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Prevention of Otic Barotrauma in Aviation: A Systematic Review

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Objective: To conduct a systematic review of the published evidence relating to the prevention of otic barotrauma in aviation. In particular, this review sought to identify procedures, techniques, devices, and medications for the prevention of otic barotrauma as well as evaluate the evidence relating to their efficacy.
Data Sources: Ten databases including Embase, MEDLINE, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials were searched using the full historical range.
Study Selection: English language articles including more than or equal to five participants or cases were included. Outcomes of interest were reduced severity or the successful prevention of otic barotrauma in participants undergoing gradual changes in pressure during air travel or its simulation.
Data Extraction: Articles and data were extracted and analyzed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses and other international guidelines.
Conclusions: This review highlights the lack of published evidence relating to what is a significant and increasingly common problem in otology. There is level 1 evidence that supports the efficacy of oral pseudoephedrine (120 mg) in preventing otic barotrauma in adults. However, oral pseudoephedrine (1 mg/kg) does not appear to be effective in children. There is insufficient evidence to support the efficacy of either nasal balloon inflation or pressure-equalizing ear plugs for the prevention of otic barotrauma. A recently reported, novel technique for insertion of temporary tympanostomy tubes is promising but requires further evaluation. **Key Words:** Aviation—Barotrauma—Middle ear—Otic barotrauma—Tympanic membrane.

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Otic barotrauma (also referred to as aerotitis media and barotitis media) is a traumatic process resulting from an unrelieved pressure difference between the middle ear and the external environment.

As a clinical entity, otic barotrauma has been present for as long as people have taken flight. Jacques Charles, the French physicist who made the first free ascent in a hydrogen balloon in 1783, described severe right ear pain on rapid ascent to an altitude of 3,000 m (1), only relieved upon descent.

Otic barotrauma is an increasingly common problem in otology. The number of passenger flights on commercial aircraft is significantly increasing (Fig. 1), giving rise to the phrase ''the city in the sky,'' with estimates putting approximately one million people in the air at any given time (2). In 2016, there were 3.7 billion passengers carried worldwide, compared with only 310 million passengers in 1970 (3). Otic barotrauma is the commonest medical problem in aviation and has been a causative factor in some aviation incidents (4,5). Recent studies have determined the incidence of subjective otalgia on a given flight to be up to 55% in children (4,6) and 20% in adults (4). Complications vary with severity, ranging from mild otalgia to more significant otologic disease including rupture of the tympanic membrane and round window (7,8). Awareness of the condition among air travelers is somewhat lacking; Mitchell-Innes et al. (9) demonstrated that 30% of airline passengers were unaware of any measures to prevent otic barotrauma. The most widely accepted classification of otic barotrauma has been proposed by Teed (10) and is based on otoscopic findings (Table 1).

To date, three reviews of the literature relating to otic barotrauma have been published (4,11,12). These reviews are either non-systematic or limited in scope. The aim of this systematic review is to present the currently available evidence relating to the prevention of otic barotrauma. Where the level of evidence in the included studies is low, we recognize these papers for providing a novel approach to the prevention of otic barotrauma.

MATERIALS AND METHODS

A systematic review, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 guidelines (13) was performed and the review protocol

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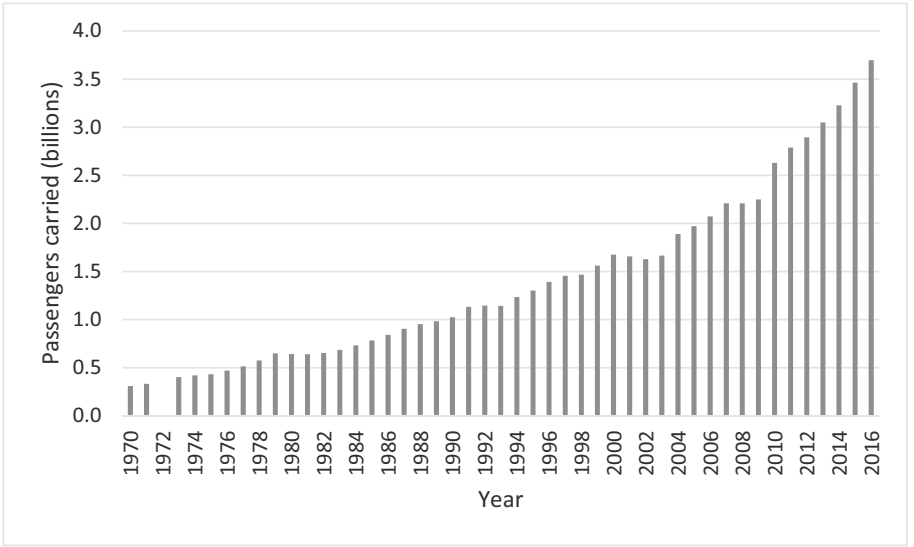

FIG. 1. Total number of passengers carried on aircraft by year (1970–2016).

registered in the PROSPERO database (14) (registration number CRD42017079924). Inclusion criteria for eligible studies are shown in Table 2.

