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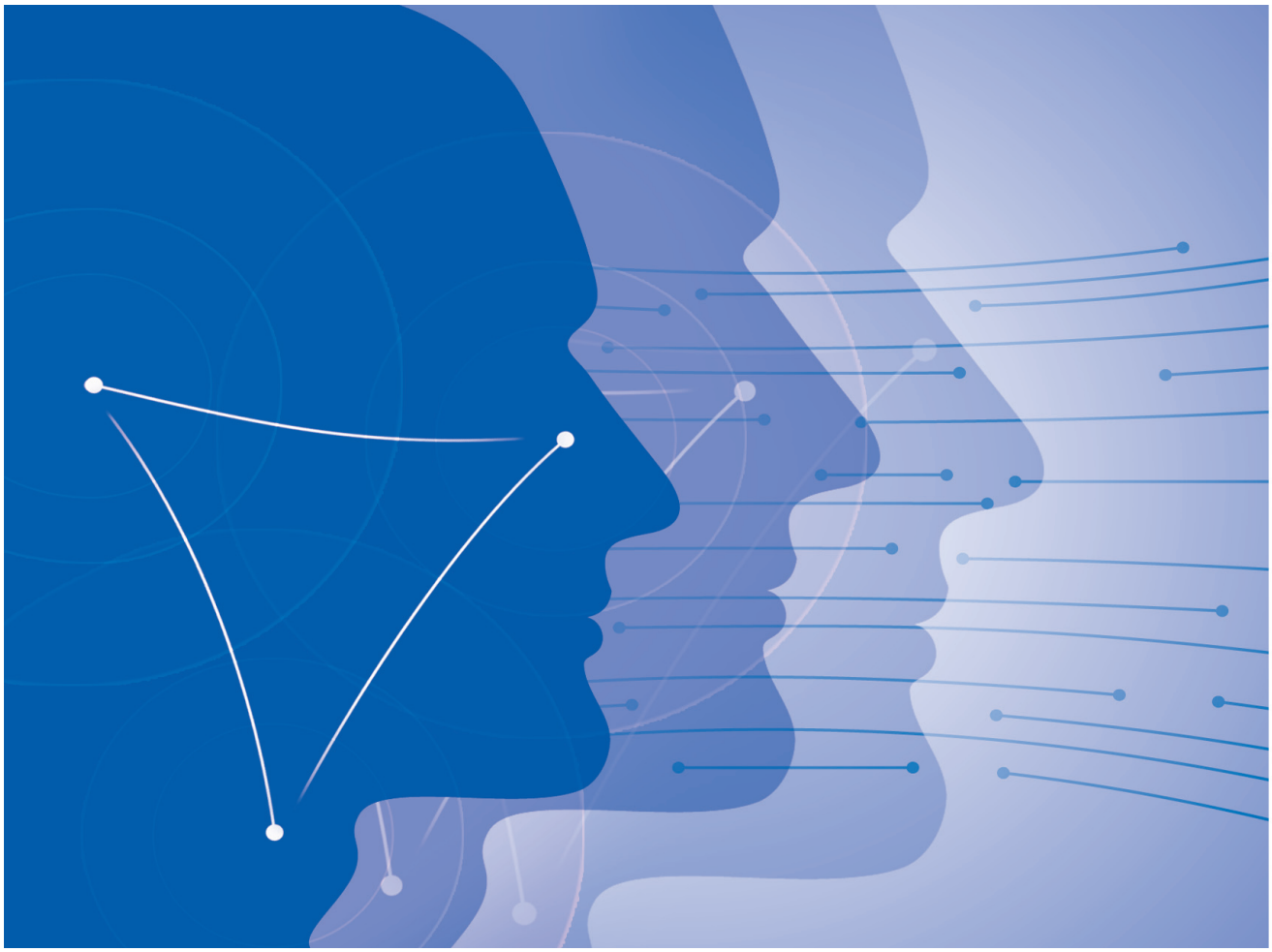

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List grant support and other assistance.

List alphabetically abbreviations used and three to ten keywords.

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Article in book:

21. Rousselot LM, Burchell AR. Splenic and arterial portography and hemodynamics in portal hypertension. In: Schiff L, ed. Diseases of the liver. Philadelphia: JB Lippincott, 1975: 368-423

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Tables must be typed and double-spaced, each on separate sheet. Number according to order of citation. Table number and title must appear above table, explanatory notes below.

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Figures should be professionally designed. Submit one set of high-quality glossy photographs in a separate envelope. They will be submitted in actual-size, as they will be printed without enlargement or reduction. Identify each figure with first's author's last name, figure number in Arabic numerals and an arrow indicating the top on the backside on each figure marked with a soft pencil or on a self-adhesive label affixed to the back of each figure. Color ilustrations are accepted if they make an exceptional contribution. Authors will be required to subsidize the publication, if have colored figures at a cost of ? BNL per figure.

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Риноликворея – обзор на диагностични методи и представяне на клинични случаи от практиката

Cerebrospinal Fluid Rhinorrhea – Diagnostic Metodes Review and Clinical Cases Demonstration

Джамбазов К., Топалова А., Марков С.

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Клиника по ушни, носни и гърлени болести

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ENT Department
UMHAT „St. George“ Plovdiv

Резюме

Въведение: Риноликвореята е изтичане на цереброспинална течност (ликвор) от субарахноидалното пространство в околоносните синуси и впоследствие в носната кухина. Определянето на точната локализация на дефекта на ринобазата представлява винаги сериозен проблем и правилният избор на метод на диагностика стои в основата на успешното хирургично лечение.
Цел: Въз основа на собствения опит и на базата на литературни данни представяме обзор на диагностичните методи при риноликворея и тяхното практично значение.
Материал и методи: За периода от 2000–2015 г. в Клиниката по УНГ-болести към УМБАЛ „Св. Георги“ ЕАД – Пловдив са диагностицирани общо 18 случая на риноликворея. Преобладаващи са спонтанни такива и вследствие на неопластичен процес. Съотношението мъже жени е 5:13. При всички пациенти като методи на диагностика са използвани глюкозо-оксидазен тест на носен секрет, компютърна томография с висока разделителна способност, като при един е приложен флуоресцеин интратекално с последваща ендоскопска ендоназална верификация. От 18-те случая на риноликворея 4-ри дебютират с риногенен менингит. При всички е осъществено ендоназално хирургично лечение – пластика на дура матер.
Резултати: При 14-те от случаите пластиката на дура матер е успешна след първата операция. Не се установява изтичане на ликвор. Ендоскопският оглед показва сигурно затваряне на дефекта. При останалите 3 случая риноликвореята персистираше, а при един случай рецидивира след едногодишен период. След повторна ендоскопска интервенция последва дефинитивно спиране на изтичането на ликвор.
Изводи: Съвременните диагностични тестове и ендоскопски ендоназални методи на пластика с алогенен материал позволяват относително сигурно доказване и локализиране на дефектите на ринобазата и дефинитивното им лечение при нисък морбидитет и ниво на компликации.

Ключови думи: риноликворея, цереброспинална фистула, ендоназална хирургия, интратекално приложение на флуоресцеин.

Abtract

Introduction: Cerebrospinal fluid rhinorrhea means a cerebrospinal fluid leakage from subarachnoid space into paranasal sinuses and from there into the nasal cavity. The exact localization of the rhinobasis defect causing cerebrospinal leak is always a serious problem and the exact choice of the diagnostic method lays in the base of the surgical success.
Aim: Using our experience and literature data, to review cerebrospinal fluid rhinorrhea diagnostic methods and their practical importance.

Material and methods: For the period 2000–2015 year in the ENT department of UMHAT „St. George“ Plovdiv 18 cerebrospinal fluid rhinorrhea cases have been diagnosed. Most of them were spontaneous or caused by neoplasm development. The correlation men to women was 5:13. In all cases several diagnostic methods were used – glucose oxidase test, high-resolution computed tomography (CT), in one case intrathecal fluorescein was used followed by endoscopic endonasal verification. Four of all 18 cerebrospinal fluid rhinorrhea cases arise with symptoms of rhinogenic meningitis. Al patients underwent endonasal surgical treatment – dura matter closure.

Results: In 14 cases there was successful dura matter closure after the first surgery. No fluid leakage was detected. The endoscopic exam showed definitely closure of the defect. As for the rest cases, in 3 of them the cerebrospinal fluid rhinorrhea persisted postoperatively and in one case there was recurrence after one year. After another endoscopic surgery an definite leakage stop was achieved in all cases.

Conclusions: Modern diagnostic tests and endoscopic endonasal methods for closure with alogenic material permit relatively sure prove and localization of the rhinobasis defects and its definitive treatment, with low mortality and complications rate.

Key words: Cerebrospinal fluid rhinorrhea, fistula cerebroslinalis, endonasal surgery, intratecal fluorescein. administration.

Въведение

Риноликвореята е патологичен процес, характеризиращ се с изтичане на цереброспинална течност (ликвор) в носната кухина и околоносните синуси, вследствие на патологична комуникация между субарахноидалното пространство и носната кухина. Първите публикувани случаи на риноликворея са през 1826 г. от Miller, последван от King през 1834 г. и Томсън през 1899 г.

Според етиологията риноликвореята може да бъде с травматичен произход (най-честа 80–90%), вродена (вродена доброкачествена интракраниална хипертензия, менингоцеле), спонтанна, ятрогенна или вследствие на неоплазма.

Дефектът на изтичане на ликвор може да е локализиран в крибриформената пластина, етмоидалния лабиринт, фронталния или сфеноидалния синус.

Риноликвореята е обвързана с висока смъртност при развитието на менингит и мозъчен абсцес, асоциирани с асцендиращи инфекции.

Успешното хирургично лечение на риноликвореята е в пряка зависимост от точната предоперативна топографска диагностика, което е в корелация с правилния избор на диагностичен алгоритъм.

Оперативното лечение на риноликвореята включва екстракраниален, интракраниален и ендоскопски ендоназален подход.

Интракраниалният достъп е описан за първи път от Dandy през 1926 г. (успешни около 60% от регистрираните случаи), а през 1948 г. Dolhman пръв съобщава за успешен екстракраниален подход и популяризиран от Hirsch през 1952 г. През 1964 г. Vrebec и Hallberg описват ендоназалния достъп в оперативното лечение на дефекти в областта на крибриформената пластина и сфеноидалния синус. През 1981 г. Wigand описва ендоскопския ендоназален подход в лечението на риноликворея и с времето той се превръща в метод на 1-ви избор в лечението на същата.

Основната цел на точното изобразяване на цереброспиналните фистули се състои в потвърждаване на диагнозата, уточняване на евентуалната етиология, локализиране на дефекта и изключване на лезии, свързани с дефекта.

Introduction

Cerebrospinal fluid rhinorrhea is a pathologic process consisting of cerebrospinal fluid leakage in the nasal cavity and in the paranasal cavities, due to a pathologic communication between subarachnoid space and nasal cavity. First cerebrospinal fluid rhinorrhea publications were in 1826 by Miller, followed by King in 1834 and Thompson in 1899.

By its etiology cerebrospinal fluid rhinorrhea can be traumatic (most common 80–90%), congenital (benignant congenital intracranial hypertension, meningocelle), spontaneous, eatrogenic or caused by neoplasm.

The cerebrospinal leakage defect can be localized in the crybtiform plate, ethmoid cells, frontal or sphenoid sinus.

Cerebrospinal fluid rhinorrhea is in a commitment with high morbidity caused by development of meningitis and brain abscess, associated with ascending infections.

Cerebrospinal fluid rhinorrhea successful surgical treatment is in a straight correlation with the exact preoperative topographic diagnosis, and this is in a correlation with the right choice of the diagnostic algorithm.

Cerebrospinal fluid rhinorrhea surgical treatment includes intracranial, extracranial and endoscopic endonasal approach.

The intracranial approach is described for the first time by Dandy in 1926 (60% success of all registrated cases), and in 1948 Dolhman first пръв announces successful extracranial approach which is popularized by Hirsch in 1952. In 1964,Vrebec and Hallberg describe the endonasal approach during the surgical treatment of the defects in the crybtiform plate area and sphenoid sinus. In 1981 г., Wigand describes the endoscopic endonasal approach in the treatment of cerebrospinal fluid rhinorrhea and step by step it turns into a first choice method for treatment of that disease.

The main aim of the exact cerebrospinal fistulas representation, consists of confirming the diagnosis, specifying the etiology, defect localization and exclusion of lesions connected with the defect.

Материал и методи

За периода от 2000–2015 г. в Клиниката по ушни, носни и гърлени болести към УМБАЛ „Св. Георги“ ЕАД – Пловдив са диагностицирани и лекувани оперативно общо 18 случая на риноликворея. Преобладаващи са спонтанни такива и вследствие на неопластичен процес. Съотношението мъже : жени е 5:13. От 18-те случая на риноликворея 4-ри дебютират с риногенен менингит.

При всички пациенти са използвани следните методи на диагностика: глюкозо-оксидазен тест на носен секрет, компютърна томография с висока разделителна способност (HRCT), магнитно-резонансна томография (MRI).

При всички е осъществено ендоназално хирургично лечение – пластика на дура матер.

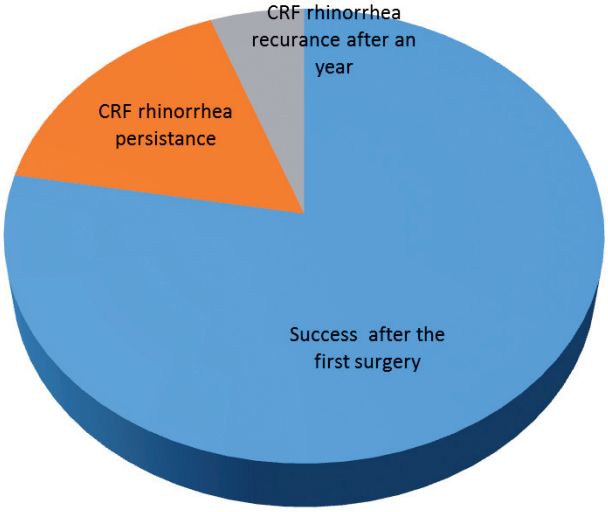
При 14-те от случаите пластиката на дура матер е успешна след първата операция. Не се установява изтичане на ликвор. Ендоскопският оглед показва сигурно затваряне на дефекта.

Material and methods

For the period 2000–2015 year in the ENT department of UMHAT "St. George" Plovdiv 18 cerebrospinal fluid rhinorrhea cases have been diagnosed and treated surgically. Most of them were spontaneous or caused by neoplasm development. The correlation men to women was 5:13. Four of all 18 cerebrospinal fluid rhinorrhea cases arise with symptoms of rhinogenic meningitis.

In all cases several diagnostic methods were used – glucose oxidase test, high-resolution computed tomography (CT), magnetic resonance imaging (MRI).

Al patients underwent endonasal surgical treatment – dura matter closure. In 14 cases there was successful dura matter closure after the first surgery. No fluid leakage was detected. The endoscopic exam showed definitely closure of the defect.



При останалите 3 случая риноликвореята персистира, а при един случай рецидивира след едногодишен период. След повторна ендоскопска интервенция последва дефинитивно спиране на изтичането на ликвор.

As for the rest cases, in 3 of them the cerebrospinal fluid rhinorrhea persisted postoperatively and in one case there was recurrence after one year. After another endoscopic surgery an definite leakage stop was achieved in all cases.

Обсъждане

Ключов момент в терапевтирането на риноликвореята е локализирането на дефекта на ринобазата. Не може да се дефинира най-правилният метод на избор при диагностиката на риноликвореята, но комплексният подход с комбиниране на образни и функционални методи във висок процент от случаите поставя диагнозата.

Discussion

Key moment in CSF rhinorrhaea treatment is the localization of the rhinobasis defect. It is impossible to define the best diagnostic method of choice in CSF rhinorrhaea cases, but the complex approach with combination of image and functional methods finds the diagnosis in most of the cases.

Методите на диагностика на риноликвореята могат да бъдат разделени на неинвазивни и инвазивни.

Неинвазивните включват:

1. Глюкозо-оксидазен тест – базира се на биохимичните различия на биологичните течности в човешкия организъм. Наличието на глюкоза в назалната секреция насочва за съдържание на ликвор в последната. Методът е неинвазивен, рентабилен, лесен за изпълнение, но с ниска чувствителност и специфичност, липсата на глюкоза не изключва риноликворея, недостоверен е, с висок процент фалшиво позитивни (при диабетици) и фалшиво негативни (при бактериална контаминация) резултати.
2. Бета-2 трансферинов тест – Бета-2 трансферинът е протеин, който се синтезира благодарение на невраминидазната активност на невроните в мозъка и се открива единствено в ликвора и перилимфата. Използва се гел-електрофореза, имуноблот или Бета-2 трансферин имунофиксационен тест. Методът е неинвазивен, с висока специфичност и отлична чувствителност, анализът изисква количество само от 10 микролитра. Техниката на изработване на резултатите изисква време (120-150 мин.) и е с висока цена, трудоемко е, не се изработва в по-голяма част от лабораториите (висока цена на индивидуалния сет). При пациенти с алкохолна зависимост и хронични заболявания се открива завишен бета-2 трансферин в серума.
3. Beta-trace протеинов тест (beta tp) – Бета-трейс протеинът е идентифициран като простагландин Д2 синтаза. Като скриниращ метод се използва имуноелектрофорезата, а като потвърдителен – нефелометър. Количественото измерване на beta tp е възможно и със сандвич Elisa-prostaglandin D2 synthase с много висока чувствителност.

Методът е неинвазивен, евтин, с висока специфичност, лесен за изпълнение, количественото изследване се извършва за 20 мин с нефелометър, и само 200 микролитра са необходими за изследването.

Методът все още се използва предимно за научна диагностика. Пациенти с ХБН или бактериален менингит имат понижени стойности на Бета-трейс протеин в ликвора и завишени в серума.

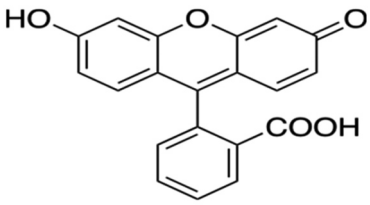
The diagnostic methods for CSF rhinorrhaea can be divided to noninvasive and invasive.

The noninvasive methods include:

1. Glucose oxidase test – it is based upon the biochemical differences between the different liquids in the human body. The glucose presence in the nasal secretion points that there are cerebrospinal liquid there also. That method is noninvasive, with low cost, easy to perform, but with low and nonspecific, the lack of glucose do not excludes CRF rhinorrhaea, the test is not reliable, with high rate of false positive (in diabetics) and false negative(when bacterial contamination is there also) results.
2. Beta-2 transferrin test – Beta-2 transferrin is a protein produced by neuraminidase activity in the brain which is uniquely found in the cerebrospinal fluid (CSF) and perilymph. Gel- electrophoresis, immunoblot or Beta-2 transferrin immuno-fixation test is used. It in an noninvasive method, very specific, and with excellent sensitivity, it needs just 10 micro liters fluid. The process of results elaboration takes time (120-150 minutes) and is expensive, it is labour-consumption process and it is not performed in most of the laboratories (high price of the individual set). In patients with alcohol abuse and chronic diseases extended levels of Beta-2 transferrin in the serum.
3. Beta-trace protein test(beta tp) – Beta-trace protein is identified as another protein with enzymatic activity (prostaglandin D2 synthase) As a screening method immunoelectrophoresis is used, and as a confirming – nephelometric assay is performed. The measurement of Beta-trace protein quantity is possible also with sandwich Elisa-prostaglandin D2 synthase with high sensitivity.

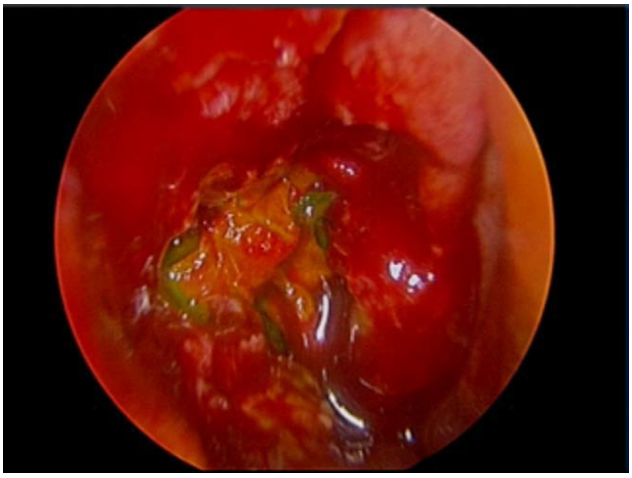
It is noninvasive, cheap method, very specific, easy to perform, the quantity measurement is performed for 20 minutes with nephelometer and only 200 micro liters are necessary for the test.

