

# An open randomised study of autoinflation in 4- to 11-year-old school children with otitis media with effusion in primary care

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## Scientific summary

### Autoinflation in children with otitis media with effusion

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# Scientific summary

## Background

As many as 46% of young school children develop otitis media with effusion (OME). Although most episodes resolve naturally, 10% will last 1 year or more. The problem with such a commonly seen condition is that it is often regarded as 'normal', even though the global and specific impacts can be as great in some children identified in primary care as in those subsequently undergoing surgery. These impacts include reported hearing difficulties, poor physical ear-related health, and behavioural and developmental concerns. Currently, there are no available evidence-based interventions suitable for primary care use to assist with temporising management. The recommendation to wait for natural resolution is often seen as unsatisfactory delay by families and children, with concurrent inappropriate use of antibiotics and other harmful, ineffective and undesired remedies compounding the problem. Autoinflation is a simple method that, in this study, involves inflating a balloon by blowing through the nose three times per day, with some preliminary hospital trial evidence for its effectiveness. However, trial data are preliminary and insufficient, with uncertain generalisability to the majority of affected children.

## Objectives

A pilot study was performed first to assess feasibility, compliance and improve the study logistics for a primary care trial.

### *Main trial objectives*

1. Tympanometry: the primary aim was to evaluate the clinical effectiveness of autoinflation in resolving OME at 1 and 3 months by assessing the proportions of children showing rigorously defined improvement, that is, tympanometric resolution of at least one type B tympanogram (fluid) ear per child back to normal pressures A/C1 types. Secondary tympanometric objectives evaluate resolution in individual ears at both 1 and 3 months.
2. Clinical outcomes: evaluation of the clinical effectiveness of the intervention on main OME symptoms (e.g. hearing difficulty, earache) using a diary score. A total ear problem (mapped) quality-of-life (QoL) measure using a patient-reported outcome measure [a 14-point questionnaire on the impact of OME (OMQ-14) item subset of the Medical Research Council-developed 30-point questionnaire on the impact of OME], compliance and adverse events were also measured.
3. Health economic: assessment of the cost-effectiveness of autoinflation in terms of the cost per additional child achieving resolution of OME at 1 and 3 months, and also in terms of cost per quality-adjusted life-year (QALY). Evaluation by notes audit of the 12-month health economic (HE) outcomes.
4. Qualitative: to describe the experience of using autoinflation, including nurse-observed competence and reported compliance, and develop an easy-to-use training package for everyday practice.

## Methods

The pilot study demonstrated excellent feasibility and compliance with the method in the target age group, and improved the logistics and costing for the main study.

### **The randomised controlled trial**

Three hundred and twenty children from 43 UK practices, aged 4–11 years and attending school, and with either reported OME symptoms/concerns in the previous 3 months or relevant notes on presentation history were enrolled in the study. Children were also required to have confirmed effusion behind one or both eardrums using tympanometry (with otoscopy). Children were individually randomised using web-based randomisation with minimisation by the nurse to either the practice's usual care alone, or autoinflation three times per day for up to 3 months [where effusion(s) remained at the 1-month assessment] plus usual care. Tympanometry outcomes at 1 and 3 months were anonymised by the Primary Care and Vaccines Collaborative Clinical Trials Unit and assessed blind by an expert panel. Analysis was by intention to treat (ITT) and per protocol (PP) according to an analysis plan.

### **The health economics methods**

The HE analyses base case took a NHS perspective for both the cost-effectiveness and the cost-utility analyses. Both analyses were based on the main clinical trial results.

### **The qualitative methods**

Semistructured face-to-face and telephone interviews were conducted with a purposive sample of 19 practice nurses and 14 parents whose children had participated in the AutoInflation Randomised Study. The interviews were digitally audio-recorded and transcribed verbatim. NVivo 10 (QSR International, Warrington, UK) computer-assisted qualitative data analysis software was used to facilitate data management and a thematic analysis was conducted.

