Interventions for recurrent idiopathic epistaxis (nosebleeds) in children (Review)

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ABSTRACT

Background

Recurrent idiopathic epistaxis (nosebleeds) in children is repeated nasal bleeding in patients up to the age of 16 for which no specific cause has been identified. Although nosebleeds are very common in children, and most cases are self limiting or settle with simple measures (such as pinching the nose), more severe recurrent cases can require treatment from a healthcare professional. However, there is no consensus on the effectiveness of the different clinical interventions currently used in managing this condition.

Objectives

To assess the effects of different interventions for the management of recurrent idiopathic epistaxis in children.

Search methods

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was 5 March 2012.

Selection criteria

We identified all randomised controlled trials (RCTs) (with or without blinding) in which any surgical or medical intervention for the treatment of recurrent idiopathic epistaxis in children was evaluated in comparison with either no treatment, a placebo or another intervention, and in which the frequency and severity of episodes of nasal bleeding following treatment was stated or calculable. The two authors reviewed the full-text articles of all retrieved trials of possible relevance and applied the inclusion criteria independently.

Data collection and analysis

We graded trials for risk of bias using the Cochrane approach. One author performed data extraction in a standardised manner and this was rechecked by the other author. Where necessary we contacted investigators to obtain missing information. We did not undertake a meta-analysis because of the heterogeneity of the treatments, procedures and quality of the included trials. A narrative overview of the results is therefore presented.
Main results

Five studies (four RCTs and one quasi-randomised controlled trial) involving 468 participants satisfied the inclusion criteria. The identified RCTs compared 0.5% neomycin + 0.1% chlorhexidine (Naseptin®) cream with no treatment, Vaseline® petroleum jelly with no treatment, 75% with 95% silver nitrate nasal cautery, and silver nitrate cautery combined with Naseptin® against Naseptin® alone; the quasi-randomised controlled trial compared Naseptin® antiseptic cream with silver nitrate cautery. Overall results were inconclusive, with no statistically significant difference found between the compared treatments upon completion of the trials, however 75% silver nitrate was more effective than 95% silver nitrate at two weeks following application. The group treated with 75% silver nitrate had 88% complete resolution of epistaxis compared to 65% in the group treated with 95% silver nitrate (P = 0.01). No serious adverse effects were reported from any of the interventions, although children receiving silver nitrate cautery reported that it was a painful experience (despite the use of local anaesthetic). The pain scores were significantly less in those treated with 75% silver nitrate, the mean score being 1 compared to a mean score of 5 in those treated with 95% silver nitrate; this was statistically significant (P = 0.001).

We carried out a 'Risk of bias' assessment of each study according to the Cochrane methodology and judged that two randomised controlled trials had a low risk of bias, two had an unclear risk of bias and the quasi-randomised controlled trial had a high risk of bias.

Authors' conclusions

The optimal management of children with recurrent idiopathic epistaxis is unknown, however if silver nitrate nasal cautery is undertaken 75% is preferable to 95% as it is more effective in the short term and causes less pain. High-quality randomised controlled trials comparing interventions either with placebo or no treatment, and with a follow-up period of at least a year, are needed to assess the relative merits of the various treatments currently in use.

Plain Language Summary

Interventions for recurrent nosebleeds of unknown cause in children

Nosebleeds in children usually just stop by themselves or after pinching the nose. However, some children get repeated nosebleeds with no specific cause (recurrent idiopathic epistaxis). The most common treatments are cautery or antiseptic cream, or both. Cautery (a method of sealing) can be painful even with local anaesthetic, and usually involves using a silver nitrate stick to seal off a visible blood vessel inside the nose that may be rupturing. Other options include ointments and nasal sprays. The review of trials found that there is not enough evidence to compare the effectiveness of different treatment options, however using a lower concentration of silver nitrate cautery is more effective in the short term and less painful. More research is needed to show the best options for reducing recurrent nosebleeds of unknown cause in children.

Background

Description of the condition

Recurrent idiopathic epistaxis in children is repeated, self-limiting nasal bleeding in patients up to the age of 16 for which no specific cause has been identified. Epistaxis is defined as acute bleeding from the nostril, nasal cavity or nasopharynx. Recurrent episodes are a source of significant distress and anxiety in children, their carers and clinicians, with the result that such nosebleeds are a common cause of morbidity and hospital referral. Currently there is no consensus on the frequency or severity of recurrences that mandates further treatment (McGarry 2008).

Prevalence

Epistaxis is very common in children, although it is rare before two years of age. Thirty per cent of all children aged 0 to 5 years, 56% of those aged 6 to 10 years, and 64% of those aged 11 to 15 years have had at least one episode of epistaxis in their lifetime (Petruson 1979), while 56% of adults with recurrent nosebleeds had problems in childhood (Beran 1986). In most children the
bleeding stops spontaneously, but children with severe or recurrent bleed may need hospital treatment. In 1979, Petruson in Sweden estimated the number of children consulting an ENT specialist due to epistaxis per 1000 children per year as 0.5 in the 0 to 5-year age group and 1.6 in the 6 to 10-year age group (Petruson 1979).