This method is still used especially for scientific diagnoses. Patients with chronic kidney diseases or bacterial meningitis have decreased values of Beta-trace protein in the cerebrospinal fluid and increased serum values.

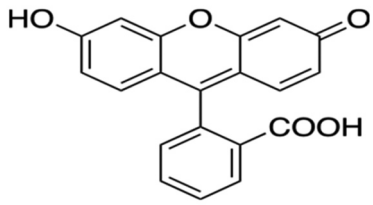


4. Интраназално приложение на флуоресцеин. Флуоресцеинът представлява флуорхромен оцветител. След извършена местна анестезия в носната кухина с ригиден ендоскоп се поставят памучни тампони, обилно напоени с флуоресцеин 0,5% в среден носов ход, в областта на крибриформената пластина и сфеноидалния рецесус. Промяната в цвета на флуоресцеина от кафяв в зелен показва наличието на ликвор.

В случаите на неактивно изтичане на ликвор се прилагат маньоври за повишаване на интракраниалното налягане (Валсава маньовър – притискане на v.jugularis interna, в позиция Trendelendurg).

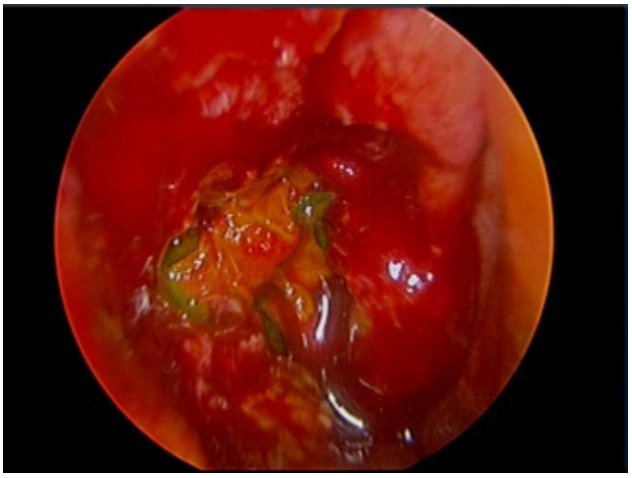


5. Компютърна томография с висока разделителна способност (HRCT) е метод на първи избор при диагностициране на дефекти на черепа. Често той е достатъчен за поставяне на диагноза, но е ограничен в откриването на дефекти само в костта. Срезове на 1–2 мм в аксиална и коронарна равнина са препоръчителни за представянето на синусите и техните стени. HRCT в комбинация с интратекално приложение на флуоресцеин акуратно локализират дефекта на ринобазата и превъзхождат останалите диагностични методи.

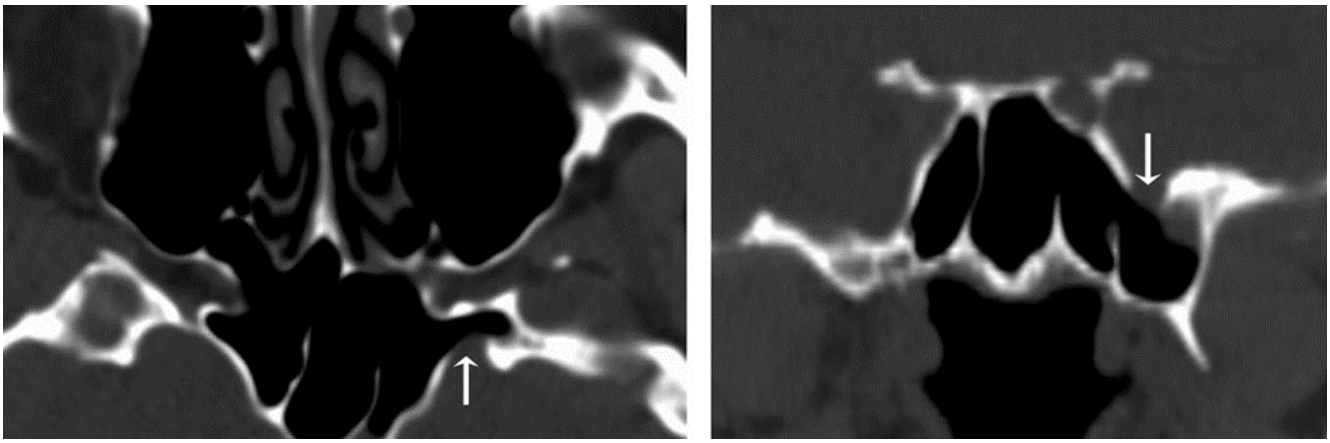


4. Intranasal fluorescein administration technique. Fluorescein is a fluorchromic paint. Under local anesthesia with rigid endoscope, in the nasal cavity cotton tampons lavishly soaked with 0,5% fluorescein are placed (in the middle meatus, in the area of cribriform plate and sphenoid recessus). The fluorescein colour change from brown to green shows cerebrospinal fluid presence.

In cases with inactive cerebrospinal fluid leakage, maneuvers for the increasing of the intracranial tension are performed (Valsalva maneuver, – pressuring v.jugularis interna in aTrendelendurg position).

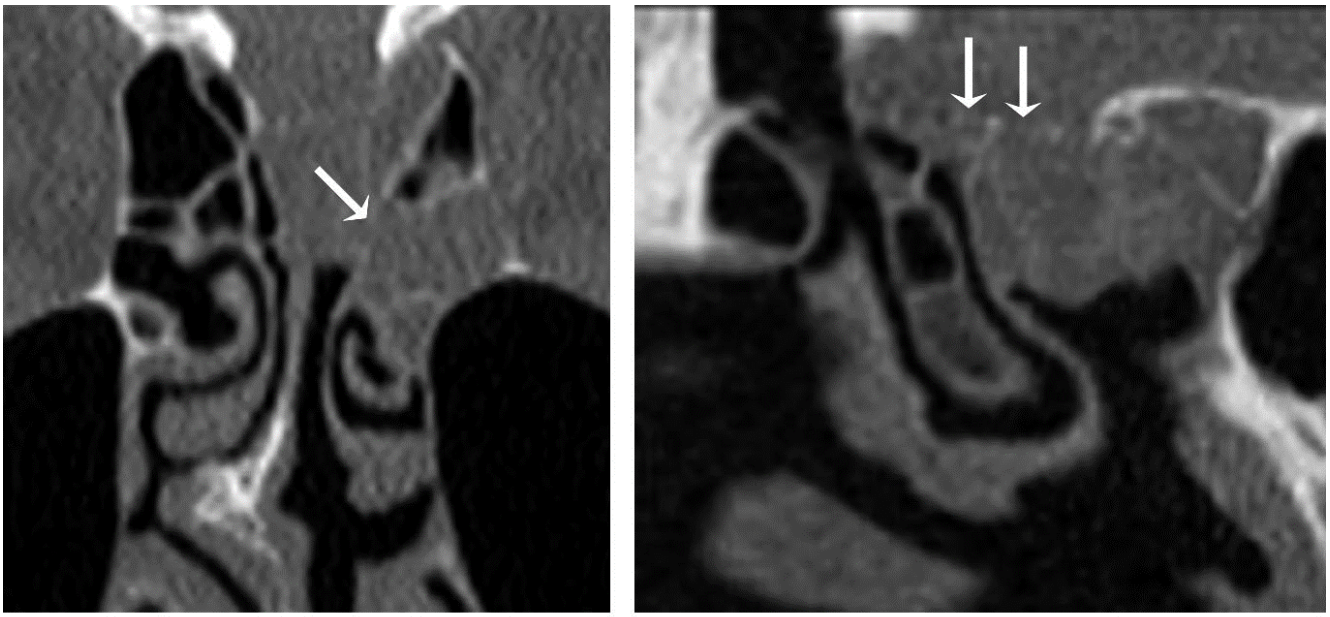


5. High-resolution computed tomography (HRCT) – is the first choice method for scull defects diagnosis. Usually it is sufficient for the diagnosis but is restricted in revealing bone defects only. 1–2 мм cuts in axial and coronal plates are recommended for presentation of sinuses and their walls. HRCT in a combination with intrathecal fluorescein administration localizes accurately the rhinobasis defect and exceeded the other diagnostic methods.



Пациентка на 29 г, с обезитас, със спонтанна риноликворея вляво, доказана интраоперативно.
КТ в аксиален и коронарен срез показва дефект в стената на ляв сфеноидален синус

Images in 29-year-old obese woman with spontaneous left-sided CSF rhinorrhea, confirmed intraoperatively.
(a) Axial and coronal CT scan shows left sphenoid defect.



a. b.

Пациентка на 40 г, със спонтанна риноликворея вляво и последващо енцефалоцеле,
доказано интраоперативно. Без данни за влияние на рискови фактори.
(a) Коронарна HRCT реконструкция през крибриформената пластина показва дехисценция на лява латерална ламела и опасификация на етмоидалния лабиринт. (b) Сагитална реконструкция на базата в областта на крибриформената пластина вляво се представя енцефалоцеле, доказано и интраоперативно.

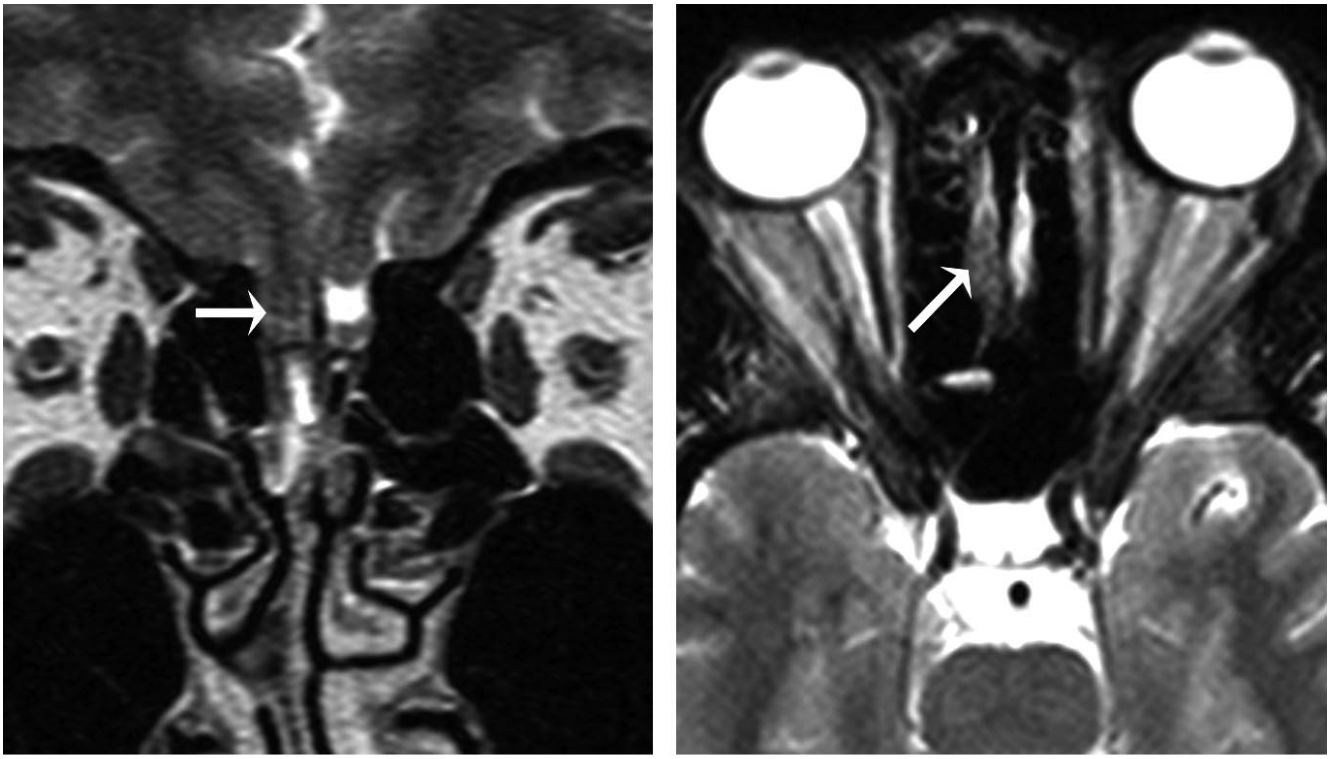
Images in 40-year-old woman with spontaneous left-sided CSF leak secondary to encephalocele,
confirmed intraoperatively. No predisposing risk factors. (a) Coronal CT reformation through cribriformplates shows dehiscence of the left lateral lamella (arrow) and opacification of the ethmoid complex. Notebilateral deep olfactory grooves. (b) Sagittal reformatted image of left cribriform skull base defect(arrows) and encephalocele, confirmed intraoperatively.

6. Магнитно-резонансна томография (МРТ) – неинвазивен, високоинформативен, допълващ HRCT, метод на диагностика. МРТ и МР-цистернография дават информация за мекотъканни възпалителни процеси и обем,

6. Magnetic resonance tomography (MPT) – Noninvasive alternative of HRCT. MPT and MP-cisternography give us information about soft tissue inflammatory processes and volumetric processes like meningocele and encephalocele

заемащи такива като менингоцеле, енцефалоцеле, тумори и др., пролабиращи през наличните костни дефекти с клинична картина на риноликворея. МРТ – Т2 в дълга секвенция контрастира сивото мозъчно вещество в светлосиво, бялото в тъмносиво, а ликвора в бяло, което позволява при неактивно изтичане на ликвор да бъде диагностицирано такова, като с това методът превъзхожда радионуклеидната цистернография и СТС. МРТ-цистернография с интратекално приложение на гадолиний е инвазивен метод с висока чувствителност, специфичност и точност (95,83%) в топографската диагностика на риноликвореята, но за съжаление все още не е оторизиран от FDA за приложение извън проучване.

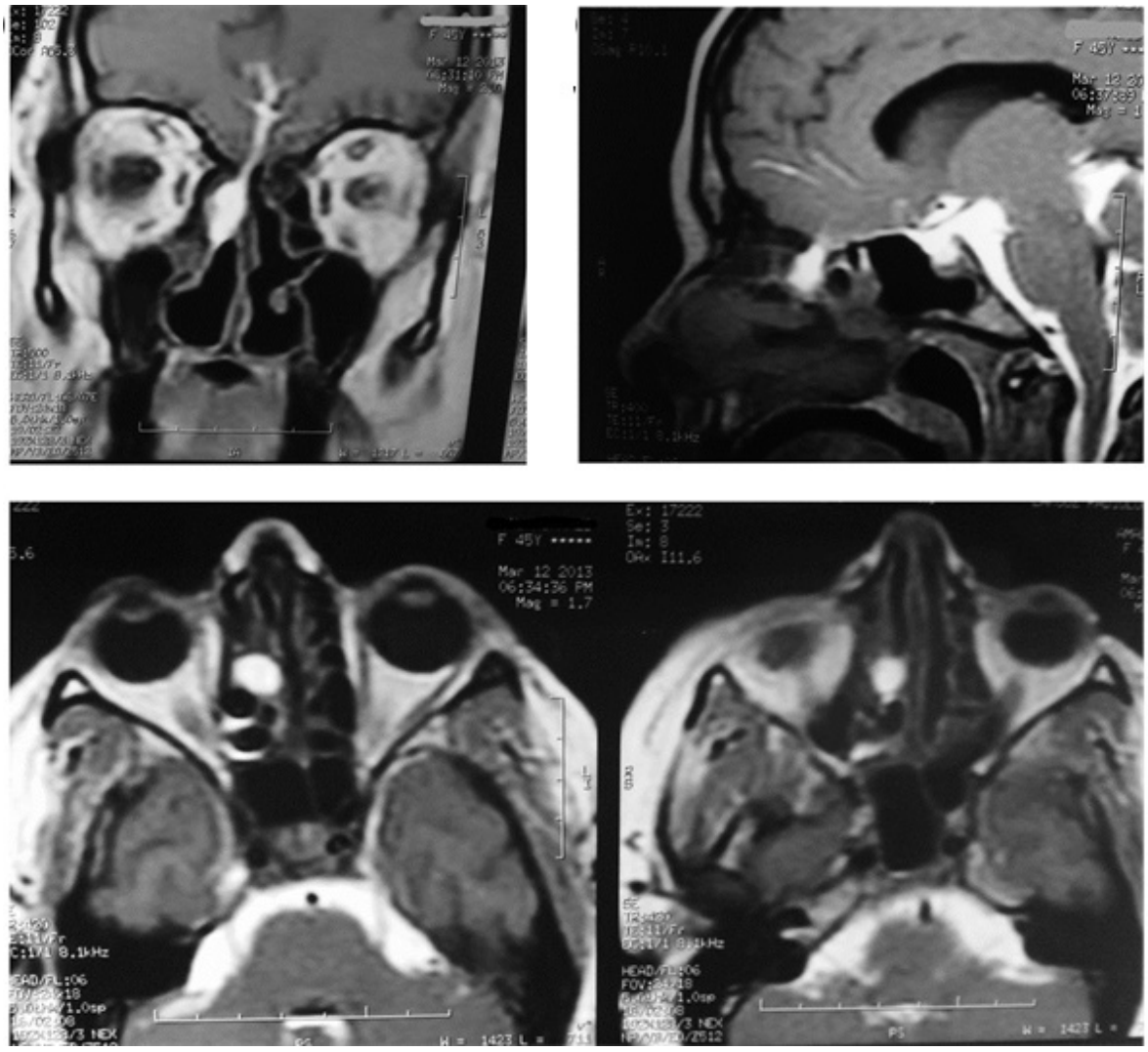
, tumors e.t.c., crawling through the available bone defects with a clinic of cerebrospinal fluid rhinorrhaea. MPT – T2 in a long sequention contrasts the grey brain substance to brightly grey, white to dark grey, and cerebrospinal fluid to white, this makes possible the inactive cerebrospinal fluid leaks to be diagnosed, this is why this method exceeds the radionuclide cisternography and CTC. MR gadolinium enhanced cisternography is an invasive method, very sensitive, specific and accurate (95,83%) at the CSF rhinorrhaea topographic diagnosis, but unfortunately it is still not approved by FDA for out of research use.



a. b.

Пациентка със спонтанна риноликворея вдясно. Коронарна и аксиална МРТ-Т2 показва енцефалоцеле в областта на дясна крибриформена пластина. Без патологични изменения вляво.

Adult woman with spontaneous right-sided rhinoliquorrhea. Coronal and axial T2-weighted MR-images reveal a small rightsided cribriform encephalocele (arrow). The left side is normal.



Пациентка на 45 г., със спонтанна риноликворея. Т1-МРТ-цистернография с интратекално приложение на гадолиний показва контрастно изтичане в десни етмоидални клетки през дефект на дясна крибриформена пластина.

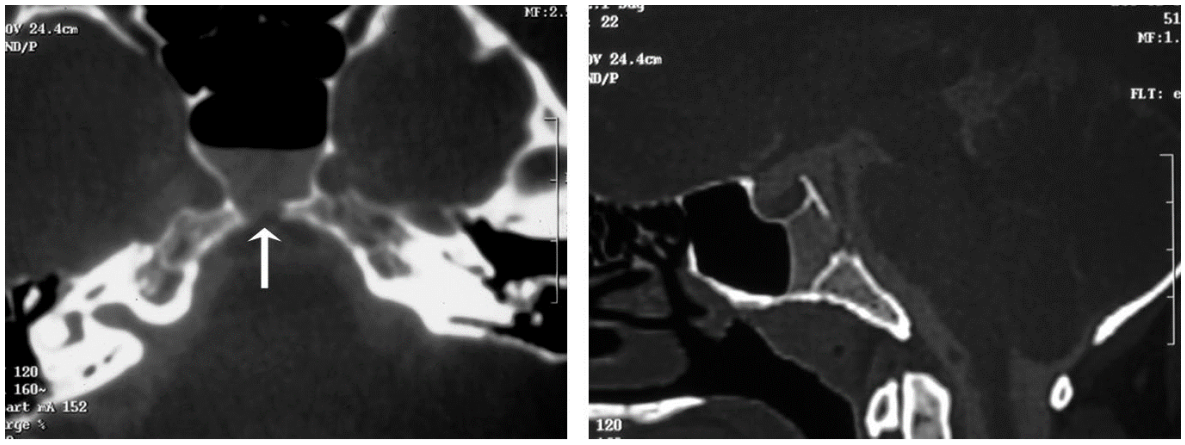
Spontaneous CSF rhinoliquorrhea in a 45-year-old female. T1–MRI intra-thecal gadolinium cisternogram shows contrast leak into the right ethmoidal air-cells trough a defect in the right aspect of cribriform plate.