## **Results**

### **Randomised controlled trial**

Among the ITT population, 109 children experienced resolution of their B-type ears to A or C1 at 1 month, 62 (47%) children in the autoinflation group and 47 (36%) children in the standard care group. At 1 month, those in the autoinflation group were 36% more likely to have resolution of at least one B-type ear [relative risk (RR) 1.36, 95% confidence interval (CI) 0.99 to 1.88;  $p = 0.0582$ ]. Sensitivity analyses using multiple imputations and a PP population analysis showed no significant differences between groups.

Pre-specified subgroups analyses of age (< 6.5 years vs.  $\geq 6.5$  years), severity (one vs. two B-type ears at baseline), OMQ-14 standardised total score (< 0 or  $\geq 0$ ) and sex were conducted on the primary outcome. In all cases no differences in treatment effects between subgroups were found. The  $p$ -values for the interaction term (treatment by subgroup) in the model ranged from 0.25 to 0.50.

The resolution of at least one B-type ear at 3 months was analysed in the same way as the 1-month primary end point. Out of 245 children, 108 experienced resolution of at least one B-type ear at 3 months, 62 of 125 (50%) in the treated group and 46 of 120 (38%) in the standard care group. At 3 months, those in the autoinflation group were 37% more likely to have resolution of at least one B-type ear (RR 1.37, 95% CI 1.03 to 1.83;  $p = 0.0283$ ).

An analysis of each ear separately was conducted, adjusting for the correlation between ears from the same child using generalised estimating equations. Results were very similar to the main per-child analyses at both 1 and 3 months [RR 1.38, 95% CI 1.01 to 1.87 ( $p = 0.04$ ); and RR 1.41, 95% CI 1.05 to 1.88 ( $p = 0.02$ ), respectively].

At the selected 3 months end point, the adjusted mean change from baseline in the standardised OMQ-14 total scores was greater in the autoinflation arm than in the routine care arm. The difference between groups was  $-0.42$  points (95% CI  $-0.63$  to  $-0.22$  points). This score difference represents an adjusted effect size of 0.48 (of a standard deviation;  $p \leq 0.0001$ ), favouring intervention.

Symptom diary days during which parents reported that their child had hearing loss, earache, sleep disturbance, problems concentrating, as well as days on which pain relief was required and days off school, were summarised in accordance with the statistics plan (to avoid multiple outcomes) as days with any problem. Overall, children in the autoinflation arm had had fewer days with any symptom/problem at 1 month [odds ratio (OR) 0.66, 95% CI 0.41 to 1.05;  $p = 0.08$ ] and at 3 months (OR 0.58, 95% CI 0.37 to 0.90;  $p = 0.02$ ).

With regard to compliance with the method, 116 out of 130 (89%) parents reported using autoinflation 'most' or 'all of the time' during the first month of treatment, consistent with the daily compliance charts. This level of compliance appears to have been maintained in those continuing treatment up to 3 months (68/85, 80%).

There was very little difference between treatment arms in terms of numbers of children with a nosebleed (15% vs. 14%), but there were more reported respiratory tract infections (RTIs) in the treated group (18% vs. 13% of children,  $n = 37$  vs.  $n = 18$  episodes). Most of the RTIs were classified, however, as mild afebrile rhinorrhoea. Eight children in the autoinflation arm (compared with two in the routine care arm) reported otalgia. One child in the autoinflation arm was hospitalised with mild/early mastoiditis that was considered by the Data Monitoring and Ethics Committee review to be non-attributable to the method and made a full recovery.

A meta-analysis of similar trials, identified in the most recent Cochrane systematic review, with outcomes at 1 month (ear-based analysis B to A/C1) favoured autoinflation (RR 1.61, 95% CI 1.26 to 2.06). When the pilot study was combined with the main study as per the statistical plan, the combined RR of the two primary care setting studies was 1.37 (95% CI 1.00 to 1.87).

