# **Original Research Article**

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# Effect of local vitamin E versus local dexamethasone on prevention of myringosclerosis

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#### **ABSTRACT**

**Background:** The objective of the study was to compare between effect of local vitamin E and local dexamethasone on prevention of myringosclerosis induced by ventilation tube in human tympanic membranes.

**Methods:** 90 children undergoing myringotomy with ventilation tube insertion were divided into 3 groups: group-I: 30 children undergoing myringotomy with ventilation tube insertion only, group-II: 30 children undergoing myringotomy with ventilation tube insertion with use of local vit E, group-III: 30 children under going myringotomy with ventilation tube insertion with use of local dexamethasone.

**Results:** The incidence of myringosclerosis occurance with otoscopic and microscopic examination was lesser in group 2 (6 ears) in which local vit E was applied than group 3 (11 ears) in which local dexamethasone was applied and also than group 1 in which no local medication was applied (21 ears).

**Conclusions:** In this study results suggest that applying local vit E in children under going myringotomy with ventilation tube insertion more effective than use of local dexamethasone in children undergoing myringotomy with ventilation tube insertion on limiting the intensity and prevalence of myringosclerosis.

**Keywords:** Ventilation tube, Vitamin E, Dexamethasone, Myringosclerosis

#### INTRODUCTION

Myringotomy associated with insertion of a ventilation tube is the most accepted treatment for otitis media with effusion and is also used as prophylactic treatment for recurrent otitis media. Tympanosclerosis is the most common sequela of myringotomy with ventilation tube treatment. 2

Tympanosclerosis occurs when high quantities of collagenic fibrosis tissue are deposited in the lamina propria which covers the ossicles, the tympanic cavity walls and the medial layer of the tympanic membrane.<sup>3</sup> The thickness because of collagen deposition makes chance for the formation of a homogenous and hyaline substance, that then lead to the deposition of crystals of calcium and phosphate.<sup>4</sup> Myringosclerosis occurs when

the deposition of crystals occurs only on the tympanic membrane, which is the most common site. This pathology has a clinical importance if it can interfere with the sound vibrations transmission through the middle ear structures.

Tympanosclerosis is the devolpment of ossification in the tympanic membrane, middle ear cavity, ossicles, and rarely in the mastoid bone, because of hyaline changes at submucosal level, when tympanosclerosis affects tympanic membrane only that is called myringosclerosis. The incidence of myringosclerosis in patients who had VT insertion is 28%-61%. The true cause of tympanosclerosis pathogenesis is unknown up till now. It is may be a special scar tissue or healed inflammation after frequent attacks of otitis media, it also may be due to the direct effect of hydrolytic enzymes in

serous fluid due to lamina propria. 9,11 Another reason is trauma. Any trauma, ranging from severe tension to the fibers in the eardrum as the simplest form to tympanic membrane perforation as the heaviest form, can lead to myringosclerosis development.<sup>12</sup> In myringotomy with VT insertions, there intraepithelial bleeding may occur and healing with fibrosis will be happened. 13 Studies suggested that the ear canal bleeding may lead to myringosclerosis development in the long term, so reducing the hemorrhage during myringotomy can minimize the myringosclerosis development in the long term. 14 The incidence of tympanosclerosis after VT insertion ranged from 25 to 35% in the literature. 15 There are recent studies that find some sort of a relationship between the reactive oxygen species and the development of myringosclerosis after tympanic membrane trauma and/or VT insertion. 16 In this study, the aim was to compare between effects of local vitamin E, as a potent chain-breaking antioxidant and local dexamethasone as steroid on the development of tympanosclerosis after VT insertion.

#### **METHODS**

A 90 children aged from 3 years to and 11 years undergoing myringotomy and VT insertion at benha University hospital, Faculty of Medicine, ENT department from September 2015 to September 2016 were included in this study. Local ethical committee approval and parental consent were taken before the onset of the study. The mean age was (Group I: 7.27 years, Group II 7.73 years, Group III: 7.93 years). 42 of the children were boys and 48 were girls. Those children complaining of hearing loss due to chronic otitis media with effusion refractory to medical treatment about three months, so these patients undergoing myringotomy and VT insertion.

Patients who underwent previous ventilation tube insertion and also patients who had previous myringosclerosis and patients who had excessive bleeding during operation were excluded.