Инвазивните методи включват:

1. КТ-цистернография (СТС) – при активно изтичане на ликвор, СТС показва движението на контраста през дефекта с 85% достоверност. Важно е прецистернографското КТ изследване с оглед отдиференциране на склеротична синусна стена и екстракраниално натрупване на контрастна материя. Недостатъкът на този тип изследване се изразява в невъзможността да установи неактивно изтичане по време на изследването. СТС е инвазивен (интратекално приложение на контраст), тромав, с висок риск от излагане на радиация метод. СТС е най-практичен тогава, когато фронталният и/или сфеноидалният синус играят роля на резервоар за ликвореята.

The invasive methods include:

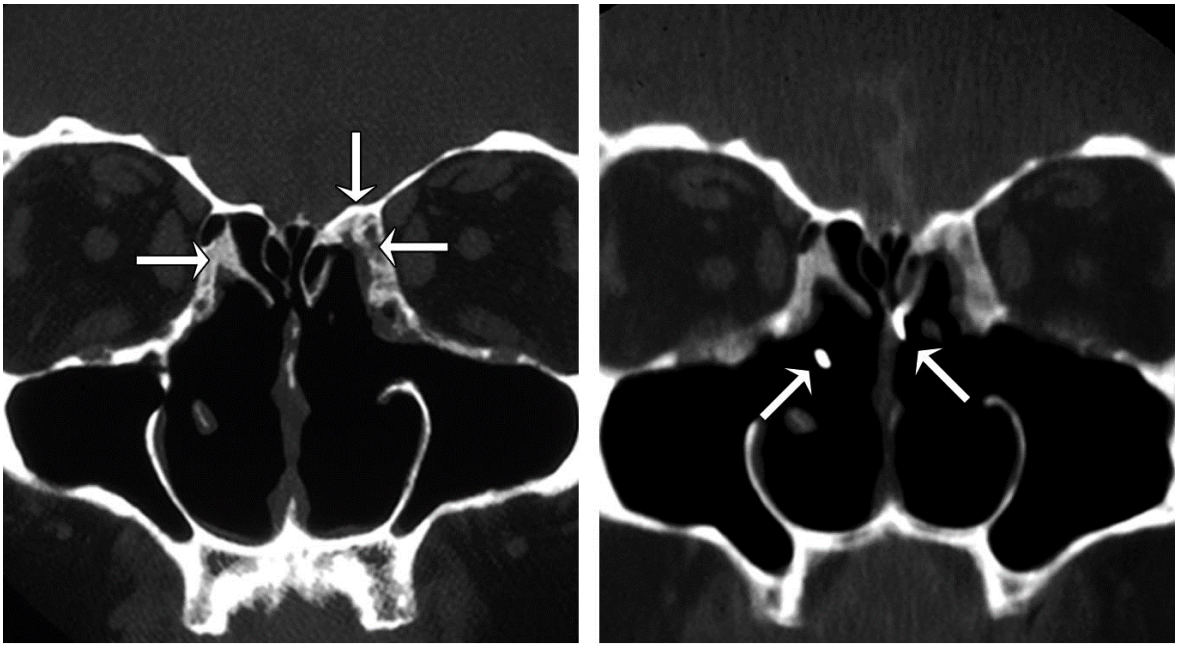
1. CT-cisternography (CTC) – when we have active CSF leak, CTC shows the movement of the contrast through the defect with 85% reliability. It is important for differentiation between sclerotic sinus wall and extra cranial contrast matter accumulation. The disadvantage of this diagnostic method consists of inability to detect inactive leak during the test. CTC is an invasive (intrathecal contrast matter application), clumsy, with high risk of radiation exposure method. It is most practical when frontal or sphenoid sinuses are in a role of a container for the cerebrospinal fluid.



a. b.

Пациентка на 38 г. с обезитас с риноликворея и позитивен бета-трансферинов тест.
а) Аксиална постконтрастна цистернограма показва натрупване на контрастна материя в сфеноидалния синус.
b) Сагиталната реконструкция позволява точното измерване на костния дефект в кранио-каудална посока.

Images in obese 38-year-old woman with rhinorrhea and positive 2-transferrin activity.
(a)Axial postcontrast cisternogram shows contrast material accumulating in the sphenoid sinus.
(b) Sagittal reformations allow accurate cranial-caudal measurement of bone defect.



a. b.

Касае се за пациентка на 35 г. с многократни FESS и ревизии.
Клиничният случай показва важността на прецистернограмското топографско изследване.
а) На коронарен срез се визуализират постоперативни особености – състояние след септопластика, двустранна унцинектомия, резекция на голяма част от двете долни носни конхи, както и средна конха, и двустранна етмоидектомия. Стените на синусите са склеротични. Остеонеогенезата е характерна находка за пациенти с хроничен синуит.
b) На коронарен срез след аплициране на контраст субарахноидално, обърнете внимание на тампоните в носната кухина. Без прецистернограмата изразеното намаляване на остеонеогенезата е възможно да бъде погрешно интерпретирано като екстракраниална акомодация на контраст.

Images in 35-year-old woman with multiple prior endoscopic sinus surgeries and revisions.
The case shows the importance of precisternogram images.
(a) Coronal image shows postoperative findings after septoplasty, bilateral uncinectomies, resection of most of both inferior and middle turbinates, and bilateral ethmoidectomies. The walls of residual sinuses are sclerotic (arrows). Osteoneogenesis is a common finding in patients with chronic sinus inflammatory disease.
(b) Coronal image after contrast material has been placed in the subarachnoid space. Note the pledgets (arrows) in the nasal cavity. The high-attenuation osteoneogenesis could be misinterpreted as extracranial accumulation of contrast material without precisternogram scan.

2. Радионуклеидна цистернография – изследването е на принципа на СТ-цистернографията, като интратекално се прилага радиофармацефтик – най-често Tc99m, последван от сцинтиграфско (гама-камерно) изследване. Методът е най-приложим при слаби и интермитентни изтичания, защото в зависимост от полуживота на радиофармацевтика изобразяването и измерването на натрупване може да отнеме часове до дни (до 54 ч). Радионуклеидната цистернография е инвазивен метод, но с по-малки възможности за локализация на дефекта и неясно изобразяване на анатомичните подробности, за разлика от СТС.
3. Интратекално приложение на флуоресцеин – методът е описан първи път от Kirchner и Proud през 1960 г. Методът е с висока информативна стойност за топографската диагноза на риноликворея. Приложението му интратекално е обвързано с усложнения (grand mal, преходна параплегия, синкоп, дисфагия), които са дозозависими.

Изследването се извършва под обща анестезия. Хиподенсен флуоресцеин 0,5%, от 0.5–1 мл се смесва с цереброспинална течност от лумбалната пункция. След като бъдат смесени, се поставят интратекално, бавно, за около 10 минути, в позиция Тренделенбург. Ендоназалната ендоскопия се извършва със син филтър след около 30 мин. след инжектирането на флуоресцеина. Дозата флуоресцеин и скоростта на неговата апликация са в пряка зависимост от последващи усложнения. Ниската доза с бавна апликация не изключва менингеално дразнене с параклинични промени (неутрофилия), с преходен характер. Процентът на изява на съществена клинична манифестация след използване на метода е сведен до минимум, спазвайки протокола за безопасното му аплициране.

2. Radionuclide cisternography – it is similar to CTC but radiopharmaceutical agent – most commonly Technetium 99m is administrated intrathecally, followed by gamma camera imaging. This method is particularly useful in low-volume or intermittent leaks because, depending on the half-life of the agent used, the imaging and measurement of uptake can be completed hours to days (up to 54 hours). Radionuclide cisternography is invasive method, has less ability for localization of the defect, and shows less fine anatomic details compared with CTC.
3. Intrathecal fluorescein – it is described for the first time by Kirchner and Proud in 1960. The method has high information value about the cerebrospinal fluid rhinorrhea topographic diagnosis. The intrathecal fluorescein administration is followed by comlications (grand mal, transitory numbness, syncope, dysphasia), which are dose related.

The test is performed under general anesthesia. Hypo dense fluorescein 0,5%, 0.5-1ml. diluted with the cerebrospinal fluid from the lumbar puncture. After that the mixed fluid is injected intrathecally, slowly for about 10 minutes in a Threndelenburg position. The endonasal endoscopy is performed by using blue filter about 30 minutes after fluorescein injection. The fluorescein dose and the injection speed are in a straight correlation with the complications followed. The low dose and slow application do not exclude meningeal irritation with transitory blood changes (neutrophil low level). Using the right safety application protocol, the percentage of significant clinical manifestation of complications after that method performance is put to a minimum.

Представяме 2 клинични случая от общо 18 за периода 2000–2015 г. при Клиника по ушни, носни и гърлени болести към УМБАЛ „Свети Георги“ – ЕАД гр. Пловдив

1-ви клиничен случай

Пациентка Ф.К.Ч. на 53 г, постъпва с приемна диагноза риноликворея, пневмоцефалия с анамнестични данни за спонтанно изтичане на бистър секрет от носа от около 2 години, като се усилва при навеждане напред. Лекувана за вазомоторна хрема, без ефект. При предходна

We present two of all 18 clinical cases for the period 2000–2015 year in the ENT department of UMHAT „St. George“ Plovdiv.

First clinical case:

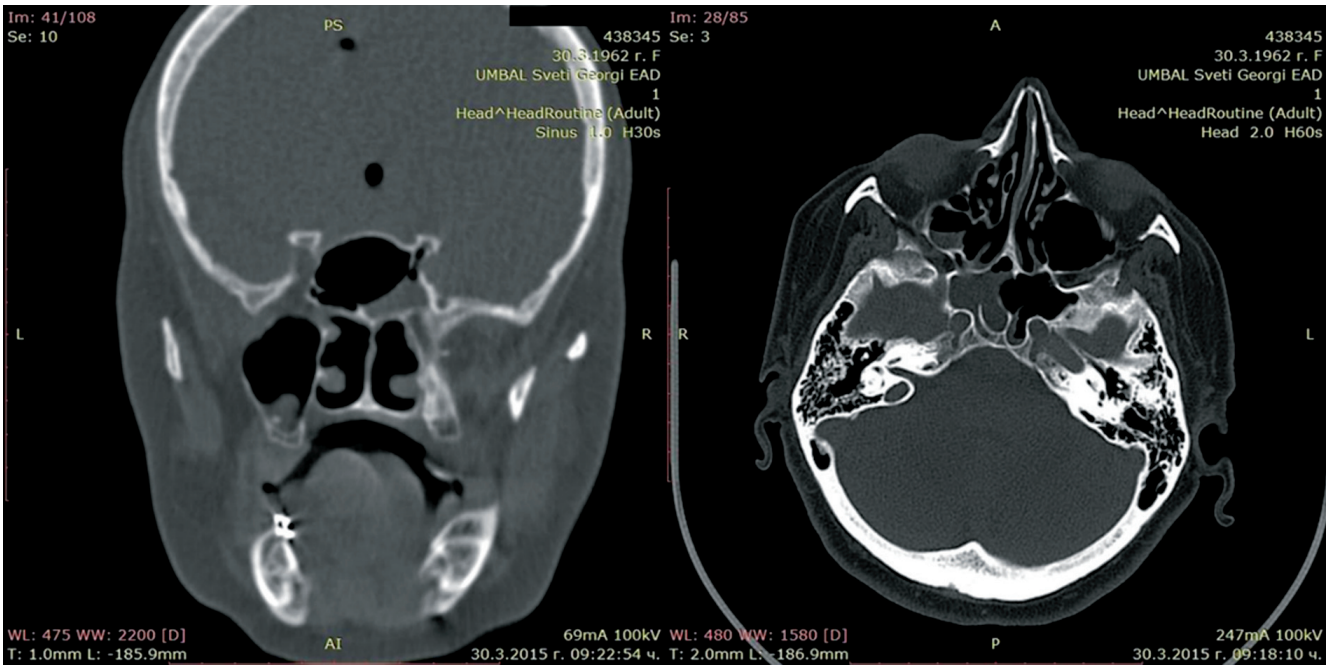
Fifty three year old female patient F.C.C. came to the hospital with diagnosis cerebrospinal fluid rhinorrhea, pneumocephalia and data from anamnesis for spontaneous nasal pellucid fluid leak for two years which increases when the patient heels ahead. Treated for vasomotor rhinitis with

хоспитализация в неврологично отделение по повод на неуточнено главоболие е извършена КТ на главов мозък, на която се визуализира дифузна пневмоцефалия. След като е бил направен глюкозен тест на назалната секреция с позитивен резултат, пациентката е насочена към Клиника по ушни, носни и гърлени болести към УМБАЛ „Св. Георги“ – град Пловдив за диагностично и терапевтично уточняване.
ПКК и биохимични субстрати – в норма. Придружаващи заболявания – Ах, ИННЗД, бронхиална астма, струма нодоза.
HRCT – данни за персистенция на пневмоцефалията. Ангажиране на 2/3 от десен максиларен синус с течна колекция, както и сфеноидален синус вдясно. Суспектни данни за единични малки прекъсвания на костния контур на хоризонталната ламина (ламина криброза) в предната ѝ част, вдясно на коронарен срез.

noeffect. During previous hospitalization in neurologic department with complains of unidentified headache, brain CT scan has been made, it shows diffuse pneumocephaly. After that, positive glucose oxidase test of the nasal secretion was made, the patient was sent to the ENT department of UMHAT „St. George“ Plovdiv for diagnostic and therapeutic specifying.

Blood picture and biochemical substrates – normal. Co morbidity – High blood pressure, ИННЗД, bronchial asthma, nodular struma.

HRCT – image data for pneumocephaly persistence. 2/3 liquid collection engagement of the right maxillary sinus, as well as right sphenoid sinus. Suspicious data for single small defects off the bony contour of the horizontal plate(cribriform plate) its anterior right part in a coronal image.



При пациентката е извършена ендоназална ендоскопска хирургия с дурапластика в областта на задна стена на десен сфеноидален синус.

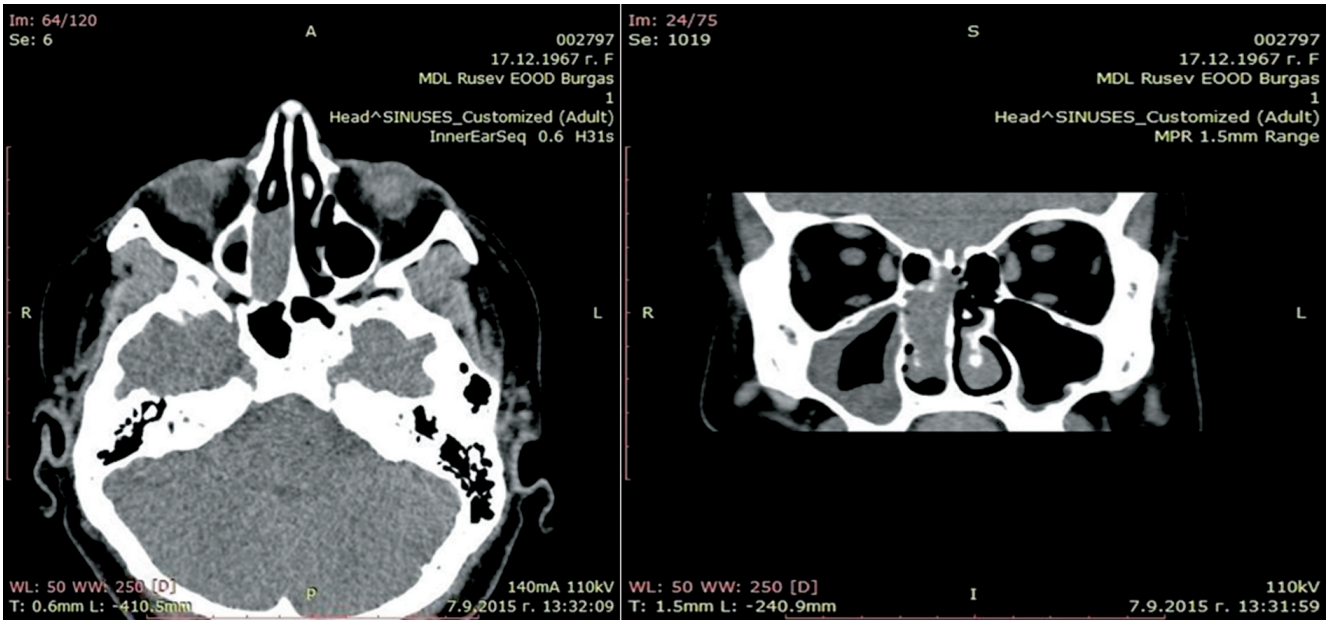
2-ри клиничен случай
Пациентка Н.Ц.Р. на 47 г. Постъпва с приемна диагноза – туморна формация в дясна носна кухина.
Анамнестични данни за оплаквания от затруднено до невъзможно носно дишане през десен

Endonasal endoscopic surgery was performed in this case, with dura matter defect plastically closure in the right sphenoid back wall area.

Second clinical case
Forty seven year old female patient came to the hospital with diagnosis – tumor formation in thr right nasal cavity.
Complains of difficult to impossible breathing through the right nasal cavity. During previous

носов ход. При предходна хоспитализация в друго болнично заведение, 5 месеца по-рано, е проведено оперативно лечение (FESS вдясно) по повод на едностранна носна полипоза с хистологичен резултат инвертен папилом.
Локален статус: полипоидна ту-формация, ангажираща дясна носна кухина.
Параклиника – без отклонения в ПКК и биохимичните субстрати.
Извършена контролна HRCT (5 месеца след FESS) – полипоидна маса, обтуриращa десен носов ход. Същата проминира краниално в етмоидалните целули, с деструкция на костните прегради на етмоидалните клетки.

hospitalization in another hospital five months earlier surgical treatment was performed (right sided FESS) as a unilateral nasal polyps treatment, with inverted papiloma histology result.
Local status: polyp lice tumor formation engaging right nasal cavity.
Blood picture and biochemical substrates – normal.
Postoperative HRCT was made (5 months after FESS) – polyp like tumor mass, with right nasal cavity obstruction. The mass has cranial extension in the ethmoid cells, with destruction of the bony walls of the ethmoid cells.



Извършена е пансинусотомия вдясно с дурапластика в областта на рима олфактория по повод на ятрогенна риноликворея.
Гладък постоперативен период. Успешна пластика на дура матер след първата операция.
И в двата клинични случаи сме използвали като метод на първи избор компютърна томография с висока разделителна способност, която бе достатъчно информативна в топографски аспект.

Right sided pansinusotomy was performed, with dura matter defect plastically closure in the olfactory region area, because of eatrogenic cerebrospinal fluid rhinorrhea.
Smooth postoperative period. Successful dura matter defect plastically closure after first surgery. In both clinical cases we used as a first choice diagnostic method high-resolution computed tomography, which gave us sufficient topographic information.

Изводи

Съвременните диагностични тестове и ендоскопски ендоназални методи на пластика с алогенен материал позволяват относително сигурно доказване и локализиране на дефектите на ринобазата и дефинитивното им лечение при нисък морбидитет и ниво на компликации.

Conclusions

Modern diagnostic tests and endoscopic endonasal methods for closure with alogenic material permit relatively sure prove and localization of the rhinobasis defects and its definitive treatment, with low mortality and complications rate.

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Чужди тела в долните дихателни пътища

Foreign bodies in the lower respiratory tract

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Резюме:

Въведение: Чуждите тела в долните дихателни пътища при децата са едни от най-сериозните спешни състояния в оториноларингологичната и педиатрична практика, можещи да доведат и до летален изход.

Материал и метод: В нашето проучване проследяваме възможните рискове и усложнения при 679 деца на възраст от 0 до 3 години с чуждо тяло в долните дихателни пътища, лекувани в УНГ клиника при УМБАЛ „Царица Йоанна-ИСУЛ“ – София и Детска клиника на УМБАЛ „Александровска“ – София. Авторите използват за сравнение данните на националната статистика за броя починали деца с чуждо тяло в долните дихателни пътища.

Резултати: През проследявания период от 20 години лечението при 667 деца е успешно приключило, докато при 59 от децата са приложени повече от една ендоскопска процедура. При 12 деца лечението е продължено в Клиника по гръдна хирургия поради невъзможност от ендоскопска екстракция на чуждите тела от долните дихателни пътища.

Заключение: Анатомичните особености на дихателните пътища на малките деца правят чуждите тела в долните дихателни пътища особено опасни. Това налага голямо внимание, опит при диагностицирането им и добра колаборация между педиатри, бронхоскопист (оториноларинголог или пулмолог), анестезиолог с опит при работа с деца и гръден хирург с оглед избягване на усложнения и летален изход.

