



ORIGINAL ARTICLE

Evolution of the tubotympanal mucociliary system activity evaluated with scintigraphy, after ventilation tube insertion in adults with chronic otitis media with effusion

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Received November 22, 2009; accepted February 1, 2010

KEYWORDS

Otitis media
with effusion;
Mucociliary clearance;
Radionuclide imaging

Abstract

Introduction and goals: Tubotympanal mucociliary function is damaged in patients with otitis media with effusion. Our objective was to study its situation and recovery after tympanostomy tube insertion.

Methods: We evaluated the mucociliary activity of the ear and Eustachian tube with scintigraphy in four groups of adults with chronic otitis media with effusion after ventilation tube insertion. The test was performed on 3 days (Group I), 6 days (Group II), 9 days (Group III) and 12 days (Group IV) after tympanostomy tube insertion.

Results: After excluding some patients with limited otorrhea, the percentages of patients that normalised mucociliary function in the different groups were: Group I, 0 of 13, 0%; Group II, 4 of 15 patients, 26,6%; Group III, 14 de 18 cases, 88,8%; and, in Group IV, 18 of 18, 100%

Conclusions: Mucociliary function is altered in patients with chronic otitis media with effusion. With the insertion of tympanostomy tubes, mucociliary clearance is restored progressively, reaching normal after 12 days in all the patients.

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PALABRAS CLAVE

Otitis media
seromucosa;
Aclaramiento
mucociliar;
Gammagrafía

Evolución de la actividad mucociliar tubotimpánica, estudiada por gammagrafía, tras la colocación de tubos de ventilación en adultos con otitis media seromucosa crónica

Resumen

Introducción y objetivos: La función mucociliar tubotimpánica está alterada en los pacientes con otitis media seromucosa. Nuestro objetivo es estudiar su situación y recuperación tras la colocación del drenaje transtimpánico.

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Métodos: Hemos evaluado la actividad mucociliar del oído medio y de la trompa de Eustaquio por gammagrafía, en 4 grupos de adultos con otitis media seromucosa crónica, tras la colocación del tubo de ventilación. La exploración se llevó a cabo 3 días (grupo I), 6 días (grupo II), 9 días (grupo III), y 12 días (grupo IV) tras la colocación del drenaje.

Resultados: Tras excluir algunos pacientes con otorrea autolimitada, los que normalizaron la función mucociliar, resultaron ser en cada grupo: grupo I, 0 de 13, 0%; en el grupo II, 4 de 15 pacientes, 26,6%; para el grupo III: 14 de 18 casos, 88,8%; y, por último, en el grupo IV, 18 de 18, 100%.

Conclusiones: En los pacientes con otitis media seromucosa crónica la función mucociliar está alterada. La inserción del tubo de ventilación reestablece el aclaramiento mucociliar de forma progresiva, alcanzando la normalidad tras 12 días en todos los pacientes.

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Introduction

Otitis media with effusion (secretory otitis media) was first described by Politzer¹ and initially called serous otitis media. From the clinical point of view, among the various definitions of the pathological process, we have chosen that of Zechner,² according to which otitis media with effusion "is a pathological process of the middle ear characterised by an accumulation of fluid in the cavity, with no signs of acute infection and behind an intact tympanic membrane".

In 1980, the Ad Hoc Committee on Definition and Classification of Otitis Media in the Second International Symposium on recent advances on serous otitis, proposed a classification based on disease duration and type of effusion; secretory otitis was classified as acute, subacute and chronic, according to duration, and as serous, mucoid and purulent depending on the type of the effusion.

Otitis media with effusion is a very common process, and its aetiopathogenesis is extremely controversial: the roles played by age, adenoid hypertrophy, allergy, climate, antibiotics, infection, impaired immunity, Eustachian tube pressure dysfunction and the secretory activity of the middle ear mucosa have been considered among the most important factors. The specific influence of each of these aspects is, in many cases, still to be clarified.

We studied the activity of the mucociliary system of middle ears affected by mucous otitis media after the insertion of tympanostomy drainage tubes, to clarify the influence of mucociliary clearance in the genesis of this condition, as well as the action of tympanostomy tubes in its healing.

To do so, we determined the transport capacity of the mucociliary system of middle ears affected by the mucosal variety of chronic otitis media with effusion, over time, after the insertion of tympanostomy tubes through the instilment of human serum albumin labelled with ⁹⁹Tc, and the performance of sequential scintigraphy.