A literature search of 10 databases was performed on October 21, 2017 using the full historical range. Articles relating to the tympanic membrane, middle ear, and eustachian tube were identified by searching abstracts, titles, and key words for the terms ''otic,'' ''otologic,'' ''ear,'' ''otitic,'' ''middle ear,'' ''tympanic membrane'' and expanding the search using the MeSH terms ''Middle Ear'' and ''Tympanic Membrane.'' Articles relating to the clinical entity of otic barotrauma were identified by searching the same fields for the terms ''barotrauma,'' ''barotitis,'' and ''aerotitis,'' expanding the search using the MeSH term ''Barotrauma.'' Duplicate results were removed from the search and the search was limited to papers published in the English language. Papers that were exclusively concerned with non-aviation causes of barotrauma (scuba diving and/or hyperbaric oxygen therapy) were excluded from the study. Table 3 lists the databases searched.

Abstracts were assessed for potential eligibility against the inclusion and exclusion criteria by two authors. Any disagreement between reviewers was resolved through discussion with the input of the senior authors. Full-text articles of all potentially eligible studies were retrieved and reviewed collaboratively by all four authors to determine final eligibility for inclusion. The reference list of each full-text article was manually searched for additional eligible studies. The process of article selection is illustrated as a PRISMA flow diagram in Figure 2. Level of evidence was classified according to the Oxford Centre for Evidence-Based Medicine's 2011 Levels of Evidence (15). Statistical results are reported as described in the included studies including measures of effect and statistical significance. The risk of bias in included studies was assessed using the Cochrane Risk of Bias Tool (16). Where the included

TABLE 1. *Teed's classification (13) of otic barotrauma*

Grade 0	Normal
Grade 1	Retraction with redness in Schrapnell's membrane
Grade 2	Retraction with redness of the entire tympanic membrane
Grade 3	Grade 2 + evidence of middle ear fluid/haemotympanum
Grade 4	Rupture of the tympanic membrane

TABLE 2. *Inclusion and exclusion criteria*

Participants	All persons undergoing gradual or incremental changes in pressure during air travel or its simulation
Intervention	Inclusion: Any intervention administered before or during flight aimed at reducing the incidence or severity of otic barotrauma
Comparators	Any intervention or none
Outcomes	Successful prevention or decreased severity of otic barotrauma
Study design	Inclusion: All study types published in peer-reviewed journals Exclusion: Case series or trials including less than five participants, and Reviews, systematic or otherwise
Language	English language only

TABLE 3. *Databases searched*

Database	Matching Articles
Embase	558
MEDLINE	439
PREMEDLINE	13
MEDLINE Epub Ahead of Print	3
Cochrane Database of Systematic Reviews	19
Cochrane Central Register of Controlled Trials	18
Health Technology Assessment Database	1
Joanna Briggs Institute EBP Database	0
NHS Economic Evaluation Database	0
ACP Journal Club	0

ACP indicates American College of Physicians; EBP, evidence-based practice; NHS, National Health Service.

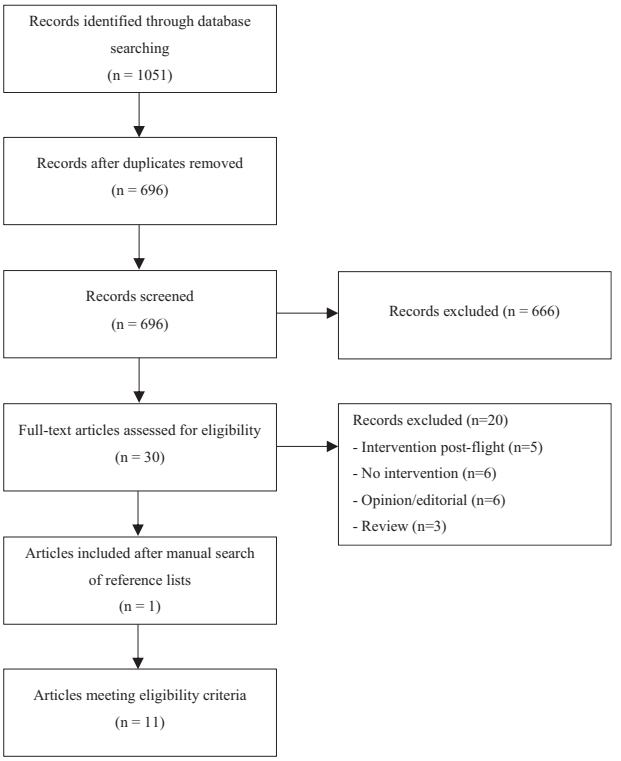

FIG. 2. Results of literature search presented as a PRISMA flow diagram.

studies were found to have broader population (e.g., inclusive of patients undergoing hyperbaric oxygen therapy), only the population subset of interest was included in the analysis.

