

## ORIGINAL ARTICLE

# Meta-Analysis of the Role of Corticosteroids in the Management of Otitis Media with Effusion

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**Background:** Otitis media with effusion is the most common reason for the child visits to the primary care physician and affects more than 80% of children under the age of 3 years. Annually, more than \$5 billion is spent in the United States on otitis media. This makes OME an important condition for the use of up-to-date evidence-based practice guidelines.

**Objective:** To determine the efficacy of corticosteroids (systemic or local) in the treatment of OME.

**Materials and Methods:** Meta-analysis of randomized control trial studies (RCT) concerned with efficacy of corticosteroids in OME treatment.

**Results:** Oral corticosteroids give better functional outcome in OME in short-term therapy.

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Annually, more than \$5 billion is spent in the United States on otitis media<sup>[1]</sup>. This makes OME an important condition for the use of up-to-date evidence-based practice guidelines<sup>[2]</sup>

The first modern era researcher of the Eustachian tube (ET) was Bartolomeus Eustachius who was a 16th century anatomist. Eustachius, for whom the ET is named, studied several areas in the human body including the ET<sup>[3]</sup>

Antonio Valsalva had done further work, a professor of anatomy at Bologna and is most recognized by his middle ear insufflating maneuver that bears his name. Valsalva was credited for naming the auditory tube, the Eustachian tube and describing its function<sup>[4]</sup>.

Adam Politzer is probably best known for his contribution to otology and probably considered as the greatest otologist of the 19th century. One of his legacies was a hand-held air bag that allowed insufflations of the middle ear space or politzerization. Further therapies developed by Politzer included a primitive middle ear ventilation tube<sup>[5]</sup>

Otitis media with effusion is the most common reason for the child visits to the primary care physician and affects more than 80% of children under the age of 3 years. Annually, more than \$5 billion is spent in the United States on otitis media<sup>[1]</sup> It remains one of the important clinical problems in otolaryngology. Conventional medical therapies for acute otitis media and otitis media with effusion (OME) include antibiotics, decongestants, auto inflations and intra nasal steroids.

As a result of failed medical intervention, 1 million children annually in the United States undergo myringotomy with insertion of a tympanostomy tube. It is the most common surgical procedure requiring general anesthesia performed to children<sup>[6]</sup>

Reflections of this entity to the society include hearing loss, learning delay and absence from school and work. As well, excessive prescription of anti microbial agents raises the spectrum of antibiotic-resistant organisms<sup>[7]</sup> This study is made to determine the efficacy of corticosteroids (systemic or local) in the treatment of OME.

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## Materials and Methods

### 1. Target disease

Is corticosteroid effective in the treatment of OME or not?

### 2. Identification and location of articles

Studies include published medical articles concerning the role of corticosteroids in the treatment of OME through searching of the Medline database using the following keywords: otitis media with effusion, steroids, OME, Middle ear effusion and secretory otitis media. Limits of the search: human, randomized controlled trials with no publication date limitation. The search was done on 31/3/2008 and yielded a total number of 171 articles and abstracts.

### 3. Screening and evaluation of articles

The following screen form of the articles was made to screen the articles that were yielded by the Medline search after blinding the article author and the journal name.

#### Inclusion criteria:

- A. Randomized control trial studies.
- B. Sample size was mentioned.
- C. The duration of treatment was reported.
- D. Study group and control group number were mentioned.
- E. Diagnostic method was present.
- F. Functional outcome was present.

#### Excluded articles:

**Table 1.** Summary of articles' results in group A1 (S= study group. C= control group)

Study	Method	Sample size	Study group No.	Age group	Results
Daly, 1991	RCT	42	S=21 C=21	2-12 years	Study group: 10 showed resolution. Control group: 3 showed resolution.
Berman, 1987	RCT	28	S=14 C=14	2-12 years	Study group: 10 showed resolution. Control group: 3 showed resolution.
Thomas, 2006	Meta-analysis	418	S=214 C=204	3-13 years	Study group: 102 showed resolution. Control group: 51 showed resolution.

