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A 'chemical help' in middle-ear surgery? A systematic review on sodium 2-mercaptoethanesulfonate

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Review Article

Dr A Moffa takes responsibility for the integrity of the content of the paper

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Abstract

Objective. Sodium 2-mercaptoethanesulfonate (Mesna) has been proposed as a chemical aid in any surgical procedure, including cholesteatoma surgery. This review investigated the benefits and safety of Mesna during surgical management of cholesteatoma and adhesive otitis media.

Method. A systematic literature review was performed to identify clinical studies evaluating topical Mesna application during ear surgery (cholesteatoma or atelectasis). A qualitative analysis based on data extracted was conducted.

Results. From 27 articles, 5 retrospective studies were selected for a full analysis for a total of 607 patients (aged 5 to 72 years). Three studies evaluated cholesteatoma recidivism after Mesna application during cholesteatoma surgery, one study evaluated the surgical success rate of Mesna application for the treatment of atelectatic ears and adhesive otitis media, and one study evaluated potential ototoxicity of Mesna during cholesteatoma surgery. All the studies showed overall improvement in recurrence and residual cholesteatoma disease after Mesna application during surgery. Sensorineural hearing loss was not encountered after Mesna application.

Conclusion. Mesna application in cholesteatoma surgery could represent a valid and safe support tool during surgical treatment carried out both with microscopy and endoscopy. More studies are required to confirm these promising results.

Introduction

Sodium 2-mercaptoethanesulfonate, also known as Mesna, is a synthetic sulfur compound that belongs to a class of thiols that produce mucolysis by disrupting disulfide bonds of the mucous polypeptide chains. It has been used in several diseases as a cytoprotective agent to prevent haemorrhagic cystitis and as a mucolytic agent to improve pulmonary function.[1] Mesna has the potential to scavenge reactive oxygen metabolites by virtue of its sulfhydryl group.[2] Many studies *in vivo* and *in vitro* suggest that Mesna plays an important role as an antioxidant drug.[3] It is widely used as a systemic protective agent against the toxicity of chemotherapy.[4] By increasing the kidney levels of free thiol, Mesna was shown to prevent renal oxidative damage in rats treated with ferric nitrilotriacetate.[5]

Only in recent years has Mesna gained attention for its potential application in facilitating surgical dissection. Traditional surgical dissection may be insufficient to remove all pathological tissue; for this reason, the use of drugs that facilitate their elimination, even in areas difficult to access, has been tried for a few decades, leading to the concept of 'chemically assisted dissection'. The fundamental principle of chemically assisted dissection lies in the rich disulfide bonds of the adhesions between the different tissue layers.[6]

In particular, Mesna has been used in revision lumbar spine surgery, significantly improving surgical dissection and reducing post-operative complications. Moreover, it has been employed to ease abdominal myomectomy procedures and excision of endometrial cysts. Finally, in ENT surgery, topical Mesna has been widely used from ear and skull base to head and neck diseases, in both out-patient and operating-room settings.[6] A variety of other chemical products have been proposed, but the majority of these substances cannot be applied intra-operatively because of severe irritation to living tissues.[7,8] In the ENT field, Mesna has been predominantly used for the treatment of most common ear disorders such as cholesteatoma, atelectatic ears, adhesive otitis media, tympanosclerosis, cholesterol granulomas and for earwax removal.

This review aims to systematically identify, summarise and critically appraise the current evidence concerning topical administration of Mesna during surgical treatment of cholesteatoma, atelectatic ears and adhesive otitis media. Specifically, we sought to evaluate the effects of Mesna application on residual and recurrent disease after tympanoplasty

with or without mastoidectomy, looking at complications with a focus on sensorineural hearing loss (SNHL).

Materials and methods

The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') guidelines.[9]

Data source and search

An electronic search was performed on Medline, Google Scholar and Ovid databases. An example of a search strategy is the one used for Medline: 'Mensa', 'Sodium 2-mercaptoethane Sulphonate', 'Chemically assisted dissection', 'CAD', 'CADISS', 'Uromitexan', 'cholesteatoma', 'chronic cholesteatomatous otitis media', 'chronic otitis media', 'atelectatic ears', 'adhesive otitis media', 'middle ear surgery', 'tympanoplasty' and 'mastoidectomy'. The other searches were adjusted to fit the specific requirements for each database. Then, a cross-reference search of the included studies was performed to minimise the risk of missing relevant data. The last search was run in March 2020.