Ключови думи: чужди тела, усложнения, ендоскопия, долни дихателни пътища

List of alphabetically abbreviations:
1. TBS-tracheobronchoscopia

Abstract:

Introduction*:* Foreign bodies in the lower respiratory tract in children are one of the most serious emergencies in otorhinolaryngological and pediatric practice, can lead sometimes to death.

Material and methods*:* In our study, we follow the possible risks and complications in 679 children aged 0 to 3 years with a foreign body in the lower respiratory tract treated in the ENT Clinic at the University Hospital "Queen Joanna-ISUL" Sofia and the Children's Clinic of the University Hospital "Aleksandrovska" Sofia. The authors use data from national statistics on the number of deaths of children with a foreign body in the lower airways to compare results.

Results*:* During the following period of 20 years treatment in 667 children is successfully completed, while 59 children have applied more than one endoscopic procedure. In 12 children continued treatment at the Clinic Thoracic Surgery due to the inability of endscopy extraction of foreign bodies from the lower respiratory tract.

Conclusion: Anatomical features of the respiratory system of young children make foreign bodies in the lower respiratory tract especially dangerous. This requires attention, experience in the diagnosis and better collaboration between pediatricians, specialist bronchoscopy (ENT or pulmonologist), anesthesiologists experienced in working with children and thoracic surgeon to avoid complications and death.

Key words*:* foreign bodies, endoscopy, complications, lower respiratory tract

List of alphabetically abbreviations:
1. TBS-tracheobronchoscopy

Въведение

Чуждите тела в долните дихателни пътища при децата са едни от най-сериозните спешни състояния в оториноларингологичната и педиатрична практика, можещи да доведат и до летален изход. [1, 2, 3, 7, 10]

Всеки предмет от екзогенен и ендогенен произход, способен да запуши частично или напълно просвета на част от дихателната система – носни ходове, ларинкс, трахея и бронхи, се приема за „чуждо тяло“. Незрялостта на дихателната система, както и на някои анатомични особености при децата са основните причини за трудностите при поставяне на диагнозата чуждо тяло в долните дихателни пътища и адекватното му лечение. Дължината на трахеята при новородените е 4 cm, а ширината ѝ е 0,5 cm. Ширината на десния главен бронх при кърмачета е 0,5–0,6 cm, а на левия – 0,4–0,5 cm. Десният главен бронх е по-широк и се явява почти директно продължение на трахеята, което обяснява почестото откриване на чужди тела в него.

Клиничната картина при децата с аспирирано чуждо тяло в долните дихателни пътища, особено при липса на инспираторен инцидент, в началото често наподобява инфекция на дихателната система или пристъп на бронхиална астма. В някои случаи това е причина за грешна или закъсняла диагноза, излагащо на риск живота на детето, както и понякога до последваща оперативна интервенция. Аспирацията на чуждо тяло в болшинството от случаите е съпроводена с много драматични моменти както за пациентите, така и за медицинския персонал. Попадането му в дихателните пътища се съпровожда от „респираторна драма“, която трябва винаги насочено да се търси при снемане на анамнезата както от личния лекар, така и от педиатъра и УНГ-специалиста. Друг важен симптом е кашлицата, но тя също не винаги е задължителна. Пристъпната кашлица и симптомът на „плющящото знаме“ са важни насочващи симптоми при нефиксирано чуждо тяло в трахеята. Ако не бъде извадено веднага, аспирираното чуждо тяло остава фиксирано в някой от отделите на дихателната система. При повечето от пациентите острите прояви на диспнея, кашлица и цианоза постепенно намаляват и изчезват – настъпва периодът на „мнимо благополучие“.

Само при малка част от пациентите оплакванията бързо прогресират и се стига до летален

Introduction

Foreign bodies in the lower respiratory tract in children are one of the most serious emergencies in otorhinolaryngological and pediatric practice, can lead sometimes to death. [1, 2, 3, 7, 10]

Any object of exogenous and endogenous origin, capable of partially or completely block of a part of the respiratory system – nasal passages, larynx, trachea and bronchi is considered a "foreign body." Immaturity of the respiratory system and some anatomical features in children are the main reasons for the difficulties in the diagnosis of a foreign body in the lower respiratory tract and its adequate treatment. The length of the trachea in newborns is 4 cm and width 0,5 – 0,6 cm. The width of the right main bronchus in infants is 0,5-0,6 cm and the left – 0,4-0,5 cm. The right main bronchus is wider and is almost a direct continuation of the trachea, which explains the frequent detection of foreign objects in it.

The clinical signs in children with aspirated foreign body in the lower respiratory tract, especially in the absence of inspiratory incident in early often resembles a respiratory infection, long standing allergies or asthma attack. In some cases this is the reason for incorrect or delayed diagnosis endangering the child's life, as well as in some times leading to subsequent surgery. Aspiration of a foreign body in the majority of cases accompanied by very dramatic moments for both patients and medical staff. Get in the airways accompanied by "respiratory drama" that has always aimed to look at history taking the GP and the pediatrician, and an ENT specialist. Another important symptom is coughing, but it also is not always mandatory. Breakthrough cough and symptoms of "flapping flag" are important guiding symptoms in non-fixed foreign body in the trachea. Aspirated foreign body, if not removed immediately, remains fixed in one of the departments of the respiratory system. Most patients who have acute symptoms of dyspnea, coughing and cyanosis gradually reduce and disappear – occurs during the „false prosperity". [25]

Only a small part of patients they complaints quickly progress and leads to death before their

изход, преди да им е оказана специализирана медицинска помощ или по време на оперативната интервенция – големи и набъбващи чужди тела, разположени най-често в областта на бифуркацията на трахеята.

Често родители и близки, грижели се за малки деца, „забравят“ да споменат за епизода на дихателния инцидент, за да не бъдат упрекнати за лошо гледане на детето, а и успокоени от факта че кашлицата и задухът са преминали и детето остава в кондиция. Периодът на „мнимо благополучие“ е с различна продължителност, което е в пряка зависимост от произхода, големината и локализацията на чуждото тяло и съответства на степента на функционалните нарушения. [25] Следва стадият на възпалителните промени в трахеобронхиалната система и белодробната тъкан. Изявява се с клиничната картина на хроничен бронхит, хронична пневмония, бронхиектазии, емпием, белодробен абсцес и др., налагащи понякога и резекция на белодробния паренхим. При тези деца се касае за „хронично чуждо тяло“. Всеки такъв случай изисква голям клиничен опит от лекуващия лекар.

Болшинството от чуждите тела са от хранителен произход. При деца на възраст до 3 години те попадат в дихателните пътища най-често по време на хранене или игра, особено когато са съпроводени от смях, говор, плач или кашлица. Намиращите се в устната кухина чужди тела или хранителни материи биват увлечени от въздушната струя и лесно преминават през гласната цепка, ако не са много големи.

Цел

Целта на нашето проучване е с направения анализ да хвърлим светлина както върху рисковете и трудностите при лечението, така и върху реалното съотношение между броя на изваденитe чужди тела и този на починали деца с тази изключително тежка патология, използвайки данните на националната статистика за броя починали деца с чуждо тяло в долните дихателни пътища за проследявания период от 20 години (1995–2014).

Материал и метод

В нашето проучване проследяваме възможните рискове и усложнения при 679 деца на възраст от 0 до 3 години с чуждо тяло в долните дихателни пътища за период от 20 години (1995–2014),

given specialized medical care or during surgery – large and swelling foreign bodies located mostly in the area of the bifurcation of the trachea.

Often parents and relatives, care for young children "forget" to mention episodes of respiratory incident, not to be blamed for poor care of the child, and reassured by the fact that cough and breathlessness are gone and the child remains in good condition. The period of „false prosperity" has a different duration, which is directly depending on the origin, size and localization of the foreign body and the degree of functional disorders. It's continued the stage of inflammatory changes in the tracheobronchial system and lung tissue. Manifested in the clinical picture of chronic bronchitis, chronic pneumonia, bronchiectasis, empyema, lung abscess, etc., and sometimes requiring resection of the lung parenchyma. This is a "chronic foreign body" in these children. Any such event requires big clinical experience of the doctor. [15]

The majority of foreign bodies have food origin. For children aged up to three years, they fall into the airways most often during the eating or a game, especially when accompanied by laughter, talk, cry or cough. Located in the oral cavity foreign bodies or food particles are carried away by the airflow and easily pass through the slit vowel if not very large. [9, 16, 20, 22, 27]

Aim

The aim of our study is with this analysis to shed light on both the risks and difficulties in treatment and on the actual ratio between the number of removed foreign bodies and that of the dead children with this extremely severe pathology, using data from the national statistics on the number of deaths of children a foreign body in the lower respiratory tract tracking period of 20 years (1995–2014).

Material and methods

In our study, we follow the possible risks and complications in 679 children aged 0 to 3 years with a foreign body in the lower respiratory tract for a period of 20 years (1995–2014) treated in the ENT

лекувани в УНГ-клиника при УМБАЛ „Царица Йоанна-ИСУЛ“ – София и Детска клиника на УМБАЛ „Александровска“ – София. Съотношението момчета/момичета беше 46% (310) към 54% (365).

За обективизиране на резултатите са използвани и данните от Националния статистически институт за броя на починалите деца по причини чуждо тяло във фаринкса и ларинкса, в трахеята, бронхите и белия дроб в България през периода 1995–2013 година по възраст. Детайлни статистически данни за умиранията по единични причини са налични в Информационна система „Демография“ от 1995 г. Статистическите разработки на умиранията по причини в България се осъществяват при спазване на изискванията на Международната класификация на болестите на Световната здравна организация. До 2004 г. в България е прилагана МКБ-IX ревизия. От 2005 г. се прилага МКБ-X ревизия. Съгласно нормативната уредба в страната приложението на 4-значния код на класификацията е въведен от 01.01.2013 г.

При всеки пациент, след щателно снета анамнеза, е извършен оглед, перкусия и аускултация на белия дроб. Винаги в началото на прегледа се сравняват дихателните екскурзии на двете половини на гръдния кош (търси се асиметрия при дихателните екскурзии). Почти винаги от страната на чуждото тяло се наблюдава по-слабо или по-силно притъпление на перкуторния тон, а при аускултация – в различна степен отслабено дишане. Чрез рентгенографско изследване (фас и профил), а при възможност компютърна томография на белите дробове (с контраст) се определя формата, размерите и разположението на чуждото тяло. [4, 5, 6, 14, 19, 23, 24] При пълна обструкция на бронхите се наблюдава ателектаза, както често и симптомът на Holzknecht – Jacobson (при вдишване медиастинумът се премества в посока на запушения бронх), а при вентилаторен тип – емфизем. Търси се също ограничение в подвижността на купола от съответната страна. В диференциалнодиагностичен аспект трябва да бъде отхвърлена пневмония, бронхиална астма, а напоследък и белодробна туберкулоза при ромския етнос. [13, 18, 21]

При всичките деца е проведена трахеобронхоскопия под обща анестезия. Използвани са ригидни бронхоскопи на фирма „Friedel“ и „Karl Storz“ Germany с инжекционно обдишване. За

Clinic at the University Hospital "Queen Joanna-ISUL" Sofia and Children clinic of the University Hospital "Aleksandrovska" Sofia. The ratio boys/girls was 46% (310) to 54% (365).

To objectify the results are used data from the National Statistical Institute, the number of dead children on grounds Foreign body in the pharynx and larynx, trachea, bronchus and lung in Bulgaria during the period 1995–2013 year old. Detailed statistics on deaths by single causes are available in Information System Demography from 1995. The statistical studies of deaths by cause in Bulgaria are carried out in compliance with the requirements of the International Classification of Diseases of the World Health Organization. Until 2004, Bulgaria has implemented ICD-IX revision. Since 2005 is applyed ICD-X revision. According to the regulations in the country application of the 4-digit code classification was introduced by 01.01.2013.

In each patient after an accurate medical history, is made a inspection, percussion and auscultation of the lungs. Always at the beginning of the examination are compared respiratory excursions of the two halves of the thorax (asymmetry is looking at respiratory excursions). Almost always on the side of the foreign body is seen less or greater dullness or tympany, while auscultation – to varying degrees weakened breathing, rhonchi, rales and local and generalized wheeles. By radiographic assessment of chest (fullface and profile) and, if possible CT of the lungs (by contrast) determines the shape, size and location of the foreign body. [4, 5, 6, 14, 19, 23, 24] In complete bronchial obstruction occurs atelectasis, as often symptoms of Holzknecht-Jacobson (during inhalation mediastinum moved in the direction of the blocked bronchus) and at valve type – emphysema. Gas exchange abnormalities are reflected in alterations of pH, pO_2 and pCO_2 in arterial blood saples. Search is also a circuscription in the mobility of the dome of the country. In the differential diagnostic aspect must be rejected pneumonia, bronchial asthma, and lately pulmonary tuberculosis in the Roma ethnic group. [13, 18, 21] Used rigid bronchoscopes company "Friedel" and "Karl Storz" Germany by injecting ventilation. To achieve maximum coverage in the surface of the foreign body without it to be crushed using differ-

постигане на максимално обхващане на страниците на чуждото тяло, без то да бъде раздробено, са използвани различни видове щипки. Раздробяване се налага единствено при много набъбнало бобено зърно с цел избутването му в един от главните бронхи за подобряване белодробната вентилация. След това парче по парче бобеното зърно се изважда. При оток на лигавицата на бронхите и вклинено чуждо тяло се прилага разтвор на адреналин 1:1000 с цел намаляването на отока. По същия начин се постъпва при екстракция на хронично чуждо тяло, обхванато от гранулации. Когато чуждото тяло минава през лумена на бронхоскопа, го изваждаме, без да променяме положението на тръбата с оглед на по-лесна ревизия на мястото. Ако тялото е по-голямо от лумена на тръбата, то тогава се изтегля до нейното отверстие и заедно се изваждат. Това крие неудобството от повторна интубация за ревизия и удължава времетраенето на интервенцията. [8, 9, 11, 17, 23, 26]

Резултати и обсъждане

При извършените бронхоскопии в 56,2% (380) чуждите тела бяха локализирани в десния главен бронх, в 35,1% (237) – в левия главен бронх, в 5,4% (36) – в трахеята и в 3,3% (22) – двустранно. При 51 пациенти или 7,5% се касаеше за хронично чуждо тяло.

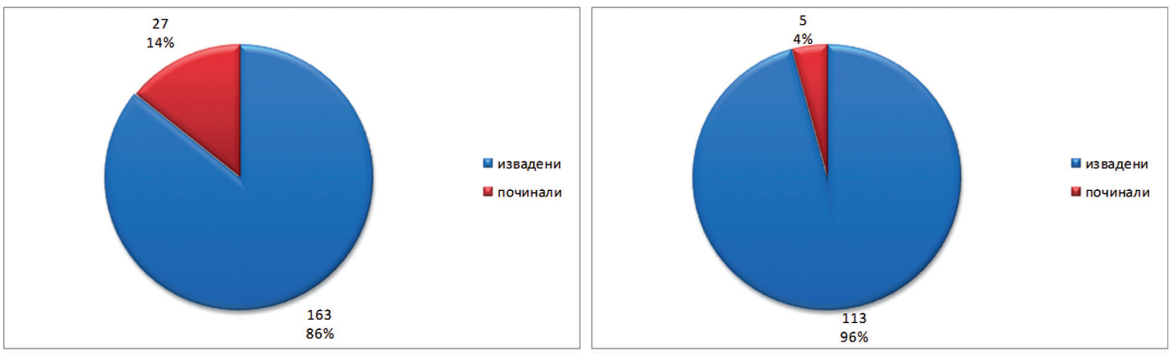
На следващите пет фигури е проследено съотношението на броя деца с извадени чужди тела в долните дихателни пътища в УНГ-клиника при УМБАЛ „Царица Йоанна-ИСУЛ“ – София и Детска клиника на УМБАЛ „Александровска“ – София спрямо брой починали деца по причини чуждо тяло в ларинкса, трахеята, бронхите и белия дроб в България през периода 1995–2013 година по възраст.

ent types of clips. Crushing necessary only in very swollen bean with the aim of pushing him into one of the main bronchi to improve lung ventilation. Then piece by piece the bean is removed. In mucosal edema of the bronchi and included foreign body is applied a solution of epinephrine 1:1000 in order to reduce edema. Similarly proceed the extraction of a chronic foreign body covered by granulation. When the foreign object passes through the lumen of bronchoscopy remove it without changing the position of the tube with a view to easier revision of the place. If the body is larger than the lumen of the tube then is drawn to its opening and, together subtracted. This hides the inconvenience of re-intubation for revision and prolongs the duration of the intervention. [8, 9, 11, 17, 23, 26]

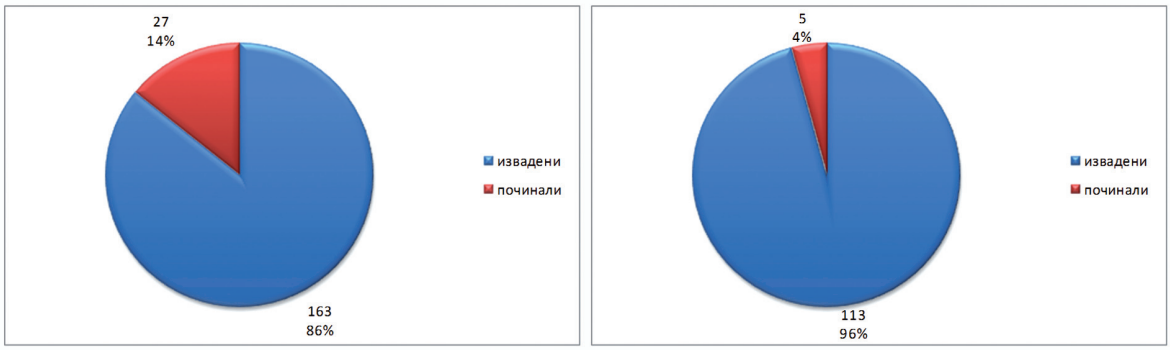
Results and discussion

Executed bronchoscopy in 56.2% (382) foreign bodies were localized in the right main bronchus, in 35.1% (238) in the left main bronchus, in 5.4% (37) in the trachea and in 3.3% (22) bilaterally. In 51 patients or 7.5% it is chronic foreign body.

The next six figures is traced ratio of the number of children removed foreign body objects into the lower respiratory tract in ENT Clinic at the University Hospital "Queen Joanna-ISUL" Sofia and the Children's Clinic of the University Hospital "Aleksandrovska" Sofia compared to the number of dead children cause foreign body in larynx, trachea, bronchus and lung in Bulgaria during the period 1995–2013 year. Both periods are significantly different and distinct age groups, and total (t-test, $p < 0.05$). In the second period, an increase in the proportion of children with a foreign body removed at the expense of reducing the deceased.