Methods

We carried out a sequential tubo-tympanic scintigraphy on 80 patients, aged between 18 and 65 years, suffering

from mucous-type chronic otitis media with effusion, of at least 12 weeks duration, who required tympanostomy tube insertion for their treatment.

In our study, serous or purulent varieties were not included, nor patients with coinciding catarrhal processes or allergic crisis of the upper airways at the time of tube insertion. There was no control group without pathology. No samples were taken for culture.

Mucociliary function was assessed by sequential tubo-tympanic scintigraphy practiced after surgery, so we created 4 groups of 20 patients, using a random assignment procedure. In Group I, the scintigraphy was performed 3 days after surgery; in Group II, 6 days afterwards; in Group III, 9 days afterwards; and in Group IV, 12 days after surgery. All patients were evaluated one week after the scintigraphic examination to assess the evolution of each case. All patients authorised their inclusion in the study and the completion of the scintigraphy scan.

All patients received, through the myringotomy, a dose of 18.5 MBq of ⁹⁹Tc human serum albumin in a volume of 0.05 cc. The transit of the radiotracer along the tube was monitored using static images acquired in lateral projection at regular intervals of time.

Two situations, depending on the activity of the tubo-tympanic mucociliary system in the scintigraphy scans performed, were distinguished³:

1. Patients with normal activity, in whom the radiopharmaceutical deposited via myringotomy reached the posterior pharyngeal wall at a normal speed (Figure 1), according to earlier experiences, and
2. The other patients lacking transport capacity of the tubo-tympanic mucociliary system, in whom the radioactive material remained at the initial point of deposit for the entire study.

Patients who, after completion of the scan, suffered an otorrhea were recorded. These patients were not considered as susceptible of being evaluated in the interpretation of the scintigraphic results. We recorded the number and percentage of patients who, in each group, obtained a normal or pathological result. We estimated the confidence intervals, with a 95% CI, of the percentages of patients with a normal scintigraphy scan in each of the groups.

Results

After instillation of the tracer, there was scarce and transient otorrhea in a variable number of patients in each study group: in Group I, there was a secondary otorrhea in 7 of 20 patients in the group, representing 35% of the study patients; in Group II, otorrhea appeared in 5 patients in the group, which represents 25% of the study patients; in Groups III and IV, otorrhea took place in 2 patients in each group, representing 10% of each of the two groups of patients studied. All these patients were excluded from the scintigraphic evaluation.

After rejecting the patients who suffered otorrhea in each study group, the following activity percentages were obtained (Table, Figure 2) for the sequential tubo-tympanic scintigraphy after completing the tympanostomy drain:

In Group I, covering the patients studied three days after insertion of tympanostomy drainage, none of the patients studied showed any transport capacity of the mucociliary system, evaluated by this procedure (95%CI: 0% to 24.7%).

In Group II, which grouped together the patients in whom scintigraphy was performed 6 days after tympanostomy drainage insertion, 4 patients of the 15 considered, that is, 26.6% (95%CI: 7.8% to 55.1%) of all patients, showed normal activity of the Eustachian tube mucociliary system.

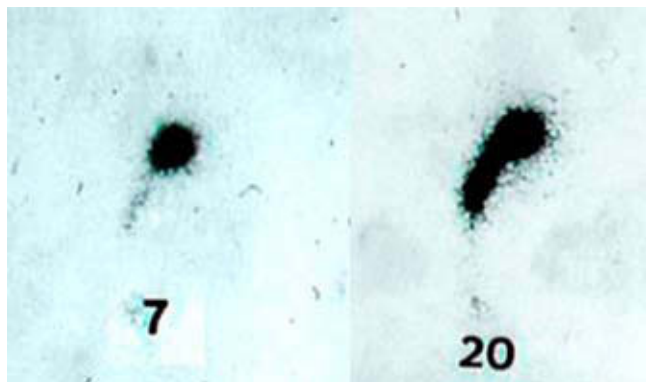


Figure 1 Images from the scintigraphy scans taken 7 and 20 min after radiotracer injection in the middle ear with normal mucociliary clearance. Note the increase of the signal emitted from the Eustachian tube.

In Group III (the patients studied nine days after tube insertion), we observed normal tubo-tympanic transport capacity of the mucociliary system in 16 of the 18 patients in this group: that is, 88.8% (95%CI: 65.3% to 98.6%).

Finally, in Group IV (patients who underwent scintigraphy 12 days after tympanostomy drainage insertion), we found normal tubo-tympanic transport capacity of the mucociliary system in 18 of the 18 patients considered; that is, 100% (95%CI: 81.47% to 100%).