Inclusion and exclusion criteria

The selection of studies was based on the Population, Intervention, Comparison and Outcome ('PICO') framework.[10] The Population, Intervention, Comparison and Outcome process is used in evidence-based medicine to frame and answer a clinical or healthcare-related question. In this study, it had the following structure. Population: paediatric and adult patients affected by cholesteatoma, retraction pockets and adhesive otitis media. Inclusion criteria were studies including patients (with no age limit) affected by cholesteatoma, atelectatic ears and adhesive otitis media who underwent surgical procedures (such as tympanoplasty with or without mastoidectomy). Exclusion criteria were studies not in English, case reports, reviews, conference abstracts, letters, and studies with unclear or incomplete data. Intervention and comparison: we included studies investigating the use of Mesna during middle-ear surgery compared with patients receiving a placebo. Outcome: the primary outcome included the frequency of residual disease and recidivism and serious adverse events. Secondary outcomes included SNHL and complications.

Data extraction and analysis

Two independent reviewers (A Moffa and V Fiore) separately searched for related scientific papers. All articles were initially screened by title and abstract, and then the authors independently assessed the full-text versions of each publication and excluded those whose content was judged not to be strictly related to the subject of this review. Data extraction from the included studies was performed systematically using a structured form, and two reviewers (A Moffa and V Fiore) independently checked it. A qualitative synthesis analysis that considered the selected studies in regard to the effects of Mesna in cholesteatoma surgery was performed.

Data extraction of the studies included the population demographics and baseline characteristics, details on intervention and control conditions, study design, outcome and time of measurement as well as risk estimates. Discrepancies were identified and resolved through discussion.

Study quality assessment

The National Institute for Health and Clinical Excellence quality assessment tool was used to evaluate the quality of the included studies.[11]

Statistical analysis and summary

It was not possible to perform the intended statistical analysis and summary of findings as described in our protocol. We were unable to do this because of the heterogenic reporting style and lack of data in individual studies included in this review. Thus, the effect on individual outcomes and overall quality assessment were solely narratively described. Available data in the retrospective studies were used. Authors of the included studies were not contacted for further information.

Results

Search criteria returned 27 articles, which were reduced to 19 after the removal of irrelevant articles and duplicates. These were screened and another 14 were excluded, resulting in 5 articles fulfilling criteria for inclusion in this review.

The flow diagram depicting the selection process is shown in Figure 1. All the original articles included were retrospective case-control studies, with only one paediatric study. The population in the included studies consisted of 607 patients aged 5 to 72 years, all with unilateral definite cholesteatoma or mean adhesive otitis media and atelectatic ears. The baseline characteristics of the studies are reported in Table 1.

From 27 articles, 5 retrospective studies were selected for a full analysis for a total of 607 patients aged 5 to 72 years. Three studies investigated the recidivism of cholesteatoma after Mesna topical application against a control group ($n = 501$) during cholesteatoma surgery, one study evaluated the surgical success rate of Mesna for the treatment of atelectatic ears and adhesive otitis media, and one study evaluated the potential ototoxicity of Mesna during cholesteatoma surgery with a control group ($n = 106$). A further description of the studies can be found in Table 2.

Primary outcomes

de la Torre and Villamor[12] evaluated the effectiveness of chemically assisted dissection with Mesna during mastoidectomy in paediatric patients affected by cholesteatoma. In this retrospective case-control study, the authors analysed 146 mastoidectomies of which 54 surgical procedures were performed with Mesna and 92 were performed without Mesna. In the study group, 4 per cent Mesna solution was applied during surgery for 10 minutes with a maximum dose of 400 mg per surgery. After the surgery, the authors evaluated recurrence and residual disease and complications. The highest rate of cholesteatoma recidivism occurred in canal wall up mastoidectomy procedures without chemically assisted dissection, whereas the lowest rate of cholesteatoma recidivism was reported in canal wall down mastoidectomy procedures with chemically assisted dissection exploiting Mesna. From the comparison of total cases (canal wall up and canal wall down procedures), the authors recorded that both recidivism and residual cases were significantly lower in the study group than the control group.