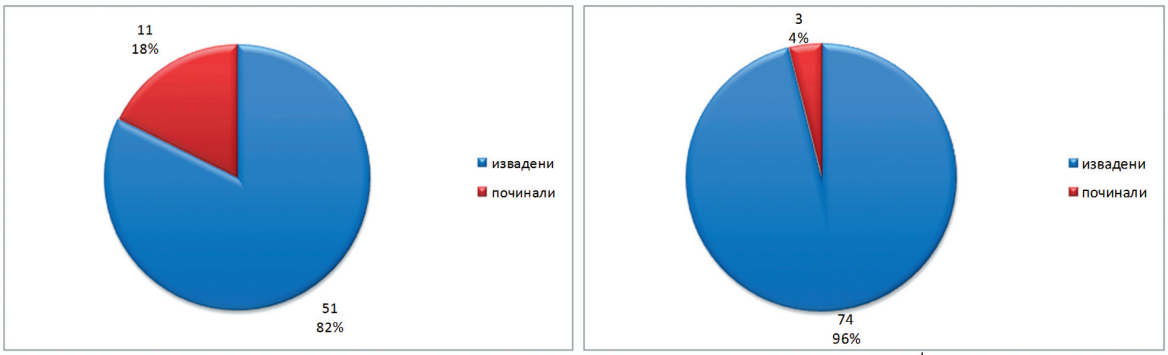


Фиг. 1. Пациенти с чужди тела в дихателните пътища на 0 години 1995–2004 г. и 2005–2013 ($p < 0.01$)
Fig. 1. Patients with foreign bodies in the airways of 0 years of 1995–2004 and 2005–2013 ($p < 0.01$)



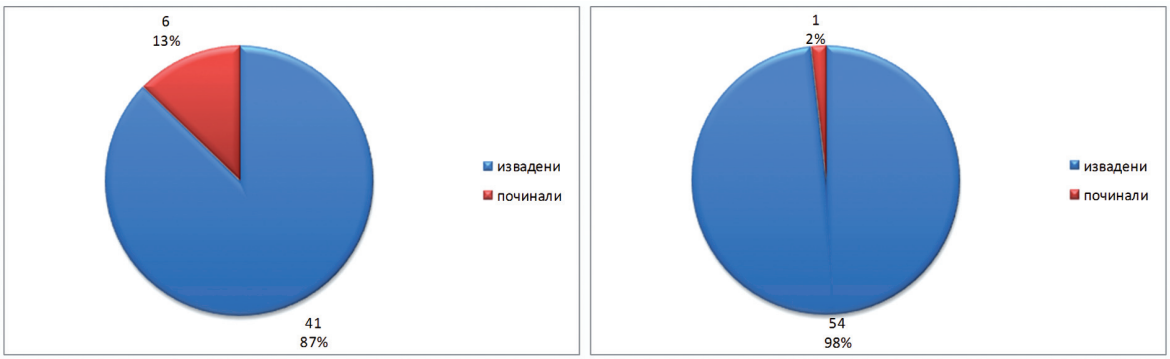
1995–2004 **2005–2013**

Фиг. 2. Пациентите с чуждо тяло в дихателните пътища на 1 година за периода (p < 0.01)
Fig. 2. Patients with foreign bodies in the airways of one year for the period 1995–2004 and 2005–2013 (p < 0.01)



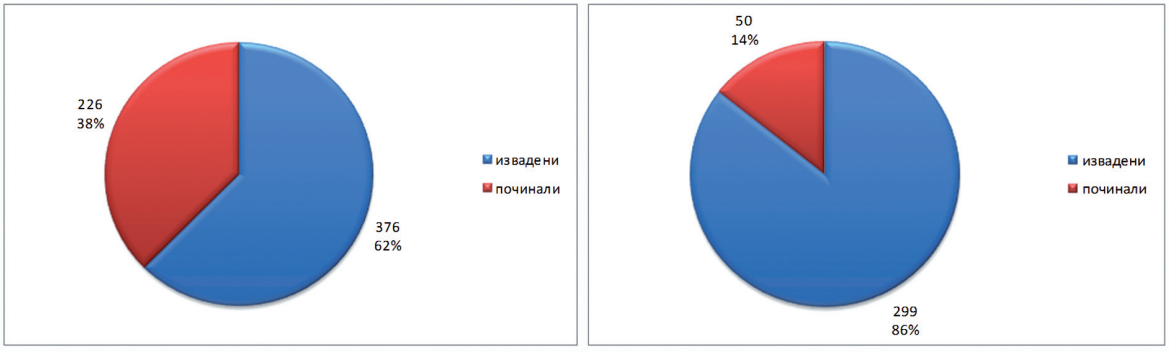
1995–2004 **2005–2013**

Фиг. 3. Пациентите с чуждо тяло в дихателните пътища на 2 години за периода (p < 0.01)
Fig. 3. Patients with foreign bodies in the airways of two years for the period 1995–-2004 and 2005–2013 (p < 0.01)



1995–2004 **2005–2013**

Фиг. 4. Пациентите с чуждо тяло в дихателните пътища на 3 години за периода (p < 0.05)
Fig. 4. Patients with foreign bodies in the airways of three years for the period 1995–2004 and 2005–2013 (p < 0.05)

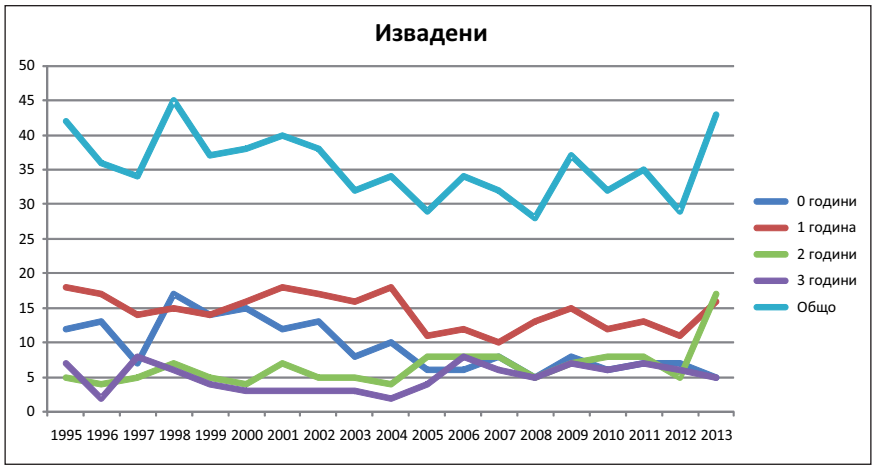


1995–2004 **2005–2013**

Фиг. 5. Съотношение на пациентите с чуждо тяло в дихателните пътища от 0-3 години за периода (p < 0.01)
Fig. 5. Proportion of patients with foreign bodies in the airways of 0-3 years for the period 1995–2004 and 2005–2013 (p < 0.01)

На фона на общото намаляване на броя на децата с чуждо тяло в трахеята и бронхите има ясна тенденция към намаляване на смъртните случаи и относително запазване на номер (с вероятно увеличение) за отстраняване на чужди тела. Делът на смъртните случаи е главно за сметка на децата 0 години – фиг. 6–8.

Against the background of a general reduction in the number of children with a foreign body in trachea and bronchi there was a clear downward trend in deaths and relatively preserving number (possibly increasing) to remove the foreign bodies. The proportion of deaths was mainly at the expense of children 0 years – Fig. 6–8.

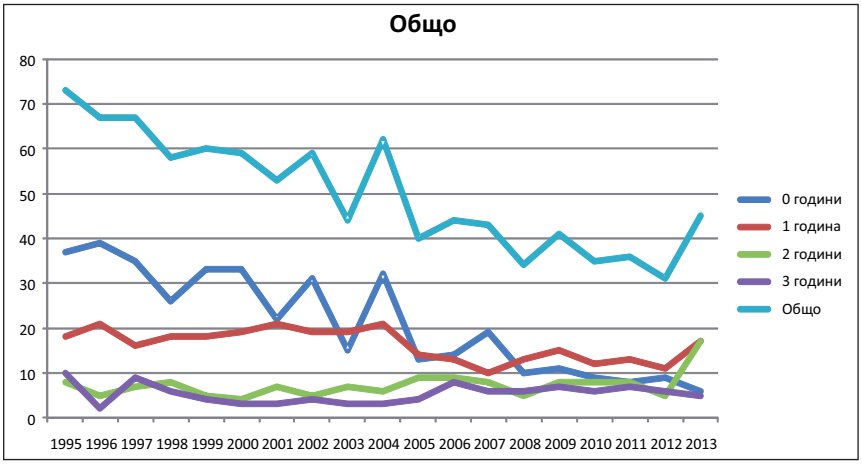


Фиг. 6. Общият брой случаи с чужди тела в дихателните пътища за периода 1995–2013 г., по възраст и общо

Fig. 6. The total number of cases out foreign bodies in the respiratory tract for the period 1995–2013, the age and general

Фиг. 7. Общият брой смъртни случаи в резултат на чужди тела в дихателните пътища за периода 1995–2013 г., по възраст и общо

Fig. 7. Total number of cases, died as a result of foreign bodies in the respiratory tract for the period 1995–2013, the age and general



Фиг. 8. Общ брой на случаи на чужди тела в дихателните пътища за периода 1995–2013 г., по възраст и общо

Fig. 8. Total number of cases of foreign bodies in the respiratory tract for the period 1995–2013, the age and general

Извадените от нас чужди тела бяха с различен произход: растителни (семки, ядки, зърна, класове от треви и др.), с неорганичен произход (метални, стъклени и пластмасови предмети), от животински произход (кости, месо) и зъби, коронки или стоматологични материали и инструменти. При някои тежки белодробни заболявания – пневмония, муковисцидоза, при посттравматични усложнения при травми на гръдния кош и следоперативни усложнения наблюдавахме така нареченото „ендогенно чуждо тяло“ в дихателните пътища.

От извадените чужди тела делът на слънчогледовите семки беше най-голям – 22,3% (151), следван от тези на фъстъците – 20% (136) и този на орехите – 17,5% (119). Делът на извадените бобени зърна е едва 2,5% (18), но трябва дебело да отбележим, че това са едни от най-опасните чужди тела, най-често водещи до смъртен изход.

В случаи на пациенти с „ендогенни“ чужди тела е препоръчително да пристъпим към бронхоскопия с флексибилен бронхоскоп. Тези тела се дължат на тежки вирусни и бактериални инфекции, при които се налага след интубиране да бъдат отстранени отливки от гъст гноен секрет и крусти. Целта е постигане на максимален ефект при минимална травма на тъканите.

Не трябва да забравяме, че при новородени и кърмачета до 6 месеца продължителността на манипулацията не трябва да е по-дълга от 20 минути, а при по-големите деца (до 3 години) – до 30 минути.

За проследявания период при 667 деца лечението приключи успешно, като при 59 от децата се наложи прилагането на повече от една ендоскопска процедура, респективно повторно пролежаване в нашите две клиники. При много малка част от пациентите 4 (0,59%) поради асфикция, дължаща се на голямо чуждо тяло в трахеята, се пристъпваше първо към трахеотомия, а след това към долна бронхоскопия. При 12 деца се наложи продължаване на лечението в Клиника по гръдна хирургия поради невъзможност от ендоскопска екстракция (вклинено или проникнало в белодробния паренхим чуждо тяло).

Въпреки внимателното боравене с апаратурата, макар и в редки случаи, сме наблюдавали следоперативни усложнения – 8 (1,2%). Много рядко наблюдаваме бързопреходен оток на ларинкса от тръбата – 6 (0,9%). При две от

Removed from us foreign bodies were of various origins: plant (seeds, nuts, grains, classes of grasses etc.), with inorganic origin (metal, glass and plastic items), of animal origin (bones, meat) and teeth, crowns or dental materials and instruments. In some severe lung diseases – pneumonia, cystic fibrosis, in post-traumatic complications of chest trauma and postoperative complications observed so-called "endogenous foreign body" in the airways. To him a thick secretions or pathological clot block the lumen of the airways. In these cases, the removal of this "plug" is imperative and survival.

Foreign bodies removed from the share of sunflower seeds was the highest – 22.3% (151), followed by those of groundnuts – 20% (136) and in walnuts – 17.5% (119). The share of the removed beans is only 2.5% (18) but must boldly note that this is one of the most dangerous foreign objects, most often leading to death.

In cases of patients with "endogenous" foreign bodies it is recommended that went to bronchoscopy with flexible bronchoscopy. These bodies are due to severe viral and bacterial infections, requiring intubation then be removed castings of thick pus and crust. The aim is to achieve maximum effect with minimum trauma to the tissues.

We should not forget that in neonates and infants up to 6 months duration of the manipulation should not be longer than 20 minutes and in older children (3 years) – 30 minutes.

At monitored period on 663 children, the treatment is successful, while 59 children have application to more than one endoscopic procedure, respectively repeated hospital stays in our two clinics. In very few patients 4 (0,59%) due to asphyxia due to large foreign body in the trachea first proceed to tracheotomy, and then to lower bronchoscopy. In 12 children have continued treatment at the Clinic for Thoracic Surgery due to the inability of endoscopical extraction (or wedge penetrated the lung parenchyma foreign body).

Despite careful handling equipment, although in rare cases, we observed postoperative complications – 8 (1.2%). Despite careful handling equipment, although in rare cases, we observed postoperative complications – 6 (0.9%). Two of the

децата (0,3%) след отстраняване на вклинено чуждо тяло сме наблюдавали затруднение на дишането и ателектаза, налагащи продължаване на лечението в клиника за интензивни грижи.

children (0.3%) after removal of the foreign body are observed difficulty in breathing and atelectasis requiring continuing treatment in hospital intensive care.

To avoid these conditions, seriously threatening the lives of children in most cases, we believe it is necessary seriously strengthen awareness-raising and prevention work by GP·s to increase the health awareness of the population. Separately, the inclusion of non-governmental organizations in this work of exclusive importance.

Заключение

Чуждите тела в долните дихателни пътища при децата, особено до 1-годишна възраст, са изключително опасни поради анатомичните особености на дихателните пътища на децата и изискват голямо внимание и опит при диагностицирането им за избягване на летален изход. Доброто снемане на анамнезата и познаване на възможностите на различните диагностични методи, бронхоскопското изследване, извършено с ригиден или флексибилен бронхоскоп, и квалификацията на екипа позволяват в болшинството от случаите ранното изваждане на чуждото тяло. Забавянето може да доведе до хронична пневмония, емпием, абсцес на белодробния паренхим, изискващи понякога и резекция на засегнатата част. Чуждите тела изискват голямо внимание, опит при диагностицирането им и добра колаборация между педиатър, бронхоскопист (оториноларинголог или пулмолог), квалифициран анестезиолог с опит при работата с деца и гръден хирург за избягване на усложнения и летален изход.

Нашият клиничен опит показва, че е необходимо да се провежда трахеобронхоскопия при всяко съмнение за наличие на чуждо тяло на долните дихателни пътища, което кореспондира със световния опит, че не съществуват абсолютни противопоказания за извършване на терапевтична трахеобронхоскопия при оправдано съмнение за чуждо тяло.

За избягване на тези състояния, сериозно застрашаващи живота на децата, в повечето случаи ние смятаме, че е необходимо сериозно засилване на разяснителната и профилактична дейност от страна на личните лекари за повишаване на здравната култура на населението. Отделно включването на неправителствени организации при тази дейност е от изключителна важност.

Conclusion

Foreign bodies in the lower respiratory tract in children, especially to 1 year of age are extremely dangerous because of the anatomical features of the respiratory system of children and require more attention and experience in diagnosing them to avoid death. Accurate history taking and knowledge of the capabilities of the various diagnostic methods, bronchoscopic examination performed with rigid or flexible bronchoscopy and qualifications of the team allow in most cases early removal of the foreign body. The delay can result in chronic pneumonia, empyema, lung abscess parenchyma sometimes requiring resection of the affected part. Foreign bodies require attention, experience in the diagnosis and better collaboration between pediatrician, endoscopist (ENT or pulmonologist), trained anesthesiologist with experience in working with children and thoracic surgeon to avoid complications and death.

Our clinical experience shows that it is necessary to conduct tracheobronchoscopy the suspected presence of a foreign body to the lower airways, which corresponds to international experience that there are no absolute contraindications to perform therapeutic tracheobronhoscopy at reasonable doubt foreign body.

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The Relation Between Noise Induced Hearing Loss and Years of Service Among Workers of a Paper Factory

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Abstract

Introduction

This study planned to investigate the occurrence time of noise induced hearing loss (NRHL) among workers in a loud work environment.

Material and Methods

For this study, the data of 70 workers who work in different departments of a paper factory was examined retrospectively. Workers were allocated in two groups as A (environment's noise level is under 80 dB) and B (over 85 dB) according to their departments' noise level. The workers with noise induced hearing loss were determined with the last Pure Tone Audiogram results.

Results

The median age was 36.98 of 70 workers included 2 females and 68 males. 15 workers with hearing loss were determined. Group B showed twice as many hearing loss results compared to the group A (5 in A and 10 in B groups), however, these results were not found to be statistically significant (p: 0.244). In the examination of the number of workers with noise induced hearing loss distributed by the years spent in this workplace, 14 of the workers who have been working in the factory over 10 years had hearing loss while only 1 worker in the group with up to 10 years of experience was affected. The difference of this distribution was statistically significant (p: 0.002).

Conclusion

The data of this study shows that there is a positive correlation between hearing loss incidence and years of service in a loud workplace. Particularly, individuals with over 10 years of experience show distinctive increase of hearing loss. Years spent in a loud workplace and accordingly, the amount of time being exposed to loud noise, increase the noise induced hearing loss.

Keywords: Hearing loss, noise induced, disease, occupational, exposure

Introduction

Noise induced hearing loss is a hearing loss related to severity of the noise and exposing time. The risk of noise induced hearing loss is considered to be increased by the years of service in a loud environment as much as the severity of the noise (1, 2).

In this study, the relation between the incidence of hearing loss, noise level of the environment and years of service were evaluated in a factory which is periodically assessed for noise level of environments and hearing levels of workers.

Material and Methods

For this study, the data of 75 workers who work in different departments with different noise levels in a factory that produces paper was evaluated retrospectively in order to determine the relation between incidence of noise induced hearing loss and years of service. Workers with symptom of otitis, sequel of otitis, autoimmune diseases, diabetes, usage of ototoxic drugs and less than a year of work experience were excluded from study, therefore the data of 70 cases were investigated.

The median age was 36.98(min.24 – max.48) of 70 workers included 2 females and 68 males. All workers' age were in range from 18 to 50 and they were evaluated in the same age group.

Environment Noise level tests

Environment Noise level tests of the factory were completed by a RION brand, NA-28 model, IEC 61672-1:2002 Class 1 and IEC 61260:1995 Class 1 mobile sound level meter and it was calibrated before each measurement.

To determine the level of noise in workers' environments, annual equivalent sound level (Leq) measurements were considered. Workers were allocated in two groups as A (environment's noise level is under 80 dB) and B (over 85 dB) according to their departments' noise levels (Table 1).

Table 1. Noise levels of the environment and staff numbers

	Environment	Leq	Number of Workers	Total	
Group A	Office	55,8	14	37	75
	Laboratory	62,8	8		
	Maintenance	69,8	15		
Group B	Coiling	88,1	8	38	
	Stokehold	88,3	5		
	Pulp preparation	89,1	10		
	Pulper	89,4	8		
	Drier	89,7	7		

Hearing Threshold Measurements

Otoscopic examination of workers was completed when they were examined periodically. All participants were examined with pure tone audiogram which determines air conduction thresholds (250, 500, 1000, 2000, 4000, 8000 Hz) and bone conduction thresholds (500, 1000, 2000, 4000 Hz). Audiometric tests were completed with Danplex DA-64 audiometer in a sound proof room. Before the measurements, workers were required to stay away from working environments for at least 16 hours. According to audiogram results, the cases which had median air-bone gaps at 1,2,3,4 KHz less than 15 dB and sensorineural hearing loss and 4000 Hz hearing loss on both ears (Boilermaker's notch) were considered to have noise induced hearing loss (3-6). Hearing loss level was calculated as the average of values on 500-1000-2000-4000 Hz.

Statistical analysis for this study was performed by Trakya University, Faculty of Medicine, Department of Biostatistics, SPSS 20.0 (license no: 10240642) computer program was used. Chi-square/Fisher test was use and significance limit was accepted as $p < 0.005$.

Results

15 workers in total were detected to have hearing loss. According to average of hearing thresholds, all cases with noise induced hearing loss showed mild hearing loss (highest score of 35 dB).

When we compare the number of workers with hearing loss in groups, according the sound level of their working area, even though group B appeared to have twice as many workers with hearing loss compared to the group A, these results were not significant statistically (p: 0.244) (Table 2).

Table 2. Noise induced hearing loss compared by noise level distribution

	Group A	Group B	Total
NRHL +	5	10	15
NRHL -	30	25	55
Total	35	35	70
Fisher test	p = 0,244		

When we evaluate the distribution of the numbers of workers with noise induced hearing loss in groups according to years of service, 14 of the workers who have been working in the factory over 10 years were affected while only 1 worker in the group with up to 10 years of experience was affected. The workers with less than 5 years of working showed no hearing loss determined. This distribution difference was statistically significant (p: 0.002) (Table 3). The median hearing loss was not higher than 35 dB for any of the workers, therefore, all cases considered as „mild hearing loss".

Table 3. Hearing loss distributed to years of service

Year	NRHL (+)	NRHL (–)	Total
1 – 5	0	0	20
6 – 10	1	11	12
11 and more	14	24	38
Total	15	55	70
Fisher Chi-square	P:0,002		

Discussion

The study showed that there was different incidence rates of hearing loss in groups with different noise levels, however, these results were not statistically significant whereas related literature indicates that it is expected to see significant difference (1, 5, 7, 8). In the work place where the study took place, the workers may visit departments with different noise levels throughout the day and the possible worker replacements between the departments with different noise levels in the previous years could be an explanation of this discrepancy. Moreover, it is worth mentioning that these results could be more significant if the sample was larger.

In this work place, personal protection wear was in use and reviewed since 2009, environment's noise level was decreased, new measures were taken about personal protection wear and application controls were implied as a discipline.