Discussion

The aetiopathogenesis of otitis media with effusion is yet to be clarified in many respects. In its pathogenesis, three possibly interrelated key factors must be considered, among others: middle ear inflammation, Eustachian tube dysfunction and decreased mucociliary clearance. The last factor was the subject of our investigation.

There is abundant evidence of the relationship between otitis media with effusion and mucociliary function impairment.⁴ Some studies provide relevant data. Ernstson⁵ studied five patients with congenital ciliary immotility syndrome, which showed the existence of chronic secretory otitis media in most patients. Chronic mucosal

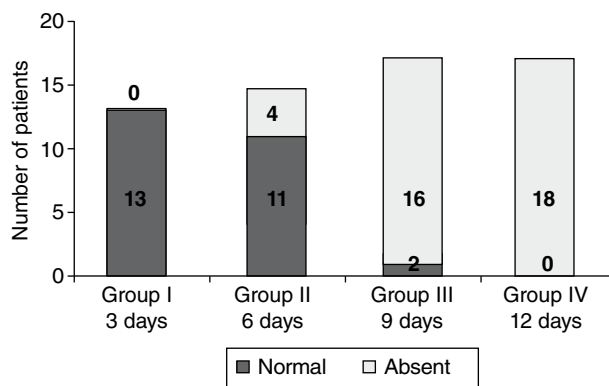


Figure 2 Number of patients with normal and pathological scintigraphy in the different patient groups created according to the days that passed after drain insertion.

Table 1 Number, percentage and confidence interval of patients with normal scintigraphy, according to the days that passed after ventilation tube insertion

Days passed until scintigraphy	Number of patients with normal scintigraphy / total cases in the group	Percentage of patients with normal scintigraphy	95% CI of patients with normal scintigraphy
3	0/ 13	0	0-24.7%
6	4/ 15	26.6	7.8-55.1%
9	16/ 18	88.8	65.3-98.6%
12	18/ 18	100	81.5-100%

otitis media is very common during childhood in patients with primary ciliary dyskinesia.⁶ Borkowski⁷ found a lower ciliary beat frequency in patients with otitis media with effusion (6.5 ± 1.83 Hz) compared to controls carried out in patients not suffering from it (10.68 ± 1.87 Hz). This suggests the existence, at least in some cases, of a ciliary activity disorder.⁴

Regarding the possible influence of mucus on the mucociliary transport system capacity, there is evidence that contact of the contents (taken from children with mucoid otitis media) with the ciliated cells in the nasal mucosa resulted in a reduction of ciliary beat after a few hours.⁸ The same result was obtained when mucus from children with mucoid otitis media was placed on guinea pigs.⁹ These alterations can be explained by the physical and chemical composition of the contents of otitis media with effusion: indeed, inflammatory mediators have been detected in it (cytokines such as TNF, interleukin [IL-8, IL-6], interferon gamma, macrophage inhibitory factor and other substances). In guinea pigs, it was found that the platelet activating factor, a substance present in the inflammatory reaction, impaired the clearance of the middle ear.¹⁰ Leukotriene C4 and D4 also caused a reduction in ciliary activity.¹¹ Bacterial endotoxins—and bacteria are common in the content of secretory otitis media—may impair ciliary clearance.¹² Even when the middle ear culture is sterile, there are viable germs in a high percentage of cases.¹³ In addition, biofilms have been demonstrated present in middle ear mucosa specimens from children with chronic otitis media with effusion.¹⁴ These circumstances facilitate the presence of endotoxins, sometimes inducing a reduced immune reaction in the host and making it easier for the process to become chronic.¹⁵ There is no conclusive data on whether endotoxins affect the mucociliary system by action on the cilia, action which may take place through cytokines, or by the characteristics of the mucus.¹⁶

It has also been considered that decreased mucociliary transport may be due to a change in the physical conditions of the mucus layer. To transport the mucus secretion, cilia beat and move in the sol phase—liquid—of the deep mucus layer and only their tips contact the thicker superficial gel layer. In chronic otitis media with effusion, metaplasia occurs in the epithelium with secretory cell proliferation and changes in the type of secretion, which is more viscous. The viscosity seems to depend on mucin concentration. Increased expression of the gene MUC5B, which produces gel-type, high molecular weight mucin, has been observed.¹⁷ This change in gene regulation could be caused by inflammatory cytokines, such as TNF- α . Increased viscosity reduces the ability of cilia to move mucus, thus decreasing mucociliary clearance.⁴ However, other studies do not show such a clear influence of mucus on the ciliary beat.^{16,18}