Yilmaz *et al.*[13] investigated the effects of Mesna application in 24 ears with retraction pockets and 17 ears with adhesive otitis media, which are important clinical entities that can

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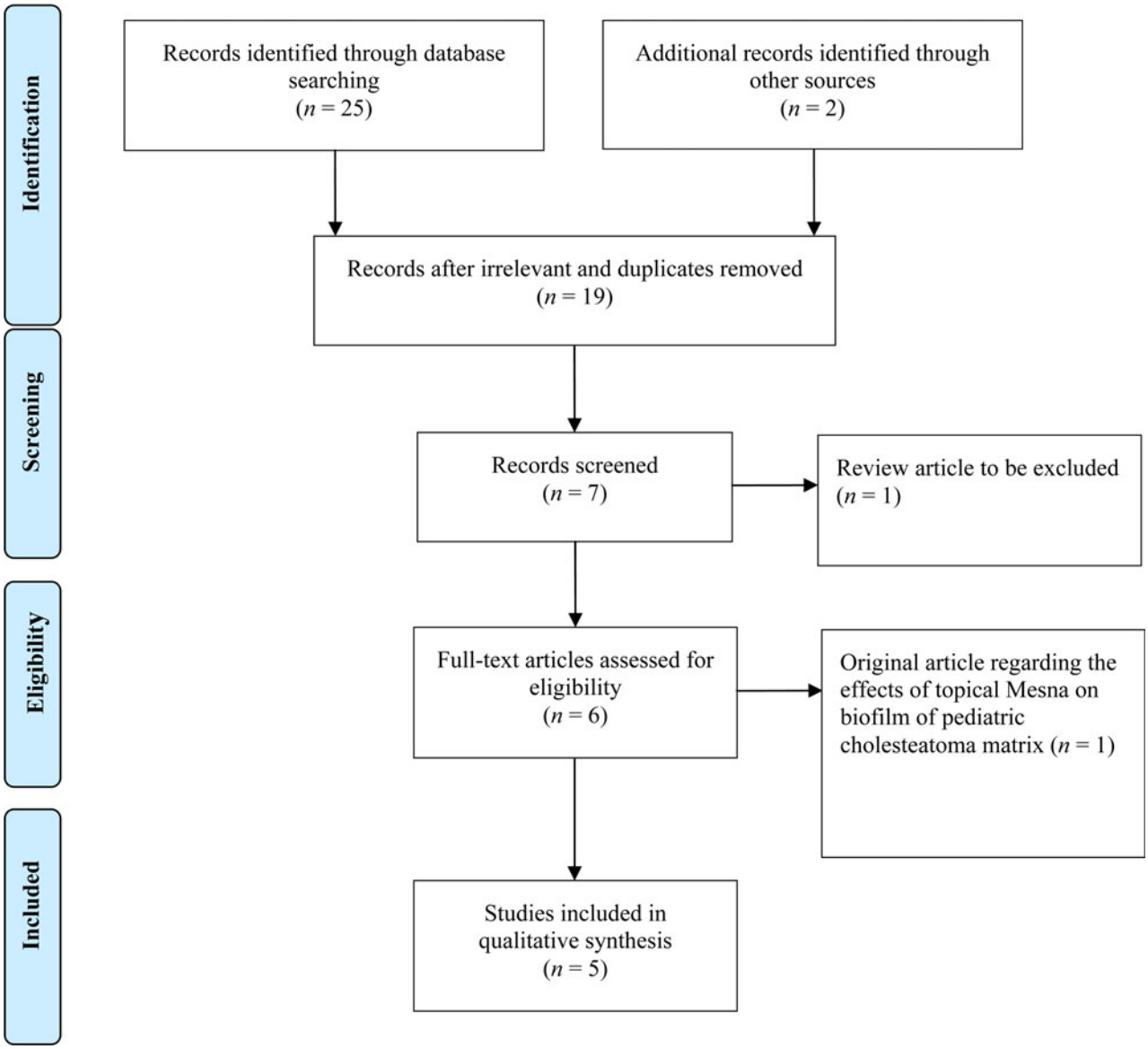

Fig. 1. Flowchart outlining the paper selection process of the systematic review (based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines).

lead to the development of cholesteatoma. Mesna injection alone has been performed for simple retractions and minor adhesions. Adhesive otitis media ears were treated with Mesna injection through the tympanic membrane initially and through the atticoantral region after mastoidectomy. The operation was successful in 79.2 per cent of ears. Overall, revision surgery was needed in 20.8 per cent of the ears. In 71.4 per cent of the ears with simple retractions and minor adhesions treated with Mesna alone, revision surgery was needed.