**Table 2.** Summary of articles' results in group A2 ( S= study group. C= control group)

Study Results	Method	Sample size	Study group No.	Age group
Cengel, 2005	RCT	63 C=29	S=34 3-15 years	Study group: 15 showed resolution Control group: 4 showed resolution
Karlıdag, 2002	RCT	40 C=20	S=20 2-12 years	Study group: 8 showed resolution Control group: 5 showed resolution
Thomas, 2006	Meta-analysis	103 C=63	S=40 2-12 years	Study group: 11 showed resolution Control group: 19 show resolution

(B): Intermediate term therapy studies (8 weeks):

**Table 3.** Summary of articles' results in group B (S= study group. C= control group)

Study	Method	Sample size	Study group No.	Age group	Results
Karlidag, 2002	RCT	40	S=20 C=20	2-12 years	Study group:8 show resolution. Control group: 5 show resolution.
Thomas, 2006	RCT	59	S=19 C=40	3-13 years	Study group: 6 show resolution. Control group: 10 show resolution.

Any article missing one or more of the inclusion criteria. Eighteen articles were found relevant to the keyword search<sup>[8-25]</sup> These articles were then subjected to inclusion and exclusion criteria<sup>[8, 10, 15, 19, 22]</sup>. Articles<sup>[2, 4, 5, 9, 10, 11, 13, 16]</sup> were excluded because of being duplicated with in study made by Daly et al<sup>[15]</sup>. The study made by Giebink et al<sup>[18]</sup> was also excluded because of not fulfilling inclusion criteria, as regard determination of sample size, study group number or treated group number.

#### 4. Data collection

The data were collected from the chosen 5 articles fulfilling the previously mentioned criteria. They were classified into 2 main groups:

(A): Short-term therapy studies (<4 weeks):

A1- Oral steroids

A2- Topical intra-nasal steroids

The following tables summarize the results of the previous articles. (Tables 1-3)

The summary of articles' results in this group focused on the use of topical intranasal steroids is demonstrated in Table 3.

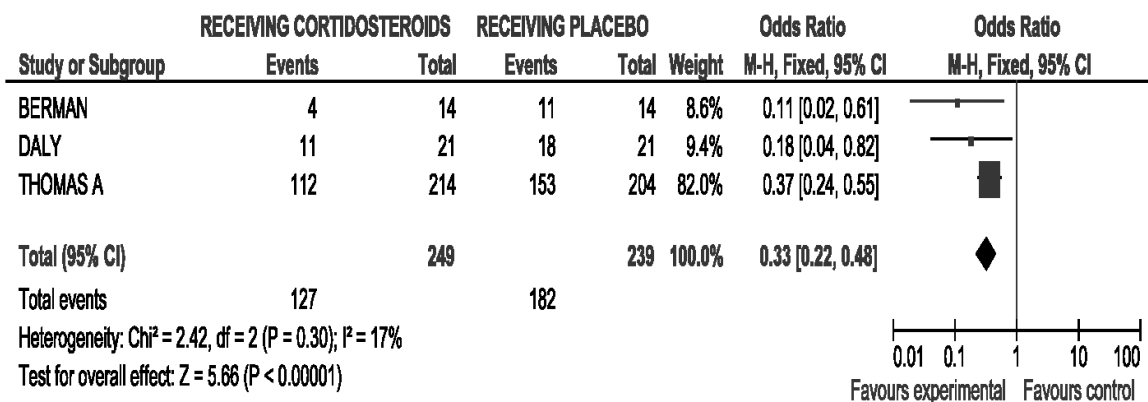
#### 5. Data analysis

Data analysis was performed using Meta-analytic Review Manager (RevMan 5) software.

The results of the data collected from the chosen articles were fed into the above-mentioned (RevMan 5) soft ware.

*a. Oral steroids use for short-term therapy (<4 weeks):*

There is highly significant difference ( $p < 0.0001$ ,  $Z = 5.66$ ) between the treatment group and control group (Figure 1). There is heterogeneity between studies involving oral steroids plus antibiotics. This could be explained by differences between studies in pharmacological interventions including steroid formulation, duration of steroid treatment, and concomitant antibiotic.



