Topical intranasal corticosteroids in children with persistent otitis media with effusion

A double-blind randomised placebo-controlled trial of topical intranasal corticosteroids in 4- to 11-year-old children with persistent bilateral otitis media with effusion in primary care

I Williamson,[1*] S Benge,[1] S Barton,[2] S Petrou,[3,4] L Letley,[5] N Fasey,[5] G Abangma,[3] H Dakin[3] and P Little[1]

[1]Primary Medical Care, University of Southampton, Aldermoor Health Centre, Southampton, UK
[2]University of Southampton Clinical Trials Unit, Southampton General Hospital, Southampton, UK
[3]Health Economics Research Centre, University of Oxford, Old Road Campus, Headington, Oxford, UK
[4]National Perinatal Epidemiology Unit, University of Oxford, Old Road Campus, Headington, Oxford, UK
[5]Medical Research Council General Practice Research Framework, London, UK

*Corresponding author

Executive summary

Health Technology Assessment 2009; Vol. 13: No. 37
DOI: 10.3310/hta13370

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk

Executive summary

Background

Otitis media with effusion (OME), which is often called glue ear, is an increasingly common presentation in primary care and the commonest reason for childhood surgery. A recent National Institute for Health and Clinical Excellence (NICE) review found that there are no proven effective medical treatments. Topical steroids delivered as a nasal spray may be beneficial, are under-researched and may be effective in a primary care setting where the majority of such children are seen.

Objectives

To determine the clinical effectiveness and cost-effectiveness of topical mometasone (a nasal steroid) in children with OME in both ears. The children in this group stand most to gain from a medical intervention because they have more disability than those who have the condition in only one ear, and are also more likely to be referred for surgery.

Methods

Design

A double-blind randomised placebo-controlled trial design was used as this is the best method for evaluating a medical intervention for which previous studies suggest there may be an effect but have been inconclusive. It involves reduction of subjective bias by blinding both observers and subjects and allocating treatments at random rather than through clinician or subject choice.

Setting

Seventy-six Medical Research Council General Practice Research Framework practices throughout the UK between the years 2004 and 2007.

Participants

Two hundred and seventeen children aged 4–11 years. The sample was selected from children presenting to the GP with one or more episodes of otitis media or ear-related problems in the previous 12 months, and whom the research nurse confirmed had glue ear on both sides using microtympanometry (B B or B C2 types using a modified Jerger classification) at entry into the main study. Tympanometry is a painless, quick and reliable method of assessing if the child has fluid behind their eardrums, by using a probe with a pressure seal at the ear canal which measures sound reflected back off the eardrum surface as the pressure is made to change.

Interventions

Mometasone furoate, a topical steroid, 50 g squirted into each nostril, or placebo spray (a dummy spray that looks and tastes the same), once daily for 3 months.

Primary outcome measure

Proportions of children cleared of glue ear assessed by tympanometry at 1 month.

Secondary outcome measures

Tympanometric clearance at 3 months and 9 months after starting the treatment; adverse events (a retrospective questionnaire-based score developed by the Medical Research Council); the OM8-30 score (a functional health status-responsive disease specific measure); reported hearing difficulty; days with earache recorded in a contemporary 3-month diary; health utilities; resource use and cost; and cost-effectiveness [measured both as the cost per quality-adjusted life-year (QALY) gained and as the cost per tympanometric cure at 1 or 3 months].

Results

For the main outcome at 1 month, 40.6% (39/96) of the topical steroid group demonstrated tympanometric cure (to C1 or A type) in one or both ears, as did 44.9% (44/98) of the placebo group. The absolute risk reduction at 1 month was calculated at –4.3% [95% confidence interval (CI) –18.05% to 9.26%]; the odds ratio (OR) was 0.84

(95% CI 0.48 to 1.48). In other words, there was no difference in the rate of resolution of children getting better irrespective of being allocated to either the treatment group or the dummy group. The absolute risk reduction in the treated group at 1 month was actually worse than in the placebo group (–4.3%). Based on these data (100/9.26), the study found that at least 11 children would require to be treated for 1 month with nasal steroids for one child to potentially benefit, and, using the average study value, the number needed to treat for one to benefit would actually be much greater than this.