Vincenti *et al.*[14] conducted a retrospective study on Mesna topical application in canal wall up mastoidectomy. They included 214 patients: 108 underwent operation with the ancillary use of Mesna (chemically assisted dissection group), and 106 were treated with the traditional mechanical technique alone (no chemically assisted dissection group). At the beginning of surgery, 10 per cent Mesna solution was obtained using saline and drawn into a syringe. Once the cholesteatoma was exposed, before starting the removal, a small amount of Mesna solution was injected and left in the middle ear and the mastoid for three minutes. During the surgical dissection, Mesna was also topically administered with continuous instillation by means of microdissectors. A residual cholesteatoma was found in 12 (11.1 per cent) of the 108 patients in the chemically assisted dissection group and in 26 (24.5 per cent) of the 106 patients in the no chemical-assisted anatomical dissection group, not before 12 months after the first-stage operation. After adjusting for potential confounders, chemically assisted dissection with Mesna was associated with a significantly lower risk of having residual cholesteatoma (odds ratio, 0.39; 95 per cent confidence interval, 0.18–0.84; $p = 0.02$).

Kalcioglu *et al.*[15] evaluated the effects of Mesna on residual cholesteatoma rates in the patients who underwent surgery. They studied 141 cases divided into two groups: 46 cases treated with 20 per cent Mesna solution intra-operatively and 95 cases without Mesna. After one year, residual cholesteatoma rates were found to be significantly higher in the group without Mesna than in the group with Mesna treatment ($p < 0.05$), regardless of the technique employed (canal wall down *vs* canal wall up: p value was not significant).

Secondary outcomes

Three of the five studies included in this review evaluated the potential ototoxicity resulting from topical administration of

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Table 1. General characteristics and quality assessment of included studies

	General characteristics of included studies								Quality assessment of included studies							
Authors & year	Study design (level of evidence)	Ears (*n*)	Side (right/ left)	Sex (male/ female)	Age (mean (range; years)	Stage of cholesteatoma (ears (*n*))	Associated lesion	Follow up (mean (range); months)	Multicentre?	Aim?	Inclusion and exclusion criteria?	Outcome?	Prospective?	Consecutive enrolment?	Main findings?	Outcomes stratified?
de la Torre & Villamor, 2019[12]	Retrospective case-control study (III)	54 cases	26/28	42/12	9.2 ± 4.2	EAC: 6; I: 2; II: 27; III: 19	–	28 ± 13.5	No	Yes	Yes	Yes	No	No	Yes	Yes
		92 controls	56/36	69/23	9.1 ± 4.3	EAC: 4; I: 10; II: 41; III: 37	–	32 ± 18.9								
Kalcioglu *et al.*, 2014[15]	Retrospective case-control study (III)	46 cases	–	26/20	27.3 (6–64)	–	–	35.2 (12–65)	No	Yes	Yes	Yes	No	No	Yes	Yes
		95 controls	–	45/50	31.4 (11–58)	–	–	39.1 (12–134)								
Vincenti *et al.*, 2014[14]	Retrospective case-control study (III)	108 cases	–	50/58	45 (18–69)	I: 29; II: 19; III: 24; IV: 26; V: 10	Eroded incus (92); eroded stapes (43); epidermisation of the facial nerve (6); labyrinthine fistula (6); bony defect of middle cranial fossa (5)	12.75 (12–15)	No	Yes	Yes	Yes	No	No	Yes	Yes
		106 controls	–	45/61	43 (18–72)	I: 32; II: 27; III: 19; IV: 23; V: 5	Eroded incus (91); eroded stapes (39); epidermisation of the facial nerve (4); labyrinthine fistula (5); bony defect of middle cranial fossa (4)	12.63 (12–15)								
Yilmaz *et al.*, 2006[13]	Retrospective case-control study (III)	24	–	–	23.3 (8–66)	–	–	6.8 (3–12)	No	Yes	Yes	Yes	No	No	Yes	Yes
Vincenti *et al.*, 2014[16]	Retrospective case-control study (III)	55 cases	–	23/32	44 (18–67)	–	–	–	No	Yes	Yes	Yes	No	No	Yes	Yes
		51 controls	–	21/30	43 (18–72)	–	–	–								