Ethical committee approval from Benha university hospitals committee was taken and all patients underwent written consent. All children were operated under general anesthesia. 90 patients were divided into 3 groups, each group consisted of 30 patients:

*Group 1:* 30 children undergoing myringotomy with ventilation tube insertion only,

*Group II:* 30 children under going myringotomy with ventilation tube insertion with use of local vitamin E.

**Group III:** 30 children under going myringotomy with ventilation tube insertion with use of local dexamethasone.

The myringotomy insicion was done in the anteroinferior quadrant. Middle ear fluid was aspirated. Grommet tubes were used bilaterally in all cases. In group I no medical treatment was applied during or after ventilation tube insertion in both ears, in group II after we made the myringotomy insicion, vitamin E drops (alpha tocopheryl acetate capsules) were used in both ears, Vitamin E was used after myringotomy incision as in Figure 1, the middle ear cavity was filled and made sure that vitamin E drops would contact all the surfaces. After 5 minutes suction of vitamin E drops was done, then grommet tube was inserted and another course of Vitamin E drops was applied as in Figure 2.

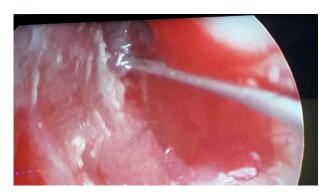


Figure 1: Local application of vit E after myringotomy incision.



Figure 2: Local application of vit E after grommet tube insertion.



Figure 3: Local application of dexamethasone after myringotomy incision.

In group III after the myringotomy insicion was done and dexamethasone drops (dexamethasone sodium-phosphate injection) 0.3 ml of 8 mg/2 ml dexamethasone instilled as in Figure 3, the middle ear cavity was filled and made sure that topical dexamethasone would contact all the surfaces. After 5 minutes suction of topical dexamethasone was done, then grommet tube was inserted and another course of local dexamethasone was applied as in Figure 4. Postoperative prophylactic ampicillin – clavulinic acid was used for 1 week.



Figure 4: Local application of dexamethasone after grommet tube insertion.

Routine follow up was scheduled by otoscopic and microscopic examination 2, 4 and 6 months after the operation as part follow up, and no other complications were encountered, The observer who performed the postoperative examinations (otoscopic and microscopic) was blind about the case examined belonged to which group in this study. Myringosclerosis formation, defined as presence of any visible white plaque by otomicroscopy in the tympanic membrane, was noted. The results were expressed as presence or absence of myringosclerosis.

10 children were excluded in this study as these children were lost during follow up (3 children in group I, 4 in group II, 3 in group III) from the study. A total 90 of children were finally evaluated. The appearance of tympanic membranes and development of myringosclerosis were evaluated according to the distribution on four quadrants.

#### **RESULTS**

A total of 180 ears were examined during the study period. Myringosclerosis was established in 38 ears, as shown in Table 1 in group I there were 21 ears with myringoscerosis, 5 patients were bilateral (10 ears), 10 myringosclerotic patches were found (16.7%), 6 myringosclerotic patches were found in right ear (10%) with no myringosclerotic patches were found in left ear in the same patients.

Table 1: Distribution of study groups according to the age, sex and site of myringosclerosis.

	Group I (30 pt) (60 ears)	Group II (30 pt) (60 ears)	Group III (30 pt) (60 ears)	Statistical test	P value
Age mean ±SD (range)	7.27 ±1.39 (5-10)	7.73±1.08 (5-9)	7.93±1.41 (6-10)	F= 2.07	0.13
Sex n (%)	(5 10)	(3 ))	(0 10)		
Male	14 (46.7)	15 (50.0)	13 (43.3)	$X^2 = 0.27$	0.88
Female	16 (53.3)	15 (50.0)	17 (56.7)	$\Lambda = 0.27$	
Myringosclerosis					
Rt	6 (10.0)	4 (6.7)	3 (5.0)	FET=24.06	<0.001**
Lt	5 (8.3)	2 (3.3)	8 (13.3)		
Bilat	10 (16.7)	0 (0.0)	0 (0.0)		
None	39 (65.0)	54 (90.0)	49 (81.7)		

Table 2: Distribution of myringosclerosis findings according to the quadrants under otomicroscopic assessment.