The study of the mucociliary transport system capacity in patients suffering otitis media with effusion is extremely complex, because the middle ear is usually a closed cavity that only occasionally communicates with the nasopharynx. We used different methods to assess mucociliary clearance in the middle ear: one consists in the introduction of various substances into the middle ear. Radiological contrasts were tested initially, but

in our opinion, these do not assess ciliary function in isolation but also include the swallowing transport mechanism of the Eustachian tube. Subsequently, we introduced substances that were transported by the mucus to assess their displacement. We used dyes such as fluorescein, observing the tubal or pharyngeal orifice of the tube continuously to record its appearance and thus evaluate displacement time. We also used sweeteners such as saccharin, which produced a sweet taste for the patient indicating that the sweetener had reached the pharynx.

Gaillard de Cologny¹⁹ used human albumin for the first time, introduced into the middle ear and labelled with ⁹⁹Tc, assessing its movement through sequential scintigraphy. This procedure allows quantification of the transport capacity of the mucociliary system in its tubo-tympanic portion.^{3,20,21} It has been used in an attempt to predict tympanoplasty outcomes.^{22,23} It has also been evaluated against study procedures of other Eustachian tube functions, such as tubal manometry.²⁴

Scintigraphy with albumin has advantages since soluble substances, such as fluorescein and sucrose, are dissolved to a further extent in the deep layer, with sol consistency, and their movement is slower, thus distorting the determination of the transport capacity of the mucociliary system. In addition, in contrast, insoluble substances, such as albumin, move over the surface layer of mucus, which is gelatinous, at the actual speed of clearance of mucus.

In our research, we chose to use the tympanostomy drain as the path for the deposition of the radiotracer, seeking a double purpose: First, to study the mucociliary system having partially withdrawn, by surgical aspiration, the accumulation of mucus that may have distorted the results of the study on the middle ear epithelium transport capacity. Second, the use of the tympanostomy drain to deposit the human serum albumin allows assessing the mucociliary transport system capacity at various periods of time after its insertion.

The evaluation of the transport capacity of the mucociliary system 3 days after tympanostomy drain insertion showed, in all our patients (13 cases), the absence of mucus transport along the Eustachian tube. Other studies with similar methodologies have shown similar results. Karja,²⁵ in 20 cases of otitis media with effusion, using the same tracer, did not detect mucociliary activity in any of the patients after instilling 0.04 ml in the 60 min after the drain insertion. In Celen's study,²⁶ 100 μ l of ⁹⁹Tc linked to macroalbumin were instilled in 32 children suffering from otitis media with effusion; in 84% of patients (27 cases), the tracer did not pass to the cavum. That study did not specify the time lapse between drain insertion and exploration, stating only that it was done within the month following the drainage tube insertion, which could explain the results.

Takeuchi²⁷ used a different method, depositing only 10 μ l of the tracer inside the middle ear through the tympanostomy drain in 34 children with otitis media with effusion, and taking measurements of the radioactivity in the tympanum cavity every 30 s for 15 min. Mucociliary clearance was estimated by the reduction of this radioactivity. In 61% of these patients, there was no clearance whatsoever.

Among the rest, the average percentage of radioactivity reduction after fifteen minutes was 5% in ears with otitis media with effusion, compared to 20.7% in ears without otitis media with effusion, but which had previously been diagnosed with it. The differences between the results of these studies may be due to the different patient and study method characteristics.

In any case, we can conclude from the results of our study, at its initial stages, as well as from the others mentioned, that mucociliary system alteration in patients with otitis media with effusion is nearly constant. We understand that this mucociliary dysfunction can act as a primary, predisposing or determining factor, which promotes the development of otitis media with effusion.

The Eustachian tube opening may assist in draining the tympanum cavity. It is therefore possible that even while suffering from a ciliary activity disorder, mucus movement is resumed after tympanostomy tube insertion, thanks to the swallowing movements that act on the middle ear. Jahrsdoerfer et al.²⁸ reported the case of two patients with Kartagener syndrome in whom the insertion of tympanostomy drainage tubes made the ears appear completely dry. That author assumed that it should be attributed to the fact that the drainage of secretions along the tube was verified even without the participation of the mucociliary system. In this sense, it was considered a muscular factor in relation to the contraction of the muscles inserted in the tube during swallowing. Under normal conditions, the muscle function can eliminate middle ear fluid content, provided that this is mucus with normal characteristics; this has been proven by Raport PN, Lim DJ and Weiss HS,²⁹ who demonstrated the existence of a surfactant agent at the level of the Eustachian tube mucus, in such a way that the opening pressures of the tube increased dramatically after washing the Eustachian tube with saline. The presence of pathological secretions in the middle ear that cannot be drained along the tube would generate a negative pressure in the middle ear when swallowing, so this muscular or swallowing factor of the Eustachian tube could not be activated.³⁰ In our patients it does not appear that this muscular factor was relevant, because in no case was the recovery of cleared labelled albumin observed after three days of surgery.