EAC = external auditory canal

Table 2. Summary of studies specifically involving the use of Mesna in the surgical management of cholesteatoma and their findings

Authors & year	Type of management	Ears (*n*)	Complications	Outcome	Method of diagnosis of recurrence	Residual cholesteatoma (*n* (%))	Recurrent cholesteatoma (*n* (%))
de la Torre and Villamor, 2019[12]	Study group: mastoidectomy with Mesna (10% for 10 minutes). Canal wall up in 19 patients & canal wall down in 35 patients)	54	Facial palsy (1); meatoplasty stenosis (11)	Variation of average of bone conduction thresholds: 2.6 ± 4.4	Diffusion-weighted magnetic resonance (23); revision surgery (24); otomicroscopy (7)	4 (7.4%). All patients had canal wall up procedure	1 (1.9%). Patient had canal wall down procedure
	Control group: only mastoidectomy (canal wall up in 67 patients & canal wall down in 25 patients)	92	Meatoplasty stenosis (5); Surgical wound infection (1)	Variation of average of bone conduction thresholds: 3.4 ± 3.3	Diffusion-weighted magnetic resonance (27); revision surgery (53); otomicroscopy (12)	63 (68.5%). Forty-six patients with canal wall up; 17 with canal wall down	12 (13%). Eleven patients with canal wall up & 1 with canal wall down
Kalcioglu *et al.*, 2014[15]	Study group: mastoidectomy with Mesna (10% for 5 minutes). Canal wall up in 22 patients & canal wall down in 24 patients	46	–	–	Diffusion-weighted magnetic resonance; revision surgery; otomicroscopy	3 (6.5%). One patient with canal wall up & 2 with canal wall down	–
	Control group: only mastoidectomy (canal wall up in 39 patients & canal wall down in 56 patients)	95	–	–		17 (17.9%). Eight with canal wall up & 9 with canal wall down	–
Vincenti *et al.*, 2014[14]	Study group: mastoidectomy with Mesna (10% for 3 minutes)	108	–	–	Revision surgery	12 (11.1%)	–
	Control group: only mastoidectomy	106	–	–		26 (24.5%)	–
Yilmaz *et al.*, 2006[13]	Mesna (20% for 5 minutes) with surgical intervention (ventilation tube (10), reinforcement (4), reinforcement + antrotomy (2), modified radical mastoidectomy (1)). Mesna alone (7)	24	Blue eardrum (1)	Bone conduction: mean pure-tone, 13.5 dB (pre-operative) & 12.1 dB (post-operative). Air conduction: mean pure-tone, 43.6 dB (pre-operative) & 16.3 (post-operative)	Otomicroscopy	5 (20.8%). All treated with only Mesna	–
Vincenti *et al.*, 2014[16]	Study group: mastoidectomy with Mesna (10% for 3 minutes)	55	No post-operative sensorineural hearing loss	Mean bone conduction threshold: 17.2 dB (pre-operative) & 17.4 dB (post-operative)	–	–	–
	Control group: only mastoidectomy	51		Mean bone conduction threshold: 16 dB (pre-operative) & 16.3 dB (post-operative)	–	–	–

Quality assessment of case series studies checklist from the National Institute for Health and Clinical Excellence: (1) was the case series collected in more than one centre (i.e., multicentre study?). (2) Is the hypothesis, aim or objective of the study clearly described? (3) Are the inclusion and exclusion criteria (case definition) clearly reported? (4) Is there a clear definition of the outcomes reported? (5) Were data collected prospectively? (6) Is there an explicit statement that patients were recruited consecutively? (7) Are the main findings of the study clearly described? (8) Are outcomes stratified (e.g., by abnormal results, disease stage, patient characteristics)?

Mesna using pure-tone audiometry results. In particular, Yilmaz *et al.*[13] did not record any statistically significant differences in pure-tone averages for bone and air conductions after Mesna topical application in patients with atelectatic ears and adhesive otitis media. Vincenti *et al.*[16] compared pre-operative and post-operative mean bone conduction threshold after Mesna application during canal wall up tympanomastoidectomy compared to those treated without Mesna. Any significant differences were analysed for any of the frequencies tested in both groups, and only a slight worsening in bone conduction at 4000 and 8000 Hz was observed. de la Torre and Villamor[12] did not register any differences in the mean variation of the average bone conduction thresholds between the Mesna and control groups.