RESULTS

Eleven studies met eligibility criteria (Fig. 2). Three of these studies, published in the 1950s, concerned the use of nasopharyngeal irradiation for the prevention of otic barotrauma in military pilots (17–19). Given such treatment could not be recommended today, these studies are not included in the qualitative analysis and are instead discussed below (''Historical perspective—Nasopharyngeal irradiation''). The remaining eight studies (20–27) were included in the qualitative analysis. Shown in Table 4, four of the eight studies were randomized control trials (23,24,26,27). Three studies did not recruit untreated controls, instead employing a crossover comparison (21), self-controlled (22), or pre-post comparison (25) study design. One study was a retrospective cohort design (20). Five out of the eight studies reported double-blinding in their protocols (21,22,24,26,27). Across the eligible studies, the effects of four interventions aimed at reducing the incidence or severity of otic barotrauma during air travel have been evaluated: modified intravenous cannulae as tubes, the Otovent® nasal balloon (ABIGO Medical AB, Sweden), pressure-equalizing earplugs, and systemic and topical nasal decongestants.

Inclusion and exclusion criteria were generally consistent across all studies. Five of the eight studies (20–22,26,27) declared their intention to specifically include participants with ear problems on previous flights. All included studies either directly or indirectly excluded participants with acute sinonsasal disease. There was a high degree of homogeneity in the outcome measures and their method of assessment with all studies employing participant (or parent thereof) report of symptoms. With respect to otic barotrauma, six studies relied exclusively on subjective reports of symptoms (20,21,24–27). Two studies (22,23) supplemented participant reports of symptoms with otoscopy and tympanometry.

Table 5 summarizes the interventions, exposure to pressure difference, and outcome measures for the eligible studies. All but one study appropriately exposed participants to an actual or simulated hypobaric environment (0.75ATA). Jumah et al. (21) instead employed a hyperbaric pressure chamber, pressurized to approximately 1.1ATA. All but one study subjected participants to a pressure difference for an appropriate duration either by simulating a cruise phase of at least 60 minutes or by studying passengers on actual flights. Jumah et al. (21) maintained hyperbaric pressure for only 8 minutes.

All eligible studies were assessed for risk of bias (Table 6). Only one study had a high risk of bias in more than one of the assessed domains (23). The three studies that evaluated either oral or topical decongestants

TABLE 4. *Summary of included studies and interventions*

Author	Year	Location	Design	Participants (n)	Intervention Studied	Level of Evidence
Zhang et al. (20)	2013	Sydney, Australia	Retrospective observational study	36 adults[a]	Modified intravenous cannulae as temporary middle ear ventilation tube	3
Jumah et al. (21)	2010	Berlin, Germany	Prospective, double-blinded, crossover comparison	21 adults	Pressure-regulating earplugs (PREP)	2
Klokker et al. (22)	2005	Copenhagen, Denmark	Prospective, double-blinded, self-controlled comparison	27 adults	Pressure-equalizing earplugs (JetEars®)	3[b]
Stangerup et al. (23)	2004	Copenhagen, Denmark	Prospective, unblinded, randomized controlled trial	134 adults	Nasal balloon	3
Buchanan et al. (24)	1999	California, USA	Prospective, double-blinded, randomized placebo-controlled trial	50 children	Oral pseudoephedrine (1 mg/kg)	1
Stangerup et al. (25)	1998	Copenhagen, Denmark	Point prevalence and prospective prepost comparison	412 adults	Nasal balloon	3
Jones et al. (26)	1998	Michigan, USA	Prospective, double-blinded, randomized placebo-controlled trial	150 adults	Topical oxymetazoline Oral pseudoephedrine hydrochloride (120 mg)	1
Csortan et al. (27)	1994	Michigan, USA	Prospective, double-blinded, randomized placebo-controlled trial	250 adults	Oral pseudoephedrine hydrochloride (120 mg)	1

[a]This study also included patients undergoing tympanostomy for prophylaxis in hyperbaric oxygen therapy and for the post-flight treatment of otic barotrauma. Only the relevant subset is included in this review.
[b]Level of evidence downgraded due to high loss to follow-up.

(24,26,27) had a low or unclear risk of bias in all assessed domains.

One study (20) evaluated typical intravenous cannulae modified to act as a temporary tympanostomy tube. This retrospective review demonstrated complete prevention of otalgia during flight in all participants.

Two studies (21,22) assessed the efficacy of commercially-available pressure-equalizing ear plugs in preventing otic barotrauma in flight. Jumah et al. (21) demonstrated a reduction in subjective otalgia in ears fitted with the active pressure-equalizing ear plug whereas Klokker et al. (22) demonstrated the opposite, finding a higher Teed grade in ears fitted with active pressure-equalizing ear plugs (1, range, 0–3) compared with placebo (0, range, 0–2) ($p = 0.033$). The level of evidence of these studies was 2 and 3, respectively.

Stangerup et al. (23,25) tested a nasal balloon in two studies. 76–80% of participants using the nasal balloon reported subjective improvement in otalgia. The more recent study (23) demonstrated a significantly higher incidence of negative middle ear pressures (15% versus 3%, $p < 0.05$) and pathological ears according to Teed's classification (15% versus 6%, $p < 0.05$) in the control group compared with the group using the nasal balloon. Both studies were level 3 evidence.