Myringosclerosis	Group I (60 ears)	Group II (60 ears)	Group III (60 ears)	Statistical test	P value
Antro-inferior Q	8 (13.3)	4 (6.7)	6 (10.0)	FET= 16.91	0.024*
Post-inf Q	6 (10.0)	2 (3.3)	5 (8.3)		
Both	5 (8.3)	0 (0.0)	0 (0.0)		
Antro-superior Q	1 (1.7)	0 (0.0)	0 (0.0)		
Postro-superior Q	1 (1.7)	0 (0.0)	0 (0.0)		
NO	39 (65.0)	54 (90.0)	49 (81.7)		

Also in group I; 5 myringosclerotic patches were found in left ear (8.3%) with no myringosclerotic patches were found in right ear in the same patients. group II, there

were 6 myringosclerotic patches founded in 6 patients,4 in right side (6.7%) and 2 in left ear (3.3%). In group III,

there were 11 myringosclerotic patches founded in 11 patients, 3 in right side (5%) and 8 in left ear (13.3%).

When the distribution of myringosclerosis was examined under otomicroscopy, myringosclerosis was found to be less developed in the tympanic membranes in group 2 than in group3 and group 1.

As showen in Table 2, in group I there were 8 myringosclerotic patches affect anterior inferior quadrant only (13.3%), there were 6 myringosclerotic patches affect posterior inferior quadrant only (10%), there were 5 myringosclerotic patches affect both anterior and posterior inferior quadrants (8.3%), one myringosclerotic patch affect anterior superior quadrants only (1.7%) and one myringosclerotic patch affect posterior superior quadrants only (1.7%). In group II: there were 4 myringosclerotic patches affect anterior inferior quadrant only (6.7%), there were 2 myringosclerotic patches affect posterior inferior quadrant only (3.3%), there were no myringosclerotic patches affect both anterior and posterior inferior quadrants, there were no myringosclerotic patches affect both anterior and posterior superior quadrants. in group III: there were 6 myringosclerotic patches affect anterior inferior quadrant only (10%), there were 5 myringosclerotic patches affect posterior inferior quadrant only (8.3%), there were no myringosclerotic patches affect both anterior and posterior inferior quadrants, there were myringosclerotic patches affect both anterior and posterior superior quadrants.





Figure 5 (A and B): Myringosclerotic ear.

#### DISCUSSION

This study showed that local vitamin E and local dexamethasone application in myringotomy with tube

insertion decreased the development of myringosclerosis but local vitamin E more potant than *local* dexamethasone.

When the tympanosclerosis affects only the ear drum that is will be called myringosclerosis. Myringosclerosis is a common sequela of OME, ROM, chronic otitis media, and VT insertion.<sup>17</sup> In spite of several hypotheses on its origin were suggested, there is no accurate information on its cause and pathogenesis, studies find differant factors that may be blamed for tissue trauma, such as intratympanic hemorrhage, hyperoxygenation foreign body reaction to VT, and autoimmune etiology.<sup>17</sup>

Mattsson et al, reported that the tympanic membrane sclerotic changes will be developed within 9 hours of myringotomy and showed that a severe histological inflammatory response will be occurred in a duration about 12-24 hours after myringotomy in pars flaccida, histological tympanosclerosis, that may be seen in 80% of cases with myringotomy, can be appear in 40% of cases only with otomicroscopy. This shows that, in fact, there is twice as much tympanosclerosis (at tissue level) in cases in which tympanosclerosis is detected by otomicroscopy.

In this study, 90 children under going myringotomy with ventilation tube insertion were divided into 3 groups: group I: 30 children undergoing myringotomy with ventilation tube insertion only, group II, 30 children under going myringotomy with ventilation tube insertion with use of local vit E group III: 30 children under going myringotomy with ventilation tube insertion with use of local dexamethasone. Although the etiology and pathogenesis of myringosclerosis are still unknown, studies show that this disease develops in three stages: the first phase, that is may be reversible and in which collagen fiber damage caused by inflammatory processes; the repair phase, which is characterized by fibroblastic invasion, and the last and final phase which is the irreversible phase and in which calcifications occur.<sup>17</sup>

In general, myringosclerosis/tympanosclerosis studies were conducted to investigate the causes of this disease to assess myringosclerosis of the tympanic membrane based on histological and otomicroscopic findings, and investigate the protectiveness of therapeutic agents. In this study, the plan was to study otomicroscopic preventive effect of topical vitamin E and topical dexamethasone on the development of myringosclerosis as myringosclerotic patch appears in 21 ears in group II but affect only 6 ears in group II and 11ears in group III.

In the literature, preventive treatments, especially with antioxidants, are commonly found in experimental myringosclerosis model studies. In the studies on myringotomized rats with different oxygen concentrations, fewer sclerotic lesions developed. In animals living in a room environment than in rats subjected to myringotomy in a hyperoxic environment.