Discussion

Mesna was introduced several years ago and marketed in several formulations as a mucolytic agent in the respiratory field because it breaks disulfide bonds between polypeptide chains of mucus. Today, it is widely used in the prophylaxis of haemorrhagic cystitis during chemotherapy with alkylating agents owing to its action as a radical scavenger.[17] In recent years, there has been an increase in indications for Mesna as a support tool for surgical dissection especially in the ENT field.[14] With the hypothesis that the physiological and pathological adhesions between different layers are rich in disulphide bonds, and bearing in mind that some drugs already in use have the ability to break these bonds, Zini *et al.*[8] developed a research project entitled 'chemically assisted dissection' and, among various substances, chose Mesna for this purpose.

Literature data that emerged from our analysis allowed us to affirm that topical Mesna can be useful as coadjutant treatment in middle-ear surgery in order to facilitate cholesteatoma removal. Additionally, it significantly reduces the incidence of residual disease without any significant side effects. Although the goal of surgery for cholesteatoma is the elimination of disease, the residual cholesteatoma rate is reported to vary from 5 to 50 per cent and develops from a remnant of keratinised epithelium that is left behind in a previous surgical procedure.[18] Cholesteatomatous matrix is largely made of keratin, a protein rich in disulfide bonds; therefore, the intra-operative use of Mesna is capable of breaking these bonds.[12] In cholesteatoma surgery, complete and accurate removal of the matrix plays a key role in minimising the likelihood of leaving in place epidermal debris that might grow to be a residual cholesteatoma.

There are several factors that promote residual disease. First of all, a defective surgical view represents a crucial problem. The middle ear has anatomical areas, such as retrotympanum and anterior epitympanum, that are difficult to reach using a microscope.[19] Recently, the use of endoscopes during middle-ear surgery has favoured the visualisation and complete resection of the lesion, supporting the role of endoscopy in reducing the incidence of residual disease.[20,21] However, although the recidivism rate in endoscopy surgery has been shown to be lower, the global rate of residual and recurrent cholesteatoma has not reached 0 per cent.[22–24] Another major cause of residual disease is incomplete cleaning of the matrix. Typical examples are cholesteatomas remaining around the ossicles or on bony defects of the middle cranial fossa, labyrinth and fallopian canal. Under these circumstances, surgical dissection has to be gentle enough to avoid iatrogenic injury, and consequently, the risk of incomplete removal of disease is heightened. Residual disease is even more frequent and difficult to prevent in the paediatric population. In particular, paediatric cholesteatoma is more aggressive and invasive with a higher recidivism rate than in adults because of its histopathological composition. Moreover, bacterial biofilms play a crucial role in antimicrobial resistance chronicity, recidivism and aggressiveness.[25]

Among the studies included in this review, the recurrent disease rate was specifically evaluated in only one study.[12] Recurrent disease differs from residual disease with regard to the presence of clinical findings. Recurrent disease presents with poorly visualised retraction pockets, perforation of the tympanic membrane and destruction of the lateral attic or posterior canal upon pre-operative microscopic examination. On the other hand, residual cholesteatoma was defined as a post-operative matrix remaining in the middle ear or mastoid cavities with simultaneous non-pathological otoscopic findings.[26]

There is a wide heterogeneity on how residual and recurrent disease were assessed. de la Torre and Villamor[12] and Kalciouglu *et al.*[15] used magnetic resonance imaging (MRI), revision surgery and otomicroscopy, Vincenti *et al.*[14] used only revision surgery, Yilmaz *et al.*[13] used only otomicroscopy, and Vincenti *et al.*[16] did not use any technique because this study analysed cochlear effects. There is a large heterogeneity among the studies included in this review regarding the treatment schedule and delivery method. Regarding Mesna dilution with saline solution, de la Torre and Villamor[12] used a solution with 10 per cent Mesna for 10 minutes, Kalcioglu *et al.*[15] used 10 per cent Mesna for 5 minutes, Vincenti *et al.*[14] and Vincenti *et al.*[16] used 10 per cent Mesna for 3 minutes and Yilmaz *et al.*[13] used 20 per cent Mesna for 5 minutes. The precise concentration of Mesna needed and how long the drug should remain in contact with the cholesteatoma matrix in order to release its action should be clarified.