Three robust, randomized control trials (24,26,27) (each level 1 evidence) assessed the effect of oral pseudoephedrine and/or topical oxymetazoline on the incidence of in-flight otalgia. Each study had a low or unclear risk of bias in each assessed domain. Csortan et al. (27) demonstrated a clinically and statistically significant reduction in the incidence of ear pain/discomfort in adults taking 120 mg oral pseudoephedrine 30 minutes before flight compared with placebo (32% versus 62%, χ^2 15.34, $p = 0.0001$). Jones et al. (26) replicated these findings in a subsequent study (34% versus 71%, χ^2 9.6, $p = 0.002$). Buchanan et al. (24) found that the same effect was not observed in children receiving oral pseudoephedrine (1 mg/kg) where a similar rate of otalgia was seen in the treated and placebo groups (risk difference 1%, 95% confidence interval (CI) −13% to 15%, $p \approx 1.0$). Jones et al. (26) found no evidence that topical oxymetazoline reduces the incidence of otalgia in flight compared with placebo (64% versus 71%, χ^2 0.15, $p = 0.695$).

Outcomes, their method of assessment and the authors' conclusions are further summarized in Table 7.

DISCUSSION

Background and Pathophysiology

Early attempts to understand the pathophysiology and manifestations of otic barotrauma in military airmen were made as early as 1918 during World War I (28). Research gained momentum toward World War II during which time otic barotrauma was one of the most common causes of in-flight discomfort (29) and interfered with the availability of airmen for combat duty up to one-third of the time (28).

Armstrong and Heim (30) proposed that otic barotrauma be defined as an ''acute or chronic, traumatic inflammation of the middle ear caused by a pressure

TABLE 5. *Summary of participant selection, intervention, comparators, and outcome measures*

	Paper	Participants and Selection	Exposure to Pressure Difference	Intervention	Comparator(s)	Outcome Measures (Method of Assessment)
Modified IVC	Zhang et al. (20)	Thirty-six adults (58 tubes) with a history of otalgia during air travel. Retrospective assembly of cohort from clinical records	Not stated	Intravenous cannula modified (ring-barked) to act as a short, temporary tympanostomy tube	Nil (observational study)	Participant-reported resolution of otalgia during air travel
Pressure-equalizing earplugs	Jumah et al. (21)	Twenty-one adults (mean age 42.4 ± 11.5 yr) with a history of pressure equalization problems in at least one ear. Exclusions: Previous ET, ME or TM surgery, present MEVT, strong nasal septal deviation, head and neck malformations, ME effusion, irritated TM or URTI within 2 weeks.	Hyperbaric pressure chamber. Pressure increased from atmospheric by 75 mmHg over 2 minutes (descent), held constant (cruise) for 8 minutes then decreased to atmospheric pressure over 2 minutes (ascent).	Silicon earplug with PREP filter (alloy filter with a milled microslot delays ambient pressure increase (flow = 0.05 cm^3/min at a constant pressure difference of 75 mmHg))	Silicon earplug without PREP filter in the same ear (≥4 h between tests)	Otalgia (participant report on VAS) Success of ET opening (continuous impedance measurement)
	Klokker et al. (22)	Twenty-seven adults (mean age 42 yr, range, 21–65 yr) with ''ear problems'' during previous travel Exclusions: Ongoing ear, nose and throat diseases, pregnancy, cardiopulmonary disease and anyone taking regular medications.	Hypobaric pressure chamber. Pressure reduced to 3/4 ATA (approx. equivalent to 8,000 ft), held constant for 60 minutes then increased to 1 ATA over 16 minutes.	Active pressure-equalizing earplug (JetEars®) (prolonged pressure equilibration) in one ear	Placebo earplug (rapid pressure equilibration) in the other ear	Barotrauma (Teed's classification (13)) Tympanometry Otalgia (participant report)
Nasal balloon	Stangerup et al. (23)	Two hundred twenty-seven adults (mean age in intervention group 39 yr, range, 18–62 yr; mean age in control group 41 y, range, 18–85 yr). Compliance with protocol and follow-up: 52% (intervention), 74% (control) Exclusions: Acute ear or sinonasal infection	Eight same-day commercial flights between Copenhagen, Denmark and London, UK in November 2001.	Nasal balloon inflation if symptomatic after Valsalva manoeuvre	Valsalva manoeuvre only	Barotrauma (Teed's classification (13)) Tympanometry Symptom relief (participant report)
	Stangerup et al. (25)	Four hundred twelve adults (median age 42 yr, range, 15–85 yr)	Eight same-day commercial flights between Copenhagen, Denmark and London, UK in May 1996.	Nasal balloon inflation if symptomatic	Nil (observational study)	Symptom relief (participant report)
Decongestants	Buchanan et al. (24)	Fifty children (aged 6 mo–6 yr) Compliance with protocol and follow-up: 91% Exclusions: Use of antihistamines or decongestants within 24 hours of flight	Commercial flights (1–4 hr duration).	Oral pseudoephedrine (1 mg/kg)	Placebo	Otalgia (parent report) Drowsiness and excitability (parent report)
	Jones et al. (26)	One hundred fifty adults (mean age 35.4 yr) with ''moderate to severe pain in one or both ears during the majority of past airplane flights'' Compliance with protocol and follow-up: 83% Exclusions: intolerance to pseudoephedrine, oxymetazoline or other sympathomimetics, decongestant or antihistamine use within 1 week, MAOI use within 2 weeks, pregnancy, acute ear or upper respiratory complaint, present MEVT, history of respiratory, endocrine, genitourinary, cardiac or neurological condition.	Commercial flights out of Michigan, USA and Ohio, USA	Oxymetazoline 0.05% (two sprays) OR Pseudoephedrine (120 mg)	Placebo Alternate intervention	Ear pain, blockage, hearing loss, dizziness/vertigo, tinnitus (participant report)