Mattsson et al reported that local applied antioxidants such as copper, zinc, superoxide dismutase, catalase, and desferoxamine prevent or reduce the development of sclerotic lesions development.<sup>18</sup> In an experimental study, Spratley et al showed, under otomicroscopy, that the topical use of ascorbic acid, which is used as an antioxidant agent, prevents myringosclerosis in the rats perforated tympanic membranes.<sup>19</sup>

Özcan et al made studies on N-acetyl cysteine use in investigating antioxidant effects in tympanosclerosis and decided that the extra use of local N-acetyl cysteine on the ear had VT insertion can be helpful in myringosclerosis development prevention.<sup>17</sup> Ovesen et al suggested that N-acetyl cystein decrease the proliferation of fibroblast and collagen release in fibroblast cultures.<sup>20</sup> So, they recommended that use of local N-acetyl cysteine in reduction of the connective tissue layer thickness in the middle ear. Kazıkdaş et al found in their study that incidence of myringosclerotic plaques were less common in animals that received alpha-tocopherol to prevent of experimentally induced myringosclerosis.<sup>21</sup> When the otomicroscopic findings of our study were examined the development of myringosclerosis was significantly higher in group1 than in group III then in group II. In addition, in group I, there were 8 myringosclerotic patches affect anterior inferior quadrant only, there were 6 myringosclerotic patches affect posterior inferior quadrant only, there were 5 myringosclerotic patches affect both anterior and posterior inferior quadrants, one myringosclerotic patch affect anterior superior quadrants only and one myringosclerotic patch affect posterior superior quadrants only.

In group II; there were 4 myringosclerotic patches affect anterior inferior quadrant only, there were 2 myringosclerotic patches affect posterior inferior quadrant only, there were no myringosclerotic patches affect both anterior and posterior inferior quadrants, there were no myringosclerotic patches affect both anterior and posterior superior quadrants, in group III; there were 6 myringosclerotic patches affect anterior inferior quadrant only, there were 5 myringosclerotic patches affect posterior inferior quadrant only, there were no myringosclerotic patches affect both anterior and posterior inferior quadrants, there were no myringosclerotic patches affect both anterior and posterior patches affect both anterior and posterior superior quadrants.

Polat et al decided that there were increase in inflammatory reactive oxygen species because of the immunological stimulation due to the tympanosclerosis formation after myringotomy and vitamin E used in reduction of this effect. Selçuk et al suggested that the local application of calcium channel blocker in guinea pigs on experimental myringosclerosis, which they had myringotomy and *Streptococcus pneumoniae* type 3 inoculation, was useful in tympanosclerosis prevention. In an animal study, Mattsson et al, determined that an increase of oxygen concentration in the atmosphere of the

ear may lead to increase in the development of myringosclerosis in ears with traumatized tympanic membranes.<sup>24</sup> Similarly, Dawes et al hypothesized that the risk of the myringosclerosis development is increased where there is traumatic ventilation tube insertion, hemorrhage, or excessive middle ear fluid aspiration.<sup>25</sup> In recent studies, some antioxidant enzymes and elements were used to decrease oxidative damage in myringotomized tympanic membranes. Polat et al, measured the levels of ROS levels in the tympanic membrane and middle ear mucosa in rats that had myringotomy and also showed that vitamin E is having a potent effect in reduction of the ROS levels.<sup>22</sup> Üneri et al reported that vitamin E-coated tube insertion both experimentally and clinically reduces the quantity of reactive oxygen species in tympanic membrane after myringotomy with ventilation tube insertion.<sup>26</sup> All these studies were suggested that myringotomy and ventilation insertion provoked development myringosclerosis.<sup>27</sup>

Topical use of oxygen free radical or topical steroid decreased the risk of the myringosclerosis development when compared to ears of control groups in rats. However, this study is unique to compare between effect of local vitamin E and local dexamethasone on prevention of myringosclerosis induced by ventilation tube in human tympanic membranes, this study revealed significant otomicroscopical differences between Vitamin E treated myringotomized ears and local dexamethasone treated myringotomized ears and non-local treated myringotomized ears.

#### **CONCLUSION**

The benefit of vitamin E treatment on myringotomized human tympanic membranes more effective than local dexamethasone treated myringotomized ears. Clinical studies employing vitamin E and other antioxidants with larger patient popullation may bring antioxidant therapy in myringotomy and tube insertion into routine clinical use.

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Institutional Ethics Committee

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