Many authors used Mesna only at the beginning of surgery whereas others applied Mesna during surgical dissection as well. Moreover, many studies did not specify the Mesna delivery method. In particular Kalcioglu *et al.*[15] used Mesna at the beginning of the surgery, but they did not specify the delivery methods. de la Torre and Villamor[12] used Mesna during the surgical dissection as well by topically instilling the drug in areas where adhesions were evident. They applied a maximum dose of 400 mg of Mesna per surgery with no details concerning the device used. Vincenti *et al.*[14] used Mesna at the beginning of surgery and during mastoidectomy, but these authors used specific microdissectors to deliver the substance. Finally, Yilmaz *et al.*[13] and Vincenti *et al.*[16] injected Mesna through the tympanic membrane or atticoantral region with a syringe at the beginning of surgery if mastoidectomy was required.

Tailored application of Mesna in cholesteatoma patients should not only consider the exact dilution ratios of the Mesna solution but also the most suitable device to deliver the drug and the most appropriate treatment schedule. Lastly, it is necessary to evaluate the surgeon's degree of satisfaction during the surgery.

Considering several toxicological, experimental and clinical studies and the large clinical use of this compound, ototoxicity was not expected from Mesna application in the middle ear.[27] In this review, three studies[12–14] evaluated bone conduction thresholds with regard to the safety of the topical administration of Mesna and auditory function. The topical administration of Mesna showed no difference in the mean variation of the average bone conduction thresholds with and without Mesna.

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Vincenti *et al.*,[16] in an experimental model of guinea pigs, evaluated the toxicity of Mesna application in middle ear on cochlear anatomy and physiology. Toxicity of Mesna was assessed by transmission electron microscopy, scanning electron microscopy, histological samples and auditory brainstem response of the cochlea, which showed no effect of this drug in inner physiology.

Mesna is a non-essential tool. However, it can be a valid aid in middle-ear surgery, supporting the use of the microscope and otoendoscope. It is necessary to understand the costs of currently available formulations on the market as well as understand which cases will benefit from Mesna. Most of the studies included in this review are retrospective; therefore, multicentre and prospective studies with a larger number of patients are needed to validate these findings. Although other substances have been used to facilitate dissection in ear surgery, such as N-acetyl cysteine, Mesna remains the most widely used.[7,28]

Currently, the only system on the market used to deliver Mesna is the Cadiss® system. This system enables a selective dissection without cutting by means of Mesna dispensed through its surgical instruments. The Cadiss system is based on the combination of mechanical dissectors and the topical application of the drug Mesna on the tissues to be separated. The combination between the mechanical dissection force and the delivery of the drug is achieved by the same instrument. The instrument differs according to the type of surgery, the configuration and the accessibility of the tissue to be dissected. Most instruments are reusable after cleaning and following recommended sterilisation procedures. The kits containing the cartridge and the tubing are delivered sterile for single use.

With Mesna topical application, surrounding organs, such as nerves and veins, are well preserved. Mesna offers many advantages to the surgeon and the patient, especially with regard to risks, organ damage or relapses. The surgeon benefits from an easier and safe surgical procedure. Moreover, by avoiding damage to healthy tissues, the patients have the advantage of a faster recovery and fewer side effects (bleeding and damage to nerves or surrounding organs).

Limitations

The analysis of five published studies on topical application of Mesna is limited by the heterogeneous and uncontrolled nature of the available studies. None of the studies were randomised, and each contained variables that confounded the outcome (various surgeons, disease variability and disease stage). The relatively short follow up probably underestimated the real incidence of residual and recurrent disease.

Conclusion

Today, Mesna is widely used in many branches of medicine, and the potential applications of Mesna in the ENT field are varied. Data deriving from the present review of five clinical studies showed that, thanks to the destruction of the disulfide bonds, topical administration of Mesna could represent a valid and safe support tool during surgical dissection performed both through the microscope and otoendoscope. More studies are required to confirm these promising results and to identify the best means of administration as well as the best treatment schedule.

Competing interests. None declared

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