(*Continued*)

TABLE 5 ***(Continued)***

Paper	Participants and Selection	Exposure to Pressure Difference	Intervention	Comparator(s)	Outcome Measures (Method of Assessment)
Csortan et al. (27)	Two hundred fifty adults with ''a history of recurrent ear pain during air travel''. Compliance with protocol and follow-up: 76% Exclusions: Intolerance to pseudoephedrine or other sympathomimetics, decongestant or antihistamine use within 1 week, MAOI use within 2 week, pregnancy or lactation, acute ear or upper respiratory complaint, present MEVT, ME effusion, history of respiratory, endocrine, genitourinary, cardiac or neurological condition.	Commercial flights out of two airports in Michigan, USA	Oral pseudoephedrine (120 mg)	Placebo	Acute pain, blockage, hearing loss, dizziness, vertigo (participant report)

ATA, atmospheres absolute (1 ATA = 760 mmHg); ET, eustachian tube; h, hours; MAOI, monoamine oxidase inhibitor; ME, middle ear; MEVT, middle ear ventilation tube; min, minutes; mo, month(s); TM, tympanic membrane; URTI, upper respiratory tract infection; VAS, visual analog scale (pain score /10); wk, week(s); y, year(s).

difference between the air and the tympanic cavity and that of the surrounding atmosphere, commonly occurring during changes of altitude in airplane flights and characterized by inflammation, discomfort, pain, tinnitus, and deafness.'' In keeping with this definition, otic barotrauma represents a spectrum of disease: milder forms are characterized by subjective otalgia ± otoscopic findings of tympanic membrane inflammation; more severe forms are associated with traumatic middle ear effusions or rupture of the tympanic membrane. There are reports in the literature of rupture of the round window and resultant perilymphatic fistula (7,8) resulting from otic barotrauma in aviation.

At cruising altitude, a plane's cabin is pressurized to approximately 0.75 atmospheres absolute (ATA) (31), approximately 570 mmHg, resulting in a pressure difference of −190 mmHg when compared with sea level (1 ATA, 760 mmHg). With an intact tympanic membrane, the middle ear relies exclusively on the eustachian tube to permit either influx or efflux of air to equalize pressures with the external environment. Pharyngeal and palatal muscles converge on the tubal cartilage and orifice to directly or indirectly facilitate its opening, most importantly tensor veli palatini, whose distal fibers actively dilate the eustachian tube (32). Therefore, actions such as chewing, yawning, and swallowing are commonly employed to open the eustachian tube during air travel. During ascent, the pressure in the middle ear becomes increasingly positive relative to cabin pressure. A pressure difference of approximately 15 mmHg is sufficient to force air out through a normal eustachian tube (30). Conversely, during descent, the pressure in the middle ear becomes increasingly negative relative to cabin pressure causing retraction of the tympanic membrane. Otalgia is experienced when the pressure difference exceeds 30 mmHg. A pressure difference of −90 mmHg exceeds the capacity of the muscles involved in tubal dilatation to open the eustachian tube (30), effectively locking it, as the mucosa acts as a valve, drawn in by the negative middle ear pressure.

This systematic review highlights the very limited amount of published literature addressing the prevention of otic barotrauma, despite the increasing prevalence of air travel across the world. The level of evidence was comparatively low in the reviewed studies with only oral or topical decongestants having been tested in level 1 studies.

The consistency of outcome measures between studies was difficult to assess, particularly with respect to patient- or parent-reported questionnaires. Several authors described, with limited detailed, the questions asked of participants in questionnaires (21,22,24,26,27) with little consistency between studies. One author used the well-known visual analog scale (21), another used a four-point scale (24); others were unclear. The subjective nature and potential lack of consistency between the survey questions used across the included studies to collect participant-reported otalgia makes comparison of outcomes challenging. This highlights the need for