The results of our research showed a recovery in the mucociliary transport system capacity, which took place over the course of days after the drainage tube insertion. Although after 3 days there was no transport of the tracer into the cavum in any of the cases studied, just over a quarter of cases showed normal activity at 6 days, almost 90% at 9 days, and normal activity in all patients evaluated was observed at 12 days after surgery.

In this sense, there are virtually no data in the literature on changes that may occur in mucociliary function after tympanostomy tube insertion in patients with chronic otitis media with effusion. After tympanostomy drainage placement in children with the aforementioned process, Karja²⁵ established a period of 3 weeks as the shortest interval after which the Eustachian tube resumed its normal function, although no other information was offered. In our patients the results show a faster mucociliary system recovery. In addition, we observed

how, at 9 days (the point at which it became normalized in almost all cases), the mucociliary transport system capacity usually showed a reversal of inflammation signs under otoscopy.

It should also be noted that mucus transport was reinitiated as a whole; that is, throughout the entire tubo-tympanic mucociliary system. We noted, as did Takeuchi,²⁷ that in all patients with this pathology in whom the tubal transport was restarted, it was not interrupted until the nasopharynx was reached. We did not identify any intermediate stage in which the mucociliary activity was only partially recovered. In any case, if there were an intermediate stage, it would be expected to occur between days 3 to 10. This contrasts with the situation in simple chronic suppurative otitis media, in which there are indeed cases where transport capacity can be observed to permanently slow down or be absent.^{3,20,21}

Another aspect to observe in this study is the appearance of slight, self-limiting otorrhea in a variable number of cases. These situations of otorrhea occurred more frequently in those determinations carried out during the first days. We understand that the initially high number of slight otorrheas should not be attributed to a defect in the method, because they were absent in patients who underwent exploration later, but perhaps to a greater presence of inflammatory factors during those experiences closer in time to the completion of the tympanostomy drain.

Eustachian tube dysfunction has traditionally been regarded as an important factor in the genesis of otitis media with effusion and should be discussed. In 1940, Holmgren³¹ already assumed that otitis media with effusion occurred as a consequence of Eustachian tube obstruction and the subsequent reabsorption of its air content by the middle ear. Much later, the absorption of gas in the middle ear was well studied and verified by Cantekin.³²

Holmquist and Renvall³³ found a pressure dysfunction in all cases of otitis media with effusion. In experimental models in which an Eustachian tube obstruction was performed, it caused the rapid appearance of a serous effusion that changed into a purulent effusion after one or two months.^{34,35} The passage of time brought about a hyperplastic alteration with formation of glandular elements and continuous vasodilatation. Moreover, serous effusion in barotrauma, where there is a situation of negative pressure inside the middle ear, constitutes an important piece of clinical evidence.

Otitis media with effusion is a clinical condition with a multifactorial origin. The inflammation of the respiratory mucosa may be triggered by viral or bacterial infections. Pressure dysfunction may be one of the initial pathogenetic factors. The persistence of the inflammatory process may be accompanied or not by bacterial infection. The multiple mediators of inflammation and changes in secretion type and quantity impair the ciliary function that allows normal middle ear clearance, which makes it easier for the process to become chronic.

Tympanostomy tube insertion, in addition to allowing the removal of a certain amount of inflammatory fluid, turns the middle ear into a cavity permanently open to

the exterior. These modifications promote the restoration of normal mucociliary system functioning. This in turn enables the reversal of the middle ear inflammation, which comes to disappear completely, for all practical purposes, after the first 12 days. This is not to say that the normalisation is irreversible and that the drainage can be removed after those 12 days, because pathogenetic factors may remain that would trigger the inflammatory situation once again if the tympanostomy drain were to be removed.

Conclusions

The mucociliary clearance of the middle ear is pathological in patients suffering from adult otitis media with effusion.

After removal of the mucous contents of the middle ear and tympanostomy tube insertion, mucociliary clearance is restored in the days after insertion, becoming standard on the twelfth day in all cases studied.

Conflict of interests

The authors declare no conflict of interests.

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