**Figure 1.** Results of meta-analysis of oral steroids use.

*b. Topical steroids with or without antibiotic versus placebo with or without antibiotic (short term resolution = up to 4 weeks):* There is insignificant difference between the treatment group and the control group ( $p > 0.05$ ,  $Z < 2$ ) in regards topical corticosteroids with or without antibiotic in the short term (up to 4 weeks) (Figure 2). There is significant heterogeneity between studies involving topical steroids plus antibiotics. This could be explained by differences between studies in pharmacological interventions including steroid formulation, duration of steroid treatment and concomitant antibiotic.

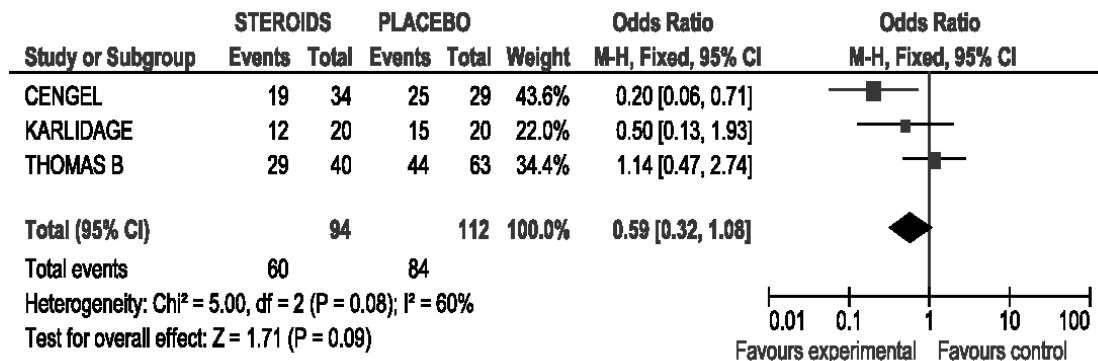
*c. Topical steroids with or without antibiotic versus placebo with or without antibiotic (intermediate term resolution = 8 weeks)* There is insignificant difference between the treatment group and the control group ( $p > 0.05$ ,  $Z < 2$ ) as regard topical steroids with OME in the intermediate term resolution (8 weeks) (Figure 3).

## 6. Reporting and interpretation of results

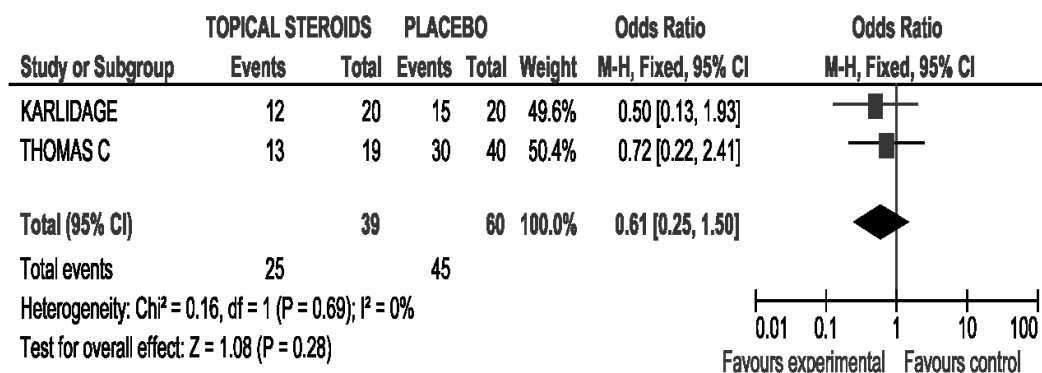
This was performed by the above-mentioned Meta-analytical soft ware, Review Manager (RevMan 5).

Our study analyzed the included three studies that compared the use of oral steroids plus antibiotic versus antibiotic only in short term therapy (4 weeks) for OME. The analysis had shown significant improvement ( $Z = 5.66$  &  $p < 0.0001$ ) in the group that received steroids [resolution occurred in 122 (49%) patients from a total number of 249 patients], in contrast to control group [57 (24%) of patients (57/239) showed resolution.