TABLE 6. *Risk of bias in included studies*

Paper	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Assessment Outcome	Incomplete Outcome Data	Selective Reporting	Other Bias
Zhang et al. (20)	N/A[a]	N/A[a]	N/A[a]	N/A[a]	Low risk. Retrospective review included all participants within scope.	Low risk. Single outcome.	Nil
Jumah et al. (21)	Low risk. ''Random order.'' Randomization effectively a coin-toss.	Low risk. The ''random order'' referred to was likely unpredictable.	Unclear. Blinding of participants and personnel reported. Not stated whether appearance and size and therefore sensation of earplugs with PREP filter was the same as earplugs without, potentially unblinding participants and personnel.	High risk. Measurements of filter-induced pressure change may have been available to the examiner real time, making determination of active versus placebo possible.	Low risk. One participant's pressure chamber test terminated early due to pain, a valid outcome despite incomplete testing time.	Low risk. All pre-specified outcomes reported.	Cross-over design introduces risk of carry-over effects of placebo or active earplug. 4 hours allowed between tests may have been insufficient for recovery from barotrauma and/or to allow adequate equalization.
Klokker et al. (22)	Low risk. One active, one placebo earplug given to participants. Randomization effectively a coin-toss.	Low risk. Simple, unpredictable allocation method.	High risk. Personnel blinded. Authors state that the active earplug had a greater noise-reducing effect than placebo, likely unblinding participants.	Low risk. Personnel blinded. Objective assessment by otoscopy by experienced examiners according to Teed's classification.	Low risk. All outcomes reported for all participants.	Low risk. All pre-specified outcomes reported.	Nil
Stangerup et al. (23)	Unclear. ''Half of the flights randomized to be ''autoinflation flights'' and the other half to be ''control flights''.''	Unclear. Allocation method not stated.	High risk. Participants not blinded. Not stated whether personnel blinded.	High risk. Participants not blinded, potentially biasing participant-reported outcomes	Low risk. 83% of participants completed questionnaire. Similar rate of missing responses in each group. Unlikely to have affected reported outcomes.	Low risk. All pre-specified outcomes reported.	Nil
Stangerup et al. (25)	N/A[a]	N/A[a]	High risk. Participants not blinded to intervention due to study design	High risk. Assessment outcome would be apparent to participants	High risk. 70% of participants completed questionnaire; only 12% attended otoscopy	Low risk. All pre-specified outcomes reported.	Nil
Buchanan et al. (24)	Low risk. ''Participants given two randomly assigned treatment syringes.'' Randomization effectively a coin-toss.	Low risk. Randomly assigned, sequential identification numbers. Identification key held by pharmacist until conclusion of study.	Low risk. Participants, their parents and personnel blinded. Pseudoephedrine and placebo syringes identical.	Low risk. Blinding of participants and parents reduced risk of bias in parent-reported otalgia	Low risk. 88% of participants completed questionnaire completely, 3% completed for ascent only. Unlikely to have affected reported outcomes.	Low risk. All pre-specified outcomes reported.	Low risk of observer bias in parent-reporting of otalgia due to randomization and identical appearance of syringes

(*Continued*)

TABLE 6 (*Continued*)

Paper	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Assessment Outcome	Incomplete Outcome Data	Selective Reporting	Other Bias
Jones et al. (26)	Unclear. Method of randomization not stated.	Low risk. Sequential identification numbers for computer coding. Identification key held by pharmacist until conclusion of study.	Low risk. Participants and personnel blinded. Pseudoephedrine and placebo tablets and oxymetazoline and placebo sprays identical.	Low risk. Blinding of participants reduced risk of bias in participant-reported otalgia	Low risk. 83% of participants completed follow-up. Very similar rate of loss to follow-up in each group. Unlikely to have affected outcomes	Low risk. All pre-specified outcomes reported.	Nil
Csortan et al. (27)	Low risk. Computer-generated random identification number.	Low risk. Identification numbers for computer coding. Identification key held by pharmacist until conclusion of study.	Low risk. Participants and personnel blinded. Pseudoephedrine and placebo tablets identical	Low risk. Blinding of participants reduced risk of bias in participant-reported otalgia	Low risk. 76% of participants completed follow-up. Very similar rate of loss to follow-up in each group. Unlikely to have affected outcomes	Low risk. All pre-specified outcomes reported.	Nil

[a]Not applicable due to study design.

a validated, patient-reported assessment tool, much like SNOT-22 (33) for chronic rhinosinusitis and ETDQ-7 (34) for chronic eustachian tube dysfunction. Such a tool would facilitate further, patient-centered prevalence studies and permit reliable comparison of outcomes across randomized control trials. Future studies should employ a broader range of outcome measures, in particular objective measures such as pre- and post-flight otoscopy by experienced examiners and tympanometry. Although it is not known whether otoscopic findings correlate with symptoms, the known pathophysiology of otic barotrauma would suggest that this outcome would be useful to include in further investigation and potentially provide a more objective measure of otic barotrauma.

Modified Tympanostomy Tubes

The pathophysiology of otic barotrauma in aviation relies on a pressure difference across the tympanic membrane. Therefore, tympanostomy tubes are the untested but very likely gold standard for otic barotrauma prophylaxis. The positive findings of Zhang et al. (20), therefore, are not surprising. The 22-gauge cannula modified and used as a temporary tympanostomy tube for barotrauma prophylaxis has a typical inner diameter of ~0.6 mm (35) and a relatively thin wall. What was more importantly tested in this retrospective cohort study was the capacity for these modified cannulae to remain patent and in situ to allow pressure equilibration as long as was necessary. This promising technique could be further validated by a randomized trial comparing the modified intravenous cannulae with a more widely used tympanostomy tube such as the Shepard grommet (inner diameter 1.14 mm (36)) or with tympanotomy alone. Outcomes of interest in any future study would include time-to-extrusion, rate of failure (blockage), complications, and contraindications.