### **Health economic evaluation**

The cost-effectiveness analysis based on the statistically significant difference in cases resolved puts the cost per case resolved at £132. Although the cost difference was not statistically significant, it was based almost entirely on the cost of the intervention.

The cost per QALY analysis showed the use of the Otovent device (ABIGO Medical, Askim, Sweden) to be just likely to be a cost-effective intervention. The uncertainty reflects the small and non-statistically significant difference in QALYs, a generic rather than condition-specific measure of outcome.

### **Qualitative study**

Three key themes emerged from the analyses that were interpreted as relevant to the research question.

#### **Rationalising**

The first point of contact for parents with concerns about their child's hearing is usually the general practitioner. Parents generally expressed a desire to take action, and a waiting period was often seen as an unacceptable delay. Access to good-quality information and advice helps parents to rationalise decisions and make informed choices for their children.

#### **Primary care management**

Nurses were sufficiently informed and skilled in screening children with tympanometry, and were seen by families as accessible and competent to fulfil this role. The collaborative relationship between the nurse, parent and child was important for co-operation with tympanometric screening and training in the use of the nasal balloon. Demonstration of autoinflation by the nurses and/or parents helped the children to master the technique.

## Engaging with monitoring and treatment

Autoinflation was reported as acceptable to families. Adherence over a period of 1 month was achievable for most parents. Some children reported initial anxieties, but this was overcome with support and encouragement. Adopting the technique as part of the child's normal routine (e.g. when cleaning teeth or using asthma inhalers) may be important for the longer-term use up to 3 months.

The nested qualitative study highlights the potential for an improved and more proactive role of general practice in the early diagnosis and treatment of this common childhood condition.

## Conclusions

Our main findings reveal that autoinflation using the balloon method is both feasible and cost-effective in a primary care setting. A number needed to treat of 9 at both 1 and 3 months was found for improved clearance of middle ear effusions, beyond natural resolution effects alone (usual care). The symptom diaries (describing hearing loss, earache, etc.) showed significant and encouraging improvements by 3 months, the recommended waiting time, as did the mapped ear-related QoL measure (OMQ-14). Although the sample is of good generalisability, children younger than 4 years may perform the method less reliably, and it does require commitment to a regular treatment plan over 1–3 months.

In terms of capacity to change clinical practice, we have demonstrated that this method is clinically effective, good value and safe and acts in a timely fashion for the majority of children likely to be treated in the NHS with symptomatic OME. It should, therefore, be an attractive initial stage option when one considers the unsatisfactory nature of present limited temporising options, which include doing nothing, giving a 'known' ineffective and harmful treatment such as antibiotics or a decongestant, and referring cases on for further evaluation for surgery (which is used to treat a minority, usually those who have experienced unacceptable delays).

From a clinical perspective, the vast majority of children with a working diagnosis of OME will be eligible for a form of empirical management – the *modus vivendi* of general practice. Thus, although there are inevitable limits to what one can conclude from a large, open pragmatic trial such as this, the sum of the new evidence appears sufficiently strong to justify much wider use of autoinflation than is the case at present.

## Suggestions for further research

Implementation and support aspects are needed to improve and refine recognition, diagnosis and impact of OME in primary care settings. This may include a web-based support intervention to promote self-efficacy and support the wider use of the nasal balloon in primary care. This could be supplemented with the further development of near-patient hearing tests and/or short-form questionnaires of impact as developed by the Medical Research Council. Development of clearer self-management plans for OME should be updated, as for asthma, in relation to best use of autoinflation. This requires further pragmatic research including HE evaluation, systematic and consensus review.

Different autoinflation methods may be compared in terms of age-related feasibility, and trials are needed of its effectiveness as a recurrent or second-line treatment in primary and secondary care settings.

The different forms of the Politzerization method that include nasal balloon autoinflation may be a productive area for new treatments. Modified devices may lend themselves to drug delivery systems that better reach the Eustachian tubes than topical nasal sprays.

## **Trial registration**

The trial is registered as ISRCTN55208702.

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