The other three studies, that compared topical steroids versus placebo of in short term therapy of OME (4 weeks), were analyzed and we found that resolution occurred in 36% (34/94) of patients in contrast to 25% (28/112) of patients in control group with insignificant



**Figure 2.** Results of meta-analysis of short term use of topical steroids.



**Figure 3.** Results of meta-analysis of intermediate term use of topical steroids use.

difference ( $Z=1.71$  &  $p=0.09$ ) between the two groups. Lastly we analyzed two studies that compared topical steroids versus placebo for intermediate term (8 weeks) treatment of OME. Fourteen (36%) of patients had resolution (14/39) in contrast to 25% (15/60) of patients in control group with insignificant difference ( $Z=1.08$  &  $p=0.28$ ) between the two groups.

## **Discussion**

Otitis media with effusion (OME) is one of the most common problems to be solved in otorhinolaryngology. There is great controversy regarding treatment of OME, whether surgical or medical.

In this study, we aimed to compare the results of corticosteroids (oral or topical) versus placebo in the treatment of OME.

Meta-analysis is a systematic approach to identify, appraise, synthesize and (if appropriate) combine the results of relevant studies to arrive at conclusions<sup>[26]</sup>.

All of the studies conducted during this meta-analysis were randomized control trials.

Our results in this Meta-analytical study, as regard response of children with OME to oral steroids plus antibiotic, showed that there is a significant difference in improvement in patients with OME receiving oral steroids plus antibiotics in the short term therapy in contrast to the other group who received placebo with antibiotics.

These results came in agreement with, Mandel et al<sup>[27]</sup>. He stated that there is a significant difference in the proportions of children who had OME of, at least, 2 months duration and were effusion-free (immediately after 14 days of treatment with prednisolone and amoxicillin) compared with those who were treated only with amoxicillin for 14 days. Hearing, as measured by pure tone audiometry (PTA), was also significantly improved after steroid treatment. However; within 2 weeks of finishing this treatment, there was no longer any significant difference in effusion status between the 2 groups, regardless of whether amoxicillin was continued or not<sup>[9]</sup>.

Thomas stated that oral steroids together with an antibiotic appear to improve resolution of effusion in the short term<sup>[22]</sup>.

Rosenfeld showed a short-term benefit for oral steroid plus antimicrobial versus antimicrobial alone in 1 out of 3 children treated. This benefit became non-significant after several weeks of finishing treatment<sup>[2]</sup>.

Mandel et al stated that trials of oral corticosteroids alone and in combination with an antibacterial agent generally suggest short-term efficacy. However, recurrence of OME was common<sup>[27]</sup>.

Our results came in against with Nuss & Berman who stated that combination therapy in the form of oral steroids with antibiotic had insignificant impact in treating OME in short term therapy<sup>[28]</sup>.

Our results showed no positive findings with the use of topical steroids with or without antibiotic in clearing effusion in patients with OME in short term therapy.

This comes in agreement with Shapiro who stated that there is no benefit with use of topical steroids in treatment of OME<sup>[29]</sup>.

Our results come in against with Tracy who demonstrated an effect in clearing effusions in the short term with the use of topical steroids plus antibiotic in treatment of OME<sup>[11]</sup>.

Our study showed no benefit using topical steroids as intermediate term therapy (8 weeks) to alleviate effusion in patients with OME.

Our results as regard intermediate outcome comes in agreement with Rosenfeld who did randomized trial showed statistically equivalent outcomes at 12 weeks for intranasal beclomethasone plus antimicrobials versus antimicrobials alone for OME<sup>[2]</sup>.

Our results come in against with Tracy who demonstrated benefit effect in the intermediate term with the use of topical steroids plus antibiotic in treatment of OME<sup>[11]</sup>.

## **Conclusion**

In our study, we used a Meta-analysis of 5 articles chosen from 171 articles. The results showed a

significant difference between the patients with OME who received oral steroids plus antibiotic versus those who received oral antibiotic only in the short term.

Patients with OME who received intranasal steroids with or without antibiotic had insignificant difference from those who received intranasal placebo with or without antibiotic in the short-term (up to 4 weeks) therapy or intermediate term (4-8 weeks) therapy.

From these findings, it is concluded that oral corticosteroids gives better functional outcome in OME in short-term therapy.

We recommend the use of oral steroids in the treatment of OME in short term.

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