Pressure-regulating Earplugs

Two studies (21,22) assessed the effect of pressure-equalizing earplugs on the incidence of barotrauma. Between these two studies, there were significant methodological differences and discordant results.

Jumah et al. (21) demonstrated a statistically significant reduction in subjective pain score with the use of pressure-equalizing earplugs. However, employing a hyperbaric pressure chamber, pressurized to approximately 1.1 ATA, for only 8 minutes and applying a relatively rapid rate of ascent and descent (pressure increased and decreased over only 2 min) significantly limits the external validity of this study. In their study, both the active and placebo ear plugs were applied to the same ear, reducing the risk of inadvertent selection bias.

Klokker et al. (22) likewise evaluated pressure-equalizing earplugs and demonstrated that ears fitted with active earplugs had a statistically significantly higher rate of barotrauma based on Teed's classification. While this effect was statistically significant ($p = 0.003$), its clinical significance was low with a median Teed's grade

TABLE 7. *Summary of study outcomes and conclusions grouped by intervention*

	Paper	Intervention Studied	Outcome Measures (Method of Assessment)	Outcomes	Conclusion
Modified IVC	Zhang et al. (20)	Modified intravenous cannulae as temporary middle ear ventilation tube	Participant-reported resolution of otalgia during air travel	Complete prevention of otalgia during air travel in all participants. 88% of tubes self-extruded, remainder were removed at 6 weeks; 100% of perforations healed.	Modified intravenous cannulae are a safe and effective option for the management of barotrauma with minimal complications.
Pressure-equalizing earplugs	Jumah et al. (21)	Pressure-regulating earplugs (PREP)	Otalgia (participant report on VAS) Success of ET opening (continuous impedance measurement)	Lower subjective pain score (VAS scale) with PREP (2.19 ± 1.50) than without PREP (3.38 ± 2.33) ($p < 0.003$); no significant difference in percentage of successful ET openings with or without PREP	Use of PREP while flying can improve the subjective state in patients with pressure equalization problems. PREP, however, has no influence on ET function.
	Klokker et al. (22)	Pressure-equalizing earplugs (JetEars®)	Barotrauma (Teed's classification (13)) Tympanometry Participant opinion on which earplug was active	Median Teed grade lower in ears with placebo plugs (0, range, 0–2) than with active pressure-equalizing earplugs (1, range, 0–3) ($p = 0.033$); No significant difference in post-decompression middle ear pressures between active and placebo earplugs 78% of participants correctly guessed which earplug was active.	Pressure-equalizing earplugs have a reverse pressure-equalizing effect with statistically significantly more ear pathology in the ears with active earplugs
Nasal Balloon	Stangerup et al. (2004) (23)	Nasal balloon	Barotrauma (Teed's classification (13)) Tympanometry Symptom relief (participant report)	Significantly more pathologic ears post-flight in control group (15% versus 6%, $p < 0.05$) Significantly more ears with high negative ME pressure (≤ -200 dPa) post-flight in control group (15% versus 3%, $p < 0.05$) 80% of participants using nasal balloon reported symptom relief with autoinflation during flight.	Nasal balloon inflation reduces the incidence of barotrauma and the development of sustained negative ME pressures in adults
	Stangerup et al. (25)	Nasal balloon	Symptom relief (participant report)	43% (n = 175) inflated the nasal balloon when symptoms developed; 76% (n = 133) reported improvement in symptoms	Nasal balloon inflation is effective in increasing middle ear pressure and may prevent painful ear conditions.
Decongestants	Buchanan et al. (24)	Oral pseudoephedrine (1 mg/kg)	Otalgia (parent report) Drowsiness and excitability (parent report)	No difference in parent-reported ear pain between pseudoephedrine and placebo groups respectively on ascent (4% versus 5%; risk difference 1%; 95% CI 9% to −8%; $p \approx 1.0$) or descent (12% versus 13%; risk difference 1%; 95% CI −13% to 15%; $p \approx 1.0$) Higher incidence of drowsiness on ascent in pseudoephedrine group compared with placebo (60% versus 27%; risk difference 33%; 95% CI 14%–52%; $p = 0.03$)	Oral pseudoephedrine does not reduce ear pain in children during air travel and is associated with early flight drowsiness
	Jones et al. (26)	Topical oxymetazoline Oral pseudoephedrine hydrochloride (120 mg)	Ear pain, blockage, hearing loss, dizziness/vertigo, tinnitus (participant report)	Decreased incidence of ear pain/discomfort with each intervention versus control. Oral pseudoephedrine versus control: 34% versus 71% (χ^2 9.6, $p = 0.002$); relative risk reduction 52% (95% CI 33–71%) Nasal oxymetazoline versus control: 64% versus 71% (χ^2 0.15, $p = 0.695$); relative risk reduction 10% (95% CI 3–17%)	Oral pseudoephedrine (120 mg) taken at least 30 minutes before flying results in a clinically and statistically significant decrease in the incidence of ear pain/discomfort while flying (number need to treat = 3). Nasal oxymetazoline pre-flight results in a small decrease in the incidence of ear/pain discomfort while flying that is not statistically significant (number needed to treat = 14)
	Csortan et al. (27)	Oral pseudoephedrine hydrochloride (120 mg)	Acute pain, blockage, hearing loss, dizziness, vertigo (participant report)	Decreased incidence of ear pain/discomfort in oral pseudoephedrine group vs control: 32% vs 62% (χ^2 15.34, $p = 0.0001$)	Treatment with 120 mg pseudoephedrine at least 30 minutes before flying appears to decrease the incidence of barotrauma in adults with a history of recurrent ear pain during air travel.