Four factors were pre-specified for inclusion in adjusting the analysis – age, season, allergy and severity of the glue ear – but only illness severity was found to affect the results. Even when an adjusted analysis was carried out, no treatment effects were found at 1, 3 or 9 months after the start of treatment as shown by the fact that the adjusted OR (AOR) at 1 month for the main outcome was 0.93 (95% CI 0.50 to 1.75). At 3 months, 58.1% of the steroid group had resolved compared with 52.3% of the placebo group, AOR 1.45 (95% CI 0.74 to 2.84). At 9 months 55.6% of the treated group remained clear in at least one ear compared with 65.3% of the placebo group, AOR 0.82 (95% CI 0.39 to 1.75).

Side effects of the spray, although relatively minor, occurred in 7–22% of children and included nasal stinging, nosebleeds, dry throat and cough. OM8-30 scores, reported hearing difficulty and days with earache were not significantly different between groups at 3 months.

The active treatment arm of the study was found to accrue slightly (but not significantly) higher costs and fewer QALYs than placebo and was therefore dominated by placebo in the cost–utility analysis. The probability that topical steroids are a cost-effective use of NHS resources at a ceiling ratio of £20,000 per QALY gained was 24.2%. Ceiling ratios comprise possible values for the maximum that society is willing to pay to gain one unit of health benefit (e.g. one QALY or one tympanometric cure), or the minimum that society is willing to accept in exchange for losing one unit of health benefit. A secondary economic evaluation used a composite end point whereby a patient was considered cured if they had resolution of OME at either 1 or 3 months after start of treatment; this end point differs from the primary and secondary end points of the trial. As slightly more patients randomised to active treatment achieved tympanometric cure at either 1 or 3 months after start of treatment, topical steroids cost £347 per additional child cured, but had only a 56.4% probability of being cost-effective at a ceiling ratio of £1000 per child cured.

Conclusions

Use of topical intranasal corticosteroids (steroid nasal spray) is very unlikely to be clinically effective for glue ear in the primary care setting.

Implications for health care

Topical nasal steroids are not an effective or worthwhile treatment for glue ear in primary care (or likely to be in secondary care because our sample was as badly affected as a large British secondary care sample).

Active monitoring in primary care for children with suspected glue ear is acceptable and satisfactory to children and families, but the current technology methods used to monitor children may require adaptation.

Relatively few children with histories of ear problems attending the GP surgery have glue ear actually confirmed on both sides and need treatment.

Active monitoring in primary care appears to have high satisfaction and low referral rates, but may be in part due to effects of a dummy medication while natural resolution is observed.

Recommendations for research

Seek alternative treatments feasible in this setting, and an evidence review (NICE 2008) suggests that first among these would be auto-inflation. A non-blinded randomised controlled trial would be required with objective outcomes such as tympanometry, and could also be used to look more specifically at accurate diagnostic methods for glue ear in this setting. (Because the condition is highly recurrent after resolving, this favours low-cost, low-side effect-type interventions in primary care.)

In the absence of a proven treatment there is a need for good information to be developed for

children, parents and guardians to support active monitoring in primary care.

Steroids may have a place in treating targeted children in secondary care. However, they are unacceptable when given orally (because of potentially severe side effects), and are very likely to be ineffective when given topically. Future studies that look at older children or those who have more marked allergies may define subgroups that benefit.

Trial registration

This trial is registered as ISRCTN38988331.

Publication

Williamson I, Benge S, Barton S, Petrou S, Letley L, Fasey N, *et al*. A double-blind randomised placebo-controlled trial of topical intranasal corticosteroids in 4- to 11-year-old children with persistent bilateral otitis media with effusion in primary care. *Health Technol Assess* 2009;**13**(37).

How to obtain copies of this and other HTA programme reports
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can be purchased only for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA programme and lists the membership of the various committees.

NIHR Health Technology Assessment programme

The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 01/72/02. The contractual start date was in September 2003. The draft report began editorial review in May 2008 and was accepted for publication in February 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

ISSN 1366-5278

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.

Printed on acid-free paper in the UK by Henry Ling Ltd, The Dorset Press, Dorchester.