The results indicates that there is a positive correlation between years of service and hearing loss. In particular, individuals with over 10 years spent working showed significantly higher rates. The results of this study could be interpreted in two ways. Firstly, the amount of time spent working in an environment with high sound level hereupon exposure to the noise, increases the risk of noise induced hearing loss. This is an expected and compatible result with the related literature (1, 2, 7). The workers with less than 5 years of work experience did not show hearing loss. This result can be perceived as noise induced hearing loss can appear after 5 years. Secondly, recent effective precautions towards noise protection can be the reason for those workers with fewer years of service showed smaller incidence of hearing loss. It is suggested to take the study further to investigate this second interpretation.

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Our experience in intratympanic vs intravenous steroids for Idiopathic Sudden Sensorineural Hearing Loss

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Abbreviations:
Dex – dexamethasone
ISSNHL – idiopathic sudden sensorineural hearing loss
IT – intratympanic
IT-Dex – intratympanic dexamethasone
IV-Dex – intravenous dexamethasone
PTA – pure-tone audiometry
ST – standard reologic and steroid therapy

PTA_{ALL} – pure tone average on all frequencies
PTA_{LF} – pure tone average on low frequencies
PTA_{MF} – pure tone average on medium frequencies
PTA_{HF} – pure tone average on high frequencies.

Keywords: idiopathic sudden sensorineural hearing loss, sudden sensorineural hearing loss, sudden deafness, intratympanic steroids.

Abstract
Background. Currently the treatment idiopathic sudden sensorineural hearing loss by steroids is considered to be the most effective and common one. It is established that intratympanic administration of steroids, even in small quantities, results in its higher concentration in the end organ compared with systemic administration. Therefore drugs that are used topically in low doses are to be preferred. We will discuss our experience for intratympanic treatment as opposed to systemic steroids
Methods. 73 patients were observed in the study. 24 patients among them were treated with intratympanic dexamethasone over a period of 6 months. 24 patients were treated with steroids and reologic substances and 25 patients were treated with intravenous dexamethasone only over a period of 10 days. Pretreatment and 1-, 3-, 6-month post-treatment using pure-tone audiograms were compared.
Results. Intratympanic and systemic therapy did not show any differences in the treatment efficiency during the first month. But intratympanic steroid therapy resulted in higher efficacy after prolonged treatment, i.e. 6 months. No differences were found between groups treated with systemic steroid monotherapy or with steroids and reologic substanses.
Conclusions. Long-term IT steroid therapy over a period of 6 months showed a more noticeable efficacy than with steroids and reologic substanses and systemic steroid monotherapy. Our experience confirms that IT therapy can be used as the primary method for treatment for patients with contraindications of systemic steroid therapy and for those with mainly high-frequency sensorineural hearing loss.

Introduction

Though there is no universal definition, ISSNHL is often defined as unexplained sensorineural hearing loss 30 dB or greater in 3 or more contiguous audiometric frequencies occuring within 72 hours. Sometimes it is clarified as unilateral and without pronounced vertigo. Steroid therapy is considered to be the most effective and common method for ISSNHL treatment alone or combined. This is confirmed in national guidelines, e.g. in Germany, Russia, Spain and the USA.
However the treatment remains challenging. Neither the optimal dosage of systemic steroids nor the treatment duration has been precisely defined, so they are often chosen empirically [1]. Paper [2] clarifies this issue: for maximum treatment outcomes the recommended doses of oral prednisone are given as 1 mg/kg/d in a single dose, with the usual maximum dose of 60 mg daily, with a treatment duration of 10 to 14 days. Data comparing treatment protocols are limited, but one representa-

tive regimen uses the maximum dose for 4 days, followed by a 10-mg tapering off every 2 days [3]. This dose is based on a maximum adrenal output of hydrocortisone (cortisol) of 200 to 300 mg/d during stress. Prednisone is 4 times, methylprednisolone is 5 times, and dexamethasone is 25 times more powerful than hydrocortisone. So the equivalent dose is for prednisone is 60 mg, 48 mg for methylprednisolone and 10 mg for dexamethasone [1].

Common side effects of glucocorticoids include insomnia, dizziness, weight gain, increased sweating, gastritis, mood changes, photosensitivity, and hyperglycemia. Severe (but rare) side effects include pancreatitis, bleeding, hypertension, cataracts, myopathy, opportunistic infections, osteoporosis, and osteonecrosis manifesting as fractures and aseptic necrosis of the femoral and humeral heads [1]. This means patients with systemic medical conditions such as insulin-dependency or poorly controlled diabetes, labile hypertension, tuberculosis, peptic ulcer disease, and prior psychiatric reactions to corticosteroids, among others, may not be suitable to receive systemic corticosteroids.

Another issue far from being evident is IT application of corticosteroids. On one hand the benefit of this route seems now to be obvious. Parnes et al. [4] published animal studies and clinical series and demonstrated higher inner ear steroid levels following IT steroid application, with benefit in one-third of patients, and higher percentages of benefit in certain otologic conditions. Subsequent laboratory data has substantiated the claim of higher perilymph steroid concentrations after IT steroid application [5].

However prospective, randomized papers showed that intratympanic treatment with 4 doses over 14 days of 40 mg/mL of methylprednisolone injected into the middle ear was no less effective than the oral prednisone treatment [6].

The IT application of steroids, even in low dosage, leads to a higher drug concentration in the inner ear fluids when compared with systemic administration [5-11].

The IT administration of steroids is associated with a low rate of side effects These are infrequent but include pain, transient dizziness, infection, persistent tympanic membrane perforation, possible vasovagal or syncopal episodes during injection, and in comparison with the oral route, higher cost, and multiple office visits [1, 12, 13].

IT application is approved in the national guidelines mentioned above.

The objective of our study is to evaluate the effectiveness of the IT application of steroid treatment in patients with ISSNHL compared with the IV application of steroids and ST.

The permission of ethical committee was obtained for our clinical research.

Materials and Methods

Only patients with ISSNHL were included in the study. The analysis of the therapy efficacy was performed on 73 patients (mean age 43.4 ±11.9 SD yr; range, 23-69 yr), consisting of 31 women and 42 men, all without previous treatment. Two of them demonstrated bilateral impairment.

The inclusion criteria during this study was as follows: patients with ISSNHL, who had not previously been treated and were older than 18 years. The time between the onset and the beginning of the therapy was less than 1 month.

The following exclusion criteria were adopted:

1. Patients with somatic pathology (such as diabetes, hypertension, gastric ulcer, tuberculosis, glaucoma, and so on), for whom systemic steroids were contra-indicated;
2. oncological patients;
3. patients with autoimmune diseases or those who were constantly or periodically taking steroids;
4. pregnant and nursing women;
5. patients with middle ear diseases, abnormal type of tympanometric curves or barotrauma in their medical history;
6. those who had intolerance for any component of treatment;
7. those who had ISSNHL in the only hearing ear.

All patients were divided into 3 groups depending on the method of therapy. The division into groups was based on mechanical randomization.

The IT-Dex group of 24 patients (25 ears) were treated with Dex intratympanically. Dex was injected through a tympanostomy tube fixed in the posteroinferior quadrant of the tympanic membrane under the local anesthesia. Dex was given according to the following dosage regimen: 4 mg (one ampoule of 1 ml) every day during 10 days, 4 mg every other day over 20 days and then 4 mg 2 times a week over 5 months. Injecting the drug in the tympanic cavity through the tympanostomy tube, we oriented patient's head in a specific position to be sure the round window membrane was covered

with the solution for 30 minutes. We asked the patient to avoid swallowing to reduce the incidence of the drug leaking through the eustachian tube.

The ST group consisted of 24 patients (25 ears) who received for 10 days Pentoxifylline, Cocarboxylase, Potassium and magnesium aspartate intravenously and vitamin B1/B6/B12-complexe intramuscularly and Dex 0.1 mg for 1 kg of body weight in 200 ml of 0.9% sodium chloride solution intravenously tapering off over 5 days.

The IV-Dex group consisted of 25 patients (25 ears) who were treated with Dex 0.1 mg for 1 kg of body weight in 200 ml of 0.9% sodium chloride solution intravenously daily over 5 days tapering off over the following 5 days .

The evaluation of the therapy efficacy was based on the PTA data before and after treatment. Hearing evaluation was based on the following criteria: A hearing restoration within 15 dB was defined as a complete recovery. An improvement of the average hearing of 50% or more from the initial test results as a partial recovery and a reduction of hearing thresholds of 15 dB or more as a hearing improvement. The average hearing levels were determined by 4 frequencies (500, 1000, 2000 and 4000 Hz).

All patients had a follow-up period of 6 months. They were observed before the treatment, 10 days after, and then 1, 3 and 6 months after the start of the therapy.

Statistical data processing was performed with the software Statistica (StatSoft Inc., release 6.1) and Biostatistics, Version 4.03, by Stanton A. Glantz, USA 1998. The statistical analysis included the following methods: descriptive statistics, analysis of variance (One-Way ANOVA), repeated measures analysis of variance, Newman-Keuls test, pared t-test, Kruskal-Wallis test, Dunn test, Chi-Squared test, Fisher exact test (one-tailed version), factor analysis of variance, analysis of covariance (ANCOVA), logistic regression, polynomial regression.

Results

There were no significant differences in sex, age, PTA (including low-, mid- and high-frequency ranges), duration between onset and treatment of the disease, association with vertigo or hearing loss degree between the three groups ($p < 0.05$).

The therapy efficacy was evaluated 1 and 6 months after the treatment beginning. At the first stage of our study, the results were divided into 2 subgroups depending on presence or absence of treatment response: with positive effect («effect+» subgroup) and without positive effect («effect-» subgroup). «Effect+» subgroup included cases of complete recovery, partial recovery and hearing improvement, whereas «effect-» subgroup consisted of cases without changes or with hearing loss.

After one month the treatment started no significant differences between groups was discovered. However 6 months after the beginning of the therapy we found a significant difference (χ^2, $p < 0.05$). The IT-Dex group represented the major component of positive clinical results (88%), whereas the ST and the IV-Dex groups differed slightly (48% and 56% respectively), which was considered to be insignificant. The difference between the IT-Dex group and the two others overall was significant (χ^2, $p < 0.05$).

At the second stage the analysis of previously revealed differences and further evaluation of the significance of differences between groups was performed. The comparative analysis of rates of complete recoveries, partial recoveries, hearing improvements («effect+» subgroup) and of cases without changes or with hearing loss («effect-» subgroup) in all groups 6 months after the therapy beginning revealed the greatest differences within the complete recovery rates between groups – in the IT-Dex group, 60% of patients demonstrated complete recovery, while in the StT group, as well as the IV-Dex group only 20% of patients recovered completely.

6 months after the treatment beginning the following results were obtained:

1. Differences of complete recoveries rates between IT-Dex group and ST group were significant ($\chi 2$, $p < 0.05$).
2. Differences of complete recoveries rates between IT-Dex group and IV-Dex group were significant ($\chi 2$, $p < 0.05$).
3. No significant differences of complete recoveries rates were seen between ST and IV-Dex groups.

Thus, in 6 months the highest efficacy was observed in the group of patients treated with IT steroids (the maximal rate of complete and partial recoveries and of hearing improvements) compared to the group of patients who had received ST therapy and systemic steroid monotherapy. The number of patients with complete recovery in the IT group was significantly higher than in the two other groups 6 months after the treatment beginning.

Moreover, the effect of the therapy on different frequencies (low, middle and high) was evaluated. Frequency range of 125 and 250 Hz was defined as low frequencies; 500, 1000, 2000 Hz – as medium frequencies and 4000, 8000 Hz – as high frequencies. Pure tone thresholds in average on these bands PTA_{LF}, PTA_{MF}, PTA_{HF} and on all the frequencies PTA_{ALL} were studied.

The PTA_{ALL} decrease in the different phases of treatment is presented in fig.1. In the IT-Dex group the maximal effect was observed 10 days after the beginning of the treatment. The PTA_{ALL} decrease 10 days after the therapy beginning and later (1, 3 and 6 months after), in comparison with the initial hearing level was significant ($p < 0.05$). The PTA_{ALL} decrease 6 months after the treatment beginning compared with one month after the treatment beginning was also significant ($p < 0.05$). The maximal effect in the ST group was also observed 10 days after the beginning of the treatment. The following changes of PTA_{ALL} during the period from the 10th day to the 6th month of therapy were not significant. In the IV-Dex group, as well as in the ST group, the maximal effect was observed 10 days after the beginning of the treatment and the following changes of PTA_{ALL} during the period from the 10th day to the 6th month of therapy were also not significant.

Thus, in the IT-Dex group improvement was registered during the whole period of the 6 months treatment, whereas in the two other groups patients had an improvement only during the first 10 days of the therapy (fig. 1).

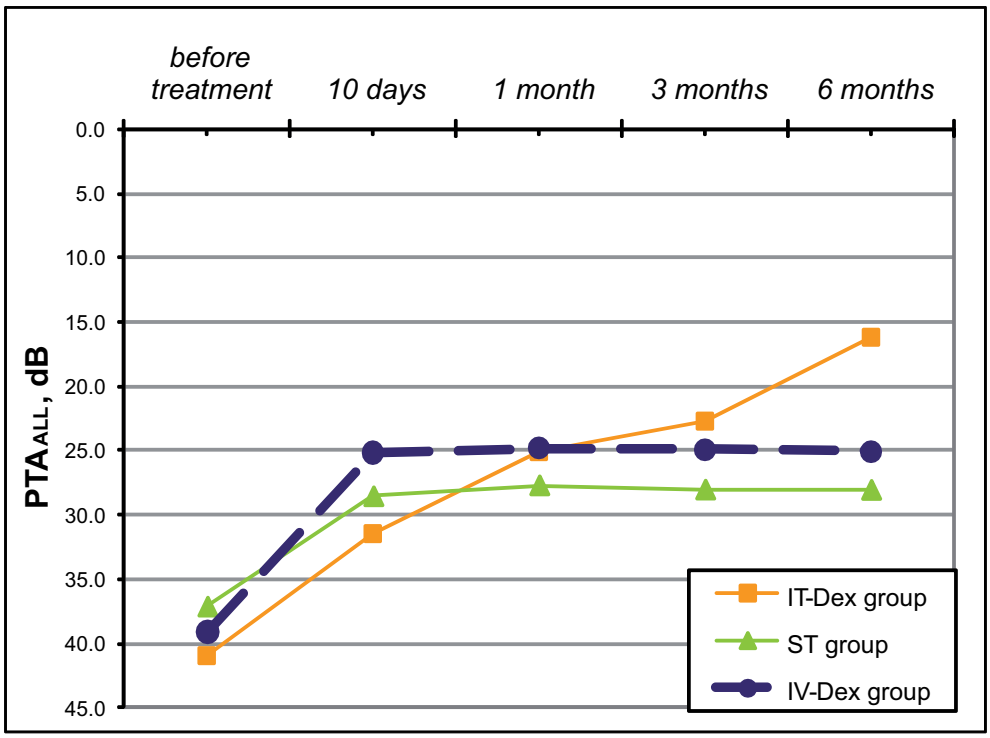

Fig. 1. Hearing changes in 3 groups during 6 months.

The analysis of variance was used to evaluate the significance of the differences of therapy efficacy within different frequency ranges in three groups 1 and 6 months after the treatment's beginning. It was found that 1 month after the therapy beginning there were significant differences between groups over the high-frequency range, whereas 6 months after – on all frequencies ($p < 0.05$). Further analysis demonstrated that this difference over the high-frequency range 1 month after the treatment's beginning was due to a more expressed effect ($p < 0.05$) in the IT-Dex group compared to the ST group. Differences between the ST and IV-Dex groups were not significant.

At the same time, 6 months after the treatment's beginning the PTA changes in the IT-Dex group were more noticeable than in the ST and IV-Dex groups within the high-frequency range and on all

frequencies overall ($p < 0.05$). No significant differences in PTA changes on all frequencies separately and in total between ST and IV-Dex groups were found ($p > 0.05$).

Thus, after 1 month of therapy, differences between groups were valid only for high frequencies because of a significantly greater efficacy in the IT-Dex group compared to the ST group. Six months after the IT-Dex group demonstrated a better effectiveness over the high-frequency range and on all frequencies in total compared to the two other groups. IV-Dex and ST didn't differ from each other for all mentioned above criteria.

Evaluation of factors associated with therapy efficacy.

The association of the treatment efficacy with patient's age, degree of hearing loss, start up time of therapy and vertigo was evaluated.

Vertigo and hearing loss degree were not associated with the therapy efficacy. Patient's age and the time between the onset of ISSHNL and the beginning of the therapy seemed to influence the effectiveness of the treatment. The rate of complete recovery was lower in patients above 35 years old and with a timescale between the onset and the beginning of the treatment of more than 7 days.

Discussion

Our study demonstrated an identical treatment efficacy of the IT and IV administration of steroids and the ST 1 month after the treatment commenced. Despite the absence of differences in one-month therapy efficacy in general between groups, the analysis of the impact on different frequencies revealed a better effectiveness of IT administered steroid on high frequencies compared with standard therapy. A. N. Salt and S. K. Plontke postulated that agents, delivered to the round window membrane locally, were not regularly distributed in the inner ear, but demonstrated a base-to-apex gradient of concentration, so that basal parts of the cochlea received far greater medicine concentrations than apical parts [8, 11]. This fact seems to explain the greater efficacy of IT steroids over the high-frequency range.

Patients who were treated with IT steroids demonstrated an improvement (PTA decrease on all frequencies) during the whole treatment period, contrary to those from the 2 other groups treated systemically, who improved only during the first 10 days of the therapy. This data lets us suppose a potential possibility of hearing improvement resulting from a longer course of treatment. The duration of treatment with systemic steroids is limited because of their side effects.

Many studies indicate that spontaneous recovery occurs in 30-65% of cases [1, 16-21]. Generally, the recovery happens within 2 weeks after the disease onset [17]. H. Zhao et al. claim that the treatment which was started within 2 weeks after the onset is more effective than the one after a fortnight of the onset and later [22].

According to our data the absence of positive response after 10 days of therapy (1, 3, 6 days after) in the groups of patients treated with systemic steroids over 10 days argues for the poor prognosis of recovery without treatment at a later date. Due to the significant differences of PTA_{ALL} obtained in our study in test time, long-term IT administration of steroids has a higher justification.

In the IT-Dex group the efficacy of the treatment was more significant than in the ST and IV-Dex groups 6 months after the beginning of the therapy. Furthermore, the rate of complete recoveries 6 months after the treatment beginning was higher for local therapy than for standard and systemic steroid therapy. This is also a proof of the capacity of hearing restoration after a longer course of treatment.

The chance of hearing improvement at the later times of therapy has been demonstrated by many authors, pointing the effectiveness of IT administration of steroids after an earlier inefficient systemic therapy [22-28].

Our results of equal efficiency of therapy for all the 3 protocols 1 month after the treatment commencement allows us to confirm the IT administration of steroids as an independent treatment mode. Generally, it concerns patients having contraindications against the systemic steroid therapy. Similar data were received by Y. Peng et al. They found that patients with hearing loss less than 70 dB showed no difference between the effectiveness of local and systemic steroid application, whereas those patients who had hearing loss more than 70 dB showed a better response to the local therapy [27]. In our study only one patient from IT-Dex group had a hearing loss more than 70 dB. However S. Kakehata et al. obtained a higher efficacy of local steroid treatment over 8 days compared to systemic steroid therapy in patients with diabetes [28].

In contradiction with the majority of aforementioned guidelines we prefer intravenous perfusion

but not per os for the systemic therapy. That was due to national custom that is confirmed in national guidelines for ISSNHL treatment and we didn't find studies for the superiority of one over another. No serious side effects related to systemic administration of steroids were observed in our study. 9 patients in ST group and 12 patients in IV-Dex group complained of sleep loss, which was completely corrected after withdrawal. That confirms the opinion that most serious side effects occur with chronic use, and adverse events are usually acceptable and manageable for the short 10- to 14-day course of steroids recommended for ISSNHL. Alexander et al. [29] reviewed the safety of high-dose steroids taken for up to 22 weeks for autoimmune inner ear disease and found that most patients completed the course, with the most frequent adverse events being hyperglycemia and weight gain. There is also evidence that osteonecrosis and fractures occur more commonly in patients with preexisting bone or joint problems in conditions such as systemic lupus erythematosis and rheumatoid arthritis [30].