CI indicates confidence interval; ET, eustachian tube; h, hours; ME, middle ear; min, minutes; mo, month(s); PREP, pressure-equalizing ear plugs; VAS, visual analog scale (pain score /10); wk, week(s); y, year(s).

FIG. 3. Photograph showing oblique beam and calliper used for delivery of radiation to the eustachian tube of a military airman. Adapted (reprinted with permission of the copyright holder) from Dickson EDD, McGibbon JEG. The treatment of recurrent otitic barotrauma by irradiation with special reference to lymphoid tissue in the sub-mucosa of the eustachian tube. J Laryngol Otol 1949;63(11):647–671.

of 1 (range, 0–3) with the active earplugs and 0 (range, 0–2) with placebo. Participants in this study were exposed to an appropriate hypobaric environment (0.75 ATA) in a hypobaric pressure chamber and the authors applied a rate of descent of 500 ft min^{-1}. The external validity of this study was therefore high. This study randomized the two ears of each participant to active and placebo earplugs. This study design potentially introduces, if participants had unilateral pressure equalizing problems, a degree of selection bias that was not controlled for in their small population.

In the two studies that evaluated pressure-equalizing earplugs, discordant results, and the limitations and bias discussed above mean that there is insufficient evidence to recommend pressure-equalizing earplugs for the prevention of otic barotrauma.

Nasal Balloon

Two studies by the same author (23,25) evaluated the effect of a nasal balloon on participant-reported otalgia during air travel and demonstrated relief of otalgia in participants using the balloon. Neither study was placebo-controlled and placebo-controlling such an intervention would be difficult, but not impossible. Future studies could randomize participants to a commercial nasal balloon or a very low-resistance balloon that would generate low intranasal pressures on inflation.

A low level of evidence (level 3), a high risk of bias in more than two domains and a lack of placebo control in both studies mean that nasal balloon inflation cannot be recommended for the prevention of otic barotrauma without further investigation.

Oral and Topical Nasal Decongestants

Three studies assessed the effect of oral and/or nasotopical decongestants (24,26,27). There is strong evidence that supports the effectiveness of oral pseudoephedrine (120 mg) in preventing otic barotrauma in adults. The results of two studies were similarly significant, both clinically and statistically (Table 7). Both of these studies excluded participants with acute ear or nose disease. There would be merit in evaluating the effectiveness of this intervention in participants with acute conditions predisposing to otic barotrauma since travellers do not always have the luxury of postponing flights if they are unwell. Oral pseudoephedrine (1 mg/kg) in children was not effective in preventing otic barotrauma in the one study that assessed it (24). Topical oxymetazoline also does not appear to be effective in adults (26).

Historical Perspective—Nasopharyngeal Irradiation

Otic barotrauma became an increasingly common and important problem in World War II, with the rapid development and use of military planes resulting in a ''small but definite waste of flying personnel'' (18). This disease prompted a rush of research into its pathophysiology and treatment. Northington (17) and Dickson and McGibbon (19) studied the effect of local application of radium to the eustachian tube and orifice, avoiding unnecessary irradiation of the surrounding tissue by using a special applicator such as that shown in Figure 3. These treatments were successful in 43 to 90% of cases. At the time, Morris (18) considered the disadvantages of external beam radiotherapy to be ''of no particular consequence'' and directed a relatively low radiation dose of 2 to 12 Gy in weekly fractions of 1 Gy at the eustachian tubes of 37 grounded airmen. Six weeks after radiotherapy, all but one of these airmen were able to resume active duty symptom-free. A large follow-up cohort study by Ronckers et al. (37) in 2001 demonstrated a higher incidence of lymphoproliferative and hematopoietic cancers in those exposed to nasopharyngeal irradiation but no excess deaths from head and neck cancers. Kang et al. (38) found a non-significant increased mortality risk from head and neck cancer in WWII submariners who underwent this treatment (odds ratio = 1.40; 95% CI = 0.54–3.58). Such a treatment could not be recommended today but is interesting to review for its historical context.

CONCLUSION

There is a lack of published evidence relating to the prevention of what is a significant and increasingly common problem in otology. Since the earlier studies that evaluated the efficacy of oral and topical decongestants (24,26,27), there have been no robust, randomized control trials. Only oral pseudoephedrine for the prevention of otic barotrauma in adults is supported by level 1 evidence. There is insufficient evidence to support the efficacy of either nasal balloon inflation or pressure-equalizing ear plugs for the prevention of otic barotrauma. The modified intravenous cannula proposed as a temporary tympanostomy tube is a novel and

relatively simple method of prevention that warrants further investigation.

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