Optimal dosage of steroids for IT administration has never been precisely estimated and treatment protocols for local steroid application have not yet been designed. Also we couldn't set an optimal duration of local treatment in our study, because the obtained data (improvement during all the period of treatment – 6 months, and different number of patients with complete hearing recovery at different moments of treatment) show that this duration is variable and specific to each patient. Therefore, it might be reasonable to continue the treatment as long as an improvement is observed, for example, until obtaining 2 similar audiograms spaced a month apart with the hearing survey being done monthly. However in these cases the outcome (benefit and harm) could be partially due to swallowing of steroids via eustachian tube during therapy, meaning this is not local in fact. In this link there are papers generating some controversy about systemic effects of IT glucocorticoids [31]. In animal studies, IT-Dex infusions resulted in higher perilymph concentrations than intravenous dexamethasone application without any systemic absorption [32]. As far as humans are concerned, small concentrations of methylprednisolone in human blood samples were detected [33]. By contrast, according to [31], steroids, after four IT applications within a 10–12 day timeframe and a 2–3 days interval between each injection did not interfere with endogenous cortisol secretion or bone metabolism. We must note however that these papers concern short term therapy so long time effects are obscured. In our study no systemic adverse effects related to IT application of steroids were noticed. We experienced one case of an acute suppurative otitis media which was eliminated by use of local antibacterial therapy. All patients demonstrated a complete healing of MT after the tympanostomy tube removal.

Keeping in mind the options of ISSNHL steroid treatment and the benefitial and potential adverse effects, our experience confirms the crucial role of the need for a shared decision making situation of doctor with his patient.

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Obstructive Sleep Apnea During Pregnancy – Myth or Functional Condition with Potentially Serious Complications

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Abstract
Sleep disordered breathing (SDB) during pregnancy covers a diverse spectrum of pathological conditions provoked by physiological changes in maternal organism and growing fetus. Most of the symptoms (sleepiness, fatigue, vomiting, snoring, obstructed nasal breathing, etc.) are considered to be „normally"-related to the physiological changes during pregnancy. In fact, that subtle complains could be a harbinger of more complex disorders, which could remain neglected and undiagnosed by the consulting obstetric and gynecology specialist or primary physician. In view of the potential serious complications related to the SDB during pregnancy it is essential to consider even the mild complains of the pregnant woman as prospective alarming symptoms. Interdisciplinary consultation with otorhinolaryngologist and subsequent detailed polysomnographic study are essential for proper diagnosis in order to avoid possible life threatening complications.

Introduction

There is a lot of "confusing" specialized terminology associated with sleep disordered breathing applicable in the daily routine clinical practice of the otorhinolaryngologists[1]. According to the second international classification of sleep disorders (ICSD II), based on the strict clinical observations and prйcised diagnostic criteria, SDB is considered to be a descriptive term for wide range of clinical pathology – simple (habitual) snoring, upper respiratory resistance syndrome (URRS), obstructive sleep apnea (OSA), central sleep apnea (CSA) and obesity-related hypoventilation syndrome (OHS)[2]. Apnea is described as a complete restriction or ≥ 90% obstruction of the airflow for minimum period of 10 seconds, which is usually associated with reduction of blood oxygen concentration (desaturation) and sleep fragmentation with abrupt change of brain activity from deep sleep to wakefulness (arousals). Hypopnea is presumably less severe condition than apnea and is caused by partial obstruction of the airway. Hypopnea is controversially defined as a different flow limitation during sleep (≥ 30% or ≥ 40%) which last at least 10 seconds and are associated with varying desaturation rate (≥ 4% or ≥ 3% respectively). AHI is the average number of apnea and hypopnea episodes for a period of 1 hour during sleep. Respiratory effort-related arousals (RERA) – arousals observed when increased respiratory efforts are generated during sleep for more than 10 seconds as an outcome of elevated resistance of the upper respiratory tract (URT). Cessation of breathing last shorter, don't meet the criteria for hypopnea and apnea, results in transition from the deeper to more superficial sleep stage and disappear subsequently. Usually RERA are ironically called "wannabe hypopnea" and are measured by nasal cannula with pressure transducer, pneumotachograph or esophageal manometry during polysomnography (PSG)[3]. Reparatory distress index (RDI) stands for the sum up of all pathologically registered breathing disturbances – RERA, apnea and hypopnea

for one hour and represent more precise predictive criterion for the gravity of sleep-related disorders. Nevertheless the simple snoring is generally considered as an annoying disturbance, it could be early and alarming symptom of obstructive sleep apnea, requiring full medical attention. Habitual snoring is not pathophysiologically associated with flow limitations, desaturations or arousals during sleep. The difference between typical clinical presentation of moderate to severe URRS and OSA in adult patients slightly differs and could be validated by ENT-specialist on the basis of clinical examination and PSG sleep characteristics as summarized in Table 1.

Table 1. Differences in clinical presentation and sleep characteristics between URRS and OSA.

Clinical presentation	URRS	OSA
age	younger	40 – 60 years old
female : male ratio	1:2	1:8
body weight	non-obese	obese
sleepiness	fatigue	excessive day-time sleepiness
blood pressure	hypotension (orthostatic)	hypertension
Seep characteristics	URRS	OSA
onset	insomnia (sleep-onset & sleep-maintenance) parasomnias (sleep walking, sleep terror)	short sleep onset
desaturation	not significant	significant
sleep fragmentation	AHI < 5	AHI ≥ 15
RERA	≥10	5-10

Obstructive sleep apnea is defined as a desaturation rate bigger than 4% from the baseline in awaken condition and minimum 50% decrease on airflow or complete stop of breathing for at least 10 seconds during sleep. The exact frequency of OSA among pregnant woman is not statistically proven by meta-analysis, but it is approximately estimated that about 6 % of reproductive female population could be affected[4]. The main reason for this inaccuracy is that the clinical assessment is based predominantly on the questionnaire survey and usually the results are not confirmed by PSG.

„Hormonal storm“ and pathophysiological changes

Normal pregnancy is usually related to the series of biochemical and hormonal changes during the first and second trimester of pregnancy, while the mechanical changes (progressive weight gain, upward displacement of the diaphragm) are associated with the growing fetus inside the maternal organism, could affect significantly the sleeping patterns during the third trimester. Estrogen and progesterone levels are noticeably elevated during pregnancy and could provoke physiological changes with pathological outcome. Estrogen induces hyperemia and edema of the nasopharyngeal mucosa[5], which result in increased upper respiratory tract resistance. During pregnancy the nasal patency could be obstructed mainly by the physiological actions of different hormones – placental trophoblastic hormone (hypertrophy of the nasal mucosa)[6], progesterone (local vasodilatation and increased blood flow) and estrogen (increased histamine receptors on the nasal epithelial cells and endothelial cells with subsequent stimulation of the neo-microvascularisation)[7]. Increased resistance of upper respiratory tract in a combination with physiological hypervolemia in pregnant women could amplify significantly the risk of SDB during pregnancy, which is more pronounced in the third trimester[8]. Estrogen disrupts significantly the sleep architecture by inhibiting REM sleep[9]. Progesterone is produced mainly by the placental tissue at the moment of implantation and overrides the effect of other hormones during the first trimester. It is considered that progesterone exerts strong sedative effect resulting in increased total sleep time and decreased sleep latency[10]. On the other hand, progesterone has a stimulating effect over the sensitivity of respiratory center towards CO_2 and thus stimulates respiration[11]. Physiological levels of cortisol start progressively to increase from 25th to 28th gestational week and rapidly normalize after delivery. The pathophysiological effect of the cor-

tisol is probably related to reduction of REM sleep duration throughout the prenancy[12]. Functional residual capacity (FRC) of the lungs is decreased by upward displacement of the diaphragm during the third trimester, which is supplementary to the physiological reduction of FRC during sleep[13]. The described pathophysiological changes are associated with diminished maternal oxygenation[14] as well as increased collapsibility of the pharynx[15].

Clinical considerations and complications

Pregnancy-related SDB could be demonstrated in the wide range of symptoms during sleep in the clinical spectrum from habitual snoring to obesity-related hypoventilation syndrome, which is arguably considered as the most severe form of the disease in pregnant women[16]. Snoring is very common clinical finding among pregnant women and the prevalence is estimated about 14%, which is significantly higher in comparison with the incidence in non-pregnant female population (approximately 4%)[17]. Furthermore snoring is a nonspecific clinical observation and usually starts at the end of the second trimester. In the same time snoring is the most frequent complaint of OSA during pregnancy, especially in obese women. Gestational rhinitis (GR) is a pathological condition which differs significantly from the more familiar and popular entity rhinitis during pregnancy (RPr). RPr encompass all types of rhinitis, which could possibly appear before, during and after pregnancy, regardless of the etiology (inflammatory, allergic, non-allergic, drug induced, vasomotor and etc.). GR typically emerges during pregnancy in the second or third trimester, lasts at least 6 weeks or longer and disappears about 2 weeks postpartum[18]. GR is not associated with allergic or inflammatory conditions and usually is attributed to the hormonal changes. On the basis of clinical signs and questionnaire survey the prevalence of GR is estimated about 9 % at the time of delivery[19]. Obstructed nasal breathing, rhinorrhea and impaired quality of life are not the only outcomes of GR. Worsening of the sleep quality, snoring and gravity of apnea of the childbearing woman with OSA could be attributed to the GR, especially in those clinical cases associated with overweight during pregnancy[20]. Furthermore, oral breathing as a result form nasal obstruction leads to decrease in nitric oxide (NO) inhalation in the lungs with further negative effect on the maternal blood pressure, preeclampsia, retarded intrauterine fetus growth, lower Apgar score of the newborn and etc.[21] Recently an attempt has been made to establish the exact prevalence of obstructive sleep apnea among pregnant women overcoming the imperfections of the traditional screening tools and has been validated that the occurrence is about 4.9%[22]. OSA is characterized by repeated cessation of the respiratory airflow, accompanied by oxygen desaturation and arousals. Significant reduction of nocturnal saturation of the peripheral blood during the third trimester of pregnancy has been reported in comparison with the results of the postpartum PSG studies of the same subjects[23]. Recurring episodes of respiratory obstruction during sleep could lead to maternal hypoxemia. Hypoxemia during sleep has been established both in normotensive and hypetrtensive pregnancies around the third trimester[24]. It has been speculated that SDB-related intermittent hypoxia could in turn provoke oxidative stress and endothelial activation[25], which are major factors in development of pregnancy-induced hypertension[26]. Maternal complications such as hypertension and preeclampsia are frequently reported to be related to OSA during pregnancy and generally have been characterized by the absence of nocturnal dipping in systolic blood pressure[27, 28]. Mild sleep-induced inspiratory flow limitations were detected during the polysomnography in preeclamptic women and subsequently disappear after continuous positive airway pressure therapy. This process is accompanied by normalization of the blood pressure, demonstrating a possible causative connection between OSA and hypertension[29]. The described minor inspiratory flow limitations couldn't be classified as apnea or hypopnea and typically are not associated with arousals. As a negative outcome in pregnant women with OSA has been also described gestational diabetes[30]. Clinical course of maternal OSA is frequently related to hypertension and peripheral vasoconstriction, which could possibly play a role in reduction of placental flow and subsequent harmful for the fetus. It has been proven by clinical survey with questionnaires and subsequently validated through PSG that even the mild OSA cases could contribute for the fetus growth retardation and increased risk of stillbirth in the late pregnancy[31]. On the other hand, increased number of pathologic conditions in the postnatal period is attributed to the OSA during pregnancy – low birth weight, small for gestation age infant, preterm birth and low Apgar scores[32].

Diagnostic approach

Questionnaires are very effective tool for screening purposes and early detection of the subtle precursors indicative for OSA during pregnancy such as: sleepiness, fatigue, snoring, witnessed apneic episodes and etc. Daytime sleepiness associated with pregnancy is considered to be normal clinical observation and taking into account the natural women hesitation to complain about snoring, gasping and other "uncomfortable" topics, frequently leads to significant delay of OSA diagnosis. Epworth Sleepiness Scale (ESS) has been routinely used for assessment of the degree of daytime sleepiness and probability to fall asleep in different situations. The maximal test score is 26 and the results ≥ 10 are with increased risk for OSA. It has to be mentioned that sleepiness is not very specific for OSA during pregnancy because of the regular daytime nap or subjective interpretation of the symptom rather as a fatigue, "unrefreshed" condition or tiredness than sleepiness. Additionally, sleepiness could not be typically observed in pregnant and preeclamtptic women[33] which requires supplementary screening tools for objective and prйcised evaluation such as multiple sleep latency test (MSLT). MSLT was originally proposed as a diagnostic tool for narcolepsy which evaluates the degree of sleepiness and how fast the patient falls asleep. MSLT is a full day test, which consists of 5 scheduled naps throughout the day separated by 2 hours intervals. The combination of ESS and MSLT could be an effective tool for early detection of OSA during pregnancy. The quality of sleep and sleep disordered breathing are effectively evaluated by another symptom based screening questionnaire, called Berlin questionnaire (BQ)[34]. BQ consists of 10 questions subdivided in 3 groups – snoring, sleepiness and body weight (plus chronic hypertension) and the effectiveness of clinical application of BQ for early OSA diagnosis in non-pregnant population has been estimated at up to 86% sensitivity and 95% specificity[35]. Controversially the high-score results from BQ in pregnant women are not reliable predictors for OSA, especially in those risk groups related to obesity[36].

ENT consultation is major diagnostic approach for establishing the presence and gravity of increased upper respiratory tract resistance during pregnancy. Anterior rhinoscopy is valuable and informative method which determines the level of obstruction (nasal septum deviation, hypertrophy of the inferior turbinate, etc). The most important anatomical sites, which could generate significant obstruction in the upper respiratory tract, lay at the level of the nasal valve and glottis area. Nasal segment of the URT is capable of creating almost 5-6 times higher resistance than the pharyngeal segment[37]. Nasal endoscopy is effective method for discovering of co-morbid pathology (sinusitis, nasal polyposis) which could contribute to increase URT resistance. Mьller's maneuver (MM) is easy to perform yet informative tool for fast evaluation of collapsibility of the retropalatal and retroglossal areas in awaken condition. Regardless the inconsistencies of result interpretation and relatively low predictive value for development of OSA, MM is still applicable in daily routine practice of otorhinolaryngologists for determining the level of obstruction. Originally developed for assessment of anatomical difficulties created by the palatal tonsil and the tongue during endotracheal intubation, the Mallampati score is easy to calculate and to determine the degree of pharyngeal edema accompanying different periods of pregnancy (mainly 12 and 38 gestation week) as a prerequisite of increased URT resistance[38].

Polysomnography is the golden standard for diagnosis of obstructive sleep apnea during pregnancy. Generally PSG study of pregnant women could be conducted in the same manner as in non-pregnant women, without any concern about possible contraindications[39]. It should be taken into consideration that generally pregnant women prefer to lay in bed in lateral position, which could affect the prйcised registration of AHI score. PSG study is recommended not only in cases with severe complications (gestational hypertension, gestational diabetes preeclampsia, intrauterine growth retardation of the fetus, etc.) and clinical cases with obesity-complicated pregnancies[40]. The evaluation of specific diagnostic criteria such as: inspiratory flow limitations (IFL) and RDI required overnight full PSG study using nasal cannula with pressure transducer and termistor, which is not possible in conventional polygraphy used predominantly for screening purposes[40]. Determining IFL is essential step in precise diagnosis of abnormal respiratory events in preeclamptic women, which are generally not associated with apneic episodes and are detected during the abnormal rise of blood pressure[41].

Treatment strategies

Symptomatic conservative treatment is defined by the application of different medication which doesn't have curative effect, but rather temporally relive of the clinical complaints. The general prophylactic measures[42] (elevated > 30° position of the head during sleep, sleeping on a lateral position, physical exercises, weight control, improving sleep hygiene, avoiding alcohol and sedatives, etc.)[43] and topical application of saline solutions (especially hypertonic) could be beneficial for the save and temporally relieve of GR symptoms[18]. Pregnant women with GR are frequently obsessed with the usage of topical decongestants for a prolonged period of time. The inadequate usage (longer than 5 days, application during the 1st trimester or close to delivery term as well as inappropriate higher dosage) of α-mimetics (phenylephrine, naphazoline, oxymetazoline and xylometazoline) leads to tachyphylaxis and negative effect on the nasal mucosa (drug-associated rhinitis), increased contractility of the uterus (preterm birth) plus possible congenital defects (pyloric stenosis, renal abnormalities)[44]. Systemic decongestants (pseudoephedrine, phenylpropanolamine) taken especially during the 1st trimester of pregnancy are associated with life threatening conditions such as: gastroschisis, endocardial wall closure defects and external ear malformations[45]. Considering the negligible clinical improvement of the natural course of GR and possible teratogenic effects of wide range of drugs (local and systemic corticosteroids, antihistamines, anti-leukotrienes inhibitors) it is not recommended to be used as a treatment strategy in co-morbid allergic rhinitis during pregnancy. In those cases it is more appropriate to use sodium cromoglycate or topical ipratropium bromide to cope with the severe rhinorrhea of moderate to severe allergic rhinitis during pregnancy[18].

Oral appliances are effective in reduction of upper respiratory tract resistance by pulling forwards genioglossus muscle, expanding pharyngeal anteroposterior dimensions. Dental appliances usually find application for treatment of habitual snoring and mild to moderate OSA. As a major drawback of mandibular advancement devices could be pointed out a relatively long period of time necessary for fabrication and adjustment (titrating) according to individual needs of the patient[46].

Positive airway pressure (PAP) is a gold standard for conservative treatment of OSA during pregnancy. Continuous positive airway pressure (CPAP) therapy is safe, generally well-tolerated and effective treatment with significant outcomes both for the mother (overcome apneic episodes, improves flow limitations, increase nocturnal oxygenation, reduce arterial pressure, etc.) and the fetus (improved fetal movements, change in movement patterns, reduced fetal hiccups) especially in preeclamptic patients[47]. The application of CPAP therapy during pregnancy is recommended for mild to moderate (AHI, 5-30/hour) and severe (AHI, > 30/hour) OSA cases associated with desaturation level ≤ 90%[48]. CPAP therapy during pregnancy is consistent with very good compliance level[39], even in cases when OSA is combined with preeclampsia as co-morbidity[49]. The usage of nasal CPAP during pregnancy is not associated with any adverse effects[50] and usually is terminated 2 weeks after delivery. The main target of CPAP therapy is to achieve favorable improvement of the saturation level (> 90%) and to acquire RDI level < 5 per hour during sleep[48]. Pregnant women diagnosed before or in the beginning of the pregnancy with SDB usually required recalibration of the CPAP equipment around the 6 month[49]. In severe cases associated with obesity-related OSA pregnancies or multiple gestations (twin pregnancies) is more favorable to use bi-level positive airway pressure (BiPAP) instead of CPAP ventilation. In order to improve the effectiveness of PAP treatment it is recommended to combine the artificial ventilation with supplementary oxygen therapy (OXT). OXT is not recommended as a primary treatment of OSA during pregnancy because of the potential risk of prolonged episodes of apnea, raised level of carbon dioxide in the circulating peripheral blood (hypercapnia) and increased ventricular irritability[51].

Surgery is limited only for the most severe cases of OSA uninfluenced by the conservative treatment, patients with low compliance rate toward CPAP therapy or those clinical cases posing high-grade risk of serious complications for the pregnant woman and her baby. In cases with severe OSA secondary to GR and refractory to conservative treatment could be recommended a volume reduction of the inferior turbinate[18]. Considering the increased surgical risk and inconsistent long-term results performing a conventional uvulopalatopharyngoplasty (UVPP)[52] is not recommended for treatment of OSA during pregnancy[53]. There is just one case in the literature reporting benefits from tracheostomy in a pregnant woman with obstructive sleep apnea [54].

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Diagnostic value of fine needle aspiration biopsy in lymphadenopathy of the head and neck

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Abstract: Lymph nodes in the head and neck region are involved in different pathological processes – metastatic, lypmhoproliferative and inflammatory. The objective of the present study was to evaluate the diagnostic accuracy of fine needle aspiration biopsy (FNAB) and define its place in the diagnostic algorithm. The results of the cytological evaluation of FNAB, confirmed with histological evaluation show that 72.8 % of space-occupying lesions of the lymph nodes were malignant, with 48.2% being metastatic. Non-Hodgkin lymphoma represented 69.1% of all lymphomas, whereas 28.3% were diagnosed as Hodgkin. Benign processes were represented almost exclusively by lymphadenitis – 93.9%. Sensitivity of malignancy was high (92.6%). FNAB had an accuracy of 79%. Specificity was low at 45.5%, mostly on account of lymphadenitis.

Key words: Lymph nodes, head and neck, fine needle aspiration biopsy

1. Introduction

Lymph nodes (LN) in the head and neck region are involved in different pathological processes – inflammatory, neoplastic and metastatic. The most commonly found malignant cell material from lymph nodes in the head and neck region represents regional metastasis from spinocellular carcinoma (SCC).[1] Distant metastases in the head and neck region are relatively rare, keeping in mind that most authors agree that only 1% of carcinomas in the head and neck region can be classified as non-regional metastasis.[2] Lymphomas account for 12% to 15% of the malignant tumors in the head and neck region.[3,4] Cervical lymphadenopathy is the first clinical sign in 70% of cases, while the frequency of extranodal lymphoma is second in the head and neck region.[5] Non-Hodgkin lymphomas comprise 75% of the head and neck lymphomas,[6] with extranodal localization in 23%-30% of cases.[7] According to Howlett et al.[8] and Gonzales et al.[9] around 30% of head and neck masses are a manifestation of reactive nodular hyperplasia and/or lymphadenitis. Granulomatous disease represents a sporadic event.

Use of imaging techniques as a single method of examination is insufficient in determining the character of disease.[8] Fine needle aspiration biopsy is an easy to perform and minimally invasive method to collect cell material for cytological examination.[9] The lymph nodes in the head and neck area are relatively easy accessible for FNAB. In cases of deep localization or small size, it is appropriate to use ultrasound navigation while performing FNAB. According to Rodjan et al.[10] ultrasound-guided FNAB has great advantages in the detection of early stage SCC and clinically nonpalpable lymph nodes (4–5 mm diameter). The diagnostic workup of other malignant neoplasms, e.g. affecting mammary and thyroid glands, includes ultrasound and FNAB.[11] Current research suggests FNAB as a specific diagnostic tool on suspicion of a cervical metastasis

from a cancer unknown primary (CUP).[12,13] Moreover, according to Balm et al.[13] only subsequent negative or nondiagnostic FNABs are an indication for incisional, excisional or tru-cut biopsy.
The aim of our research is to evaluate the diagnostic value of FNAB and to define its place in the diagnostic treatment algorithm.

2. Materials and Methods

2.1 Examined contingent

The present research was approved by the ethics commission of Medical University of Varna. For the period between 2008 and 2014 in the division of Maxillofacial surgery (University Hospital "Sv. Marina") were tracked 146 patients with lymph node pathology of the head and neck region, which underwent FNAB. In 13 cases the results were uninformative, which necessitated a second biopsy. The present research included 114 patients with diagnostic cytology, which were treated surgically. The cohort included 65 men (57%) and 49 women (43%) aged between 4 and 95, with the highest rate of morbidity being in the sixth and seventh decade.

2.2 FNAB execution

FNAB was performed using disposable needles size 25 (0.5 mm Ч 38 mm/ 25 Gauge Ч 1 1/2) and disposable syringes with a volume of 2 to 5 ml and freehand aspiration technique. Cell material was extracted from the center and periphery of the mass.

2.3 Cytopreparatory technique

The extracted cell material was applied to a slide, which was pushed into another with a sliding motion. This way the suspension was distributed evenly and four smears were obtained (2 center and 2 periphery smears). The smears were left to air dry for an hour, fixed in methanol for five minutes and subsequently dyed with Giemsa (methylene blue, eosin, and Azure B).

2.4 Diagnostic categories of FNAB

Diagnostic categories of FNAB stratified the risk of malignancy. The diagnostic classification concerning the assessment of FNAB was conducted in six categories: 0 – non-diagnostic; I – definitely benign; II – probably benign; III – possibly malignant; IV – probably malignant; V – definitely malignant.
The applied diagnostic categorization used two negative for malignant process categories, I and II, respectively definitely benign and probably benign. Three positive categories stratified the risk of a malignant process – III, IV, V, respectively possibly malignant, probably malignant and definitely malignant.

2.5 Statistical Analysis

Data were analyzed by the means of descriptive, non-parametric tests – chi-square test, cross-tabulation (IBM SPSS Statistics for Windows, v. 21.0, Armonk, NY, USA). The significance level was adjusted at $P < 0.05$.
Sensitivity, specificity, diagnostic accuracy, the positive predictive value (PPV) and the negative predictive value (NPV) of FNAB were calculated. Sensitivity was defined as the percentage of patients who were correctly diagnosed to have malignancy on FNAB. Specificity was defined as the percentage of patients who were correctly diagnosed to have benign disease on FNAB.

3. Results

FNAB was non-diagnostic in 8.9% of cases (13 out of 146). Histologic verification of the results of FNAB showed that 72.8% of space-occupying lesions are malignant. Lymph node metastasis represented about half (48.2%) of all malignant neoplastic processes (Table 1). Among these, SCC was most common – 48.7% (n = 19) of all metastatic tumors, followed by poorly differentiated carcinoma – 7.7% (n = 3), undifferentiated carcinoma – 7.7% (n = 3) and malignant melanoma – 7.7% (n = 3), metastasis from adenocarcinoma (n = 2) and mucoepidermoid carcinoma (n = 2). Non-Hodgkin/Hodgkin lymphoma represented, respectively, 69.1% and 28.6% of the malignant lymphoproliferative disorders. Lymphadenitis accounted for 94.9% of all space-occupying benign lesions, while only two cases of lymphangioma were noted.

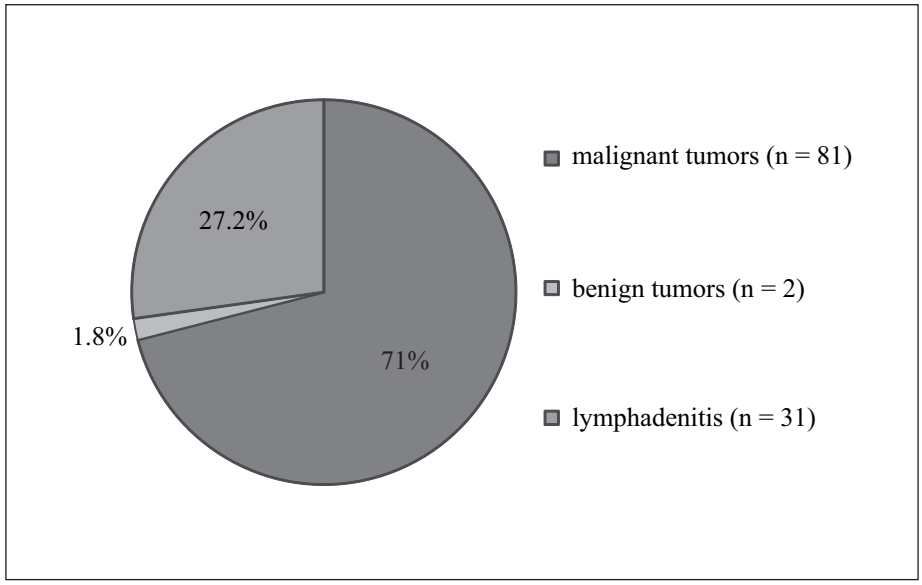

Figure 1. Lymph node pathology as confirmed by histological examination

Table 1. Histopathology of the lymph nodes

	Histological classification	Number
Metastatic tumours	1. Squamous-cell carcinoma	19
	2. Poorly differentiated carcinoma	3
	3. Undifferentiated carcinoma	3
	4. Malignant melanoma	3
	5. Poorly differentiated adenocarcinoma	2
	6. Mucoepidermoid carcinoma	2
	7. Papillary carcinoma	2
	7. Basal cell adenocarcinoma	1
	8. Small cell carcinoma	1
	9. Mesothelioma	1
	10. Medullary carcinoma	1
	13. Neuroendocrine carcinoma	1
Lymphoma	1. Non-Hodgkin	29
	2. Hodgkin	12
	3. Other malignant lymphoproliferative processes	1
Benign neoplasms	Lymphangioma	2
Inflammatory disorders	Lymphadenitis	31

The statistical analysis showed that the extracted data was statistically significant ($P < 0.05$). Sensitivity and diagnostic accuracy are, respectively, 92.6% and 79%. The most common false negative results (5) were found with lymphoma. Interestingly the specificity is only 45.5%. This was mainly due to the fact that 17 out of 18 false positive results are from FNAB of lymphadenitis.

Table 2. Diagnostic value of FNAB of lymph node lesions

TP (n)	75
FP (n)	18
TN (n)	15
FN (n)	6
PPV (%)	80.7
NPV (%)	71.4
Sensitivity (%)	92.6
Specificity (%)	45.5
Diagnostic accuracy (%)	79

4. Discussion

In the present study 8.9% of FNABs were non-diagnostic. Other autors came to similar results.[14] The most common reason for low diagnostic yield are metastases (from SCC, thyroid cancer, malignant melanoma)[13] with cystic degeneration, the cyst wall being lined by relatively mature, benign-appearing squamous cells.[14] FNAB in these cases can turn out non-diagnostic, due to aspiration of centrally located cystic fluid, which is evacuated mostly because of its lower resistance.[14] Another reason for a non-diagnostic FNAB are fibrous lesions, which frequently do not provide enough cell material for interpretation, due to difficulties with the aspiration.[15] Lesions with high of blood volume, presence of necrosis and fibers with scattered atypical cells are also difficult for cytological analysis.[15]

Publications about sensitivity for malignancies in the head and neck region are few as a whole and/or do not provide separate data about the diagnostic accuracy of FNAB of lymph nodes. The majority of autors discuss staging of oral and oropharyngeal SCC.[12,14,16,17] A study of Souren et al.,[14] comparing FNAB, ultrasound and magnet resonance imaging for staging of oral and oropharyngeal SCC, reported a high sensitivity (81%) and specificity (100%) of ultrasound guided FNAB of lymph nodes. In a similar study Geetha et al.[16] report 67% sensitivity and 100% specificity. These results are not entirely comparable with the present outcome, because our cohort had unspecified lymphadenopathy at initial presentation. Nonetheless, in the present investigation all metastases were recognized correctly by FNAB as malignant (sensitivity 100%) and the overall sensitivity for malignant process was high – 92.6%. Despite the presence of five false negative results (predominantly FNAB of lymphoma), the sensitivity for lymphoma was high – 88%. Karimi-Yazidi et al.[18] confirm these observations. They reported a sensitivity of 88% and a specificity of 82.1%. A possible reason for a false negative result can be the presence of Reed-Sternberg cells, which on rare occasions can be found not only in Hodgkin, but also in Non-Hodgkin lymphoma (after initial treatment), viral infections, such as infectious mononucleosis as well.[7] Moreover, FNAB is problematic in the differentiation of a low-grade Non-Hodgkin lymphoma from reactive nodal hyperplasia.[7] Flow cytometry in combination with FNAB can increase the diagnostic accuracy in these cases.[7] Nonetheless, the application of FNAB in lymphoma remains controversial and many pathologists use it only for the diagnosis of relapse or in the most obvious cases of lymphoma.[19]

In the present study more than half of the benign processes (lymphadenitis and lymphangioma) were recognized as malignant – 17 out of all 18 false positive results were from FNAB of inflammatory disorders of the lymph nodes, resulting in a low specificity of 45.5%. Koo et al.[20] reported that metastatic lymph nodes (*e. g.* nasopharyngeal carcinoma, pulmonary small cell carcinoma, papillary thyroid carcinoma, malignant melanoma and rhabdomyosarcoma) have the characteristics of a granulomatous inflammation. This can be attributed to necrotic tissue response or T-cell mediated hypersensitivity to antigens.[20]

Contingent selection undergoing FNAB could lead to a substantial increase of specificity. Inclusion of patients only suspicious for malignancy or for restaging would exclude the majority of inflammatory lymphadenopathies. On the other hand, the application of FNAB in all patients with lymphadenitis can be advantageous. A recent study[21] showed that 45% of the cases of FNAB of lymph nodes represent a non-specific inflammatory lymphadenopathy, not necessitating inpatient treatment. The same investigation showed that in children this percentage is 85%. Other authors report that the application of FNAB can reduce excisional/incisional biopsy by 40%-75% in pediatric head and neck masses.[22]

Fine needle aspiration cytology is associated with less complications than excisional lymph node biopsy, the latter having a complication rate of 5% to 10%.[11] Moreover, FNAB can be conducted without anesthesia and reduce treatment costs for staging of malignant disease[20] with up to 55% in comparison to excisional lymph node biopsy.[11]

It can be concluded that FNAB is highly recommended in the diagnostic work-up of head and neck lymphadenopathy, avoiding unnecessary hospitalization in many cases.

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Dear Friends,

On behalf of the 4th International Pediatric Sleep Association Congress in conjunction with the 14th Annual Meeting of Taiwan Society of Sleep Medicine and the 1st Conference of Asian Society of Sleep Medicine (IPSA 2016), we are extremely happy to invite you to participate in the Congress which will be held on March 10-13, 2016, in Taipei International Convention Center, located in the heart of Taipei, Taiwan. We sincerely hope the beauty of our city and the theme of our conference will attract you all.

IPSA 2016 serves as a premier event on the international calendar of pediatric sleep bringing together physicians, educators, basic scientists, sleep technician and clinical investigators from hospitals, industry, and academia to present and share the latest cutting-edge research results and innovative solutions in the related fields.

We believe you will have a fruitful and enjoyable time during your stay in Taipei based on our solid program and the hospitality of Taipei, Taiwan, known as „Formosa“ (“beautiful Island“ in Portuguese), as used by the Portuguese mariners centuries ago to describe Taiwan

We look forward to seeing you in Taipei, Taiwan in 2016!

Best Regards,

Dr. Yu-Shu Huang, Chair of IPSA 2016 and Local Organizer
Dr. Daniel KK Ng, Co-Chair of IPSA 2016
Dr. Oliviero Bruni, President of IPSA
Dr. Chia-Mo Lin, President of Taiwan Society of Sleep Medicine

INVITATION

Dear Colleagues,

Mediterranean Society of Otology and Audiology (MSOA) is an organization that supports scientific activities with a scientific journal and scientific meetings since its establishment in 1987. We are very pleased to announce that 15th International Meeting of The Mediterranean Society of Otology and Audiology will be organized in Cappadocia-Turkey on 28-30 April, 2016.

As in the past congresses, the scientific program will provide an ideal platform to share and discuss the latest advances in Otology and Audiology. Moreover, current standards will be reviewed with distinguished otologists and audiologists.

Three plenary panels about the cochlear implantation, vestibular diagnostic tests and middle ear surgery will follow the plenary lectures. Moreover, round tables, short communications and panels on otology, neurotology and audiology will enrich our scientific program. Hands-on-courses will be held with a limited number of participants.

We are also pleased to inform you that the best video presentation and free paper will be awarded in the 15th International Meeting of The Mediterranean Society of Otology and Audiology.Cappadocia is considered one of the natural wonders of the world. Chimney rocks, cave houses and churches, underground cities and open-air museum attract a lot of visitors from all over the world. Moreover air ballooning and trekking in Ihlara Valley, Monastery Valley (Guzelyurt), Urgup and Goreme are very popular activities. Half-day tour will be planned in these areas in the social program besides other activities. Webpage of the 15th International Meeting of The Mediterranean Society of Otology and Audiology (http://www.msoa2016.org/) is being update regularly.

We are honoured to invite you to the 15th International Meeting of The Mediterranean Society of Otology and Audiology, which will take place in Cappadocia-Turkey, 28-30 April 2016. We are looking forward to welcoming you in order to make an unforgettable congress together.

Prof. Dr. S. Armagan Incesulu

Глубокоуважаемые коллеги!

Приглашаем Вас принять участие в работе
XXIX-ой Международной Конференции Молодых Оториноларингологов имени проф. М.С.Плужникова
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Заявки на участие в конференции, *пожалуйста, высылайте* **до 15 февраля 2016 года** *в* **технический комитет** *конференции.*

Заявки на доклад *с названием докладов (8 мин.) на английском языке, пожалуйста, высылайте* **до 15 февраля 2016 года** *в* **научный комитет** *конференции.*

Abstract/Тезис *(1 стр.) на английском языке для публикации в материалах конференции в журнале "Folia Otorhinolaryngologiae et Pathologiae Respiratoriae", пожалуйста, высылайте* **до 15 марта 2016 года** *в* **научный комитет**. *Оформление в соответствии с требованиями к рукописям, направляемым в журнал "Folia Otorhinolaryngologiae et Pathologiae Respiratoriae" (***www. foliaopr.spb.ru***)*

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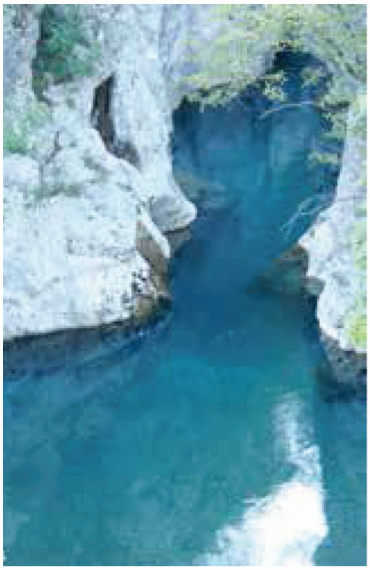

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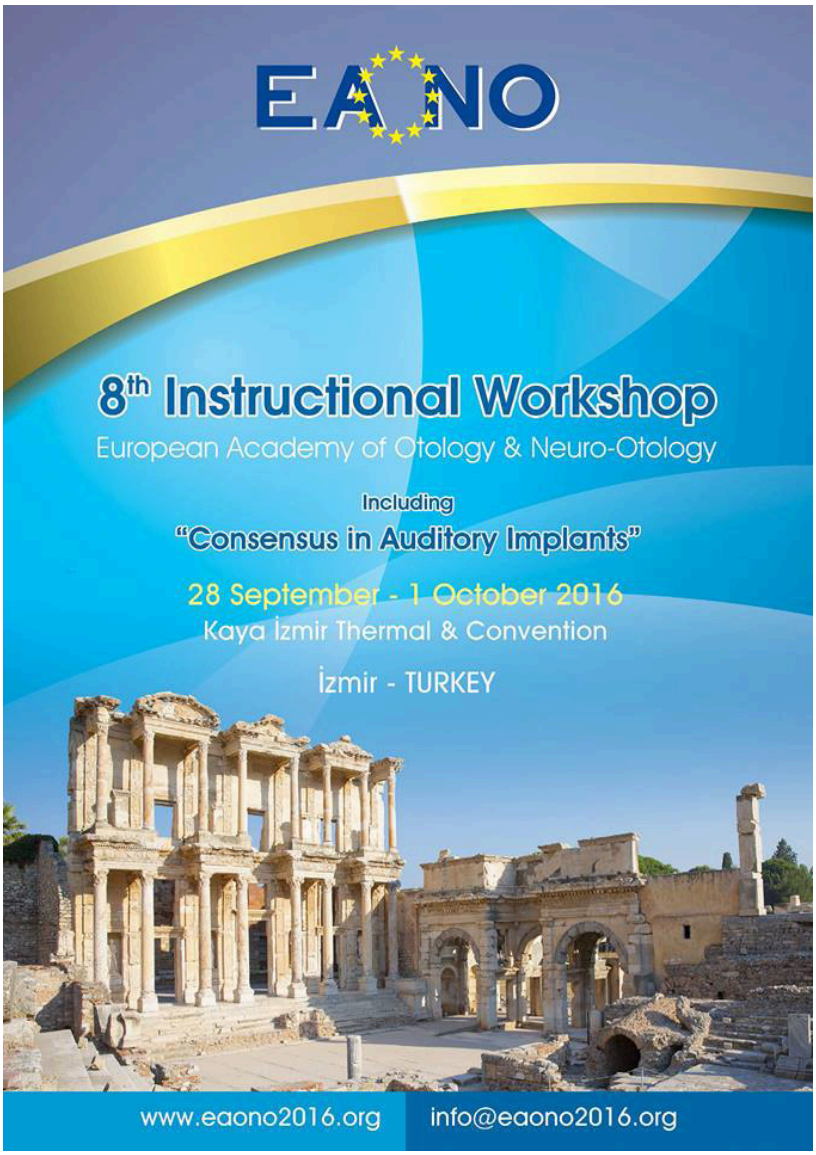

Dear Friends,

The next EAONO Instructional Course will be organized in Izmir on **28 September – 1 October** 2016. Traditionally the instructional courses will be the main theme and will be presented by the remarkable European Otologists as well as the invited speakers from other Continents. Besides; Research sessions, „Residents Sessions" as already initiated in Siena; Plenary Sessions and Panels will be part of it. Of course the „Consensus on Auditory Implants" will couple with the scientific sessions.

The Temporal Bone Dissection Courses will take part in two different formats. Registrations will be received either for advanced dissection to be accomplished by using full cadaver heads or for basic dissection on temporal bones to take place in two different anatomy departments.

We shall be regularly updating the webpage www.eaono2016.org for the details and also will keep on mailings through the EAONO Online Forums.

Until then, please keep in touch.

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