Aetiology

Epistaxis is classified as anterior or posterior depending upon the primary bleeding site and is thought to be more common in males (Sengupta 2010). Anterior epistaxis is more common in children and young adults, whereas posterior nasal bleeding is more often seen in older adults with hypertension or arteriosclerosis (Watkinson 1997). In the majority of children, spontaneous haemorrhage is almost always venous and originates from Little’s area, the anterior region of the nasal septum, where a number of arteries anastomose with each other forming a plexus of vessels (Kiesselbach’s plexus) under the thin mucosa. Bleeding often results when this region is exposed to dry air or minor trauma. The subsequent crusts and scabs can then cause itching, which in turn leads children to traumatisate the area again by picking and rubbing. Childhood recurrent idiopathic epistaxis is usually attributed to crusting, nasal vestibulitis (an infection of the skin of the nasal vestibule producing soreness, inflammation, fissuring and crusting) and/or digital trauma (‘nose picking’), although in many cases no direct cause can be established (Guarisco 1989; McGarry 2006; Petruson 1974). Staphylococcus aureus may have a role in this process; its colonisation of the nasal cavity is thought to produce a chronic low-grade inflammation resulting in septal neovascularisation which, along with irritation and digital trauma, may explain the sequence of events resulting in recurrent epistaxis (Montague 2011).

The incidence of idiopathic epistaxis in all ages is thought to be highest during the colder winter months in northern climates, when upper respiratory tract infections (a frequent precursor to episodes of epistaxis) are more frequent and when indoor humidity decreases to low levels at both home and in the work place (Nunez 1990). Changes from a cold outside environment to a warm dry one may cause variations of the normal nasal cycle of alternating congestion and decongestion, which can then lead to sinonasal congestion, engorgement of the nasal mucosa and ultimately epistaxis. Airborne environmental pollutants are thought to increase the incidence of epistaxis (Bray 2004). Epistaxis is also more common in hot dry climates with low humidity; however this view is not universal as work has suggested temperature to have no causal relationship with epistaxis (Bray 2005).

Patients who suffer from allergic rhinitis are more prone to epistaxis because the nasal mucosa is more inflamed and friable (Watkinson 1997). In only a small number of cases can epistaxis in children be attributed to a well-defined primary cause, for example a blood dyscrasia (a problem with blood clotting), a blood vessel abnormality (such as telangiectatic vessels in Little’s area), a viral infection (such as dengue haemorrhagic fever, a mosquito-borne viral disease which sometimes presents with a few days of recurrent epistaxis) or vestibulitis. In the majority of cases, bleeding arises from a normal vein (or, occasionally, an artery) without any obvious abnormality to account for it. The terms ‘spontaneous’ or ‘idiopathic’ epistaxis have therefore been used to describe this most common category of epistaxis.

It should be noted that occasionally tumours such as juvenile angiofibroma may present as epistaxis (especially in teenage boys), as may certain bleeding disorders, such as von Willebrand’s disease, haemophilia or idiopathic thrombocytopenic purpura, the latter being the most common systemic cause of epistaxis. Studies suggest that as many as 5% to 10% of children with recurrent nosebleeds may have mild, previously undiagnosed von Willebrand’s disease (Katsanis 1988; Kiley 1982). Hereditary haemorrhagic telangiectasia may also present in this way. Nevertheless, for more than 90% of all paediatric patients with epistaxis, there is no underlying systemic cause.

Management

Most children’s nosebleeds are self limiting or settle with simple measures such as pinching the nose, but more severe recurrent cases require treatment from a health professional. There is no consensus on how frequent or severe recurrences need to be to warrant such treatment. Once a careful history has been taken to exclude bleeding secondary to systemic disease, direct examination (with or without a flexible or rigid endoscope) usually reveals an engorged vessel on the septum (Watkinson 1997).

Description of the intervention

The most common interventions used to treat idiopathic recurrent nosebleeds in children are cautery of visible vessels on the anterior part of the nasal septum (usually with a silver nitrate stick under local anaesthetic) and/or the application of an antiseptic nasal cream in order to reduce vestibulitis and crusting. Silver nitrate acts as an oxidising agent. In an aqueous solution the silver cation of the salt (Ag(I)) is readily reduced to neutral silver metal (Ag(0)) which precipitates, resulting in free radicals. The chemical stress associated with this reaction oxidises organic tissue. Two commercially available concentrations of silver nitrate (75% and 95%) are used by otorlaryngologists for the treatment of epistaxis. The silver nitrate is supplied in the form of tips fused with potassium nitrate onto thin plastic handles (Glynn 2011). It remains unknown whether the use of the stronger 95% preparation has any benefit over the 75% preparation (Glynn 2011), however studies have shown 95% silver nitrate to be associated with greater tissue damage and a higher potential for complications (Amin 2007).
Other treatments include the instillation of nasal saline spray to moisten the nasal cavity and prevent excessive drying and crust-ing (Wurman 1992), or the use of bland oils or ointments (in particular petroleum jelly) to cover the mucosa and blood vessels and thereby prevent them from becoming dry and friable. These are frequently advocated as initial treatments for less severe cases (e.g. Barelli 1977; Watkinson 1997). Various other topical pharmacological agents have been advocated, including: oxymetazoline, a topical nasal decongestant (Krempl 1995); intranasal sprays containing desmopressin, an anti-haemorrhagic agent (Lethagen 1993); and epsilon-aminocaproic acid (Jash 1972) and tranexamic acid gel (Tibbelin 1995), both antifibrinolytic agents (i.e. agents that inhibit the dissolution of blood clots). An alternative treatment, fibrin sealant, has also been evaluated (Vaiman 2002). Galvanocautery (a form of electrocautery) under local anaesthetic is not recommended in children (Watkinson 1997) but can be performed under general anaesthetic using bipolar diathermy.

Adverse effects

There remains no consensus concerning the effectiveness of these interventions. Silver nitrate cautery, in particular, can be painful for the patient and has been said to have a high failure rate (McGarry 2006; Ruddy 1991). Cautery is only useful when the site of bleeding is clearly visible and not bleeding too briskly. It relies on destroying the blood vessels with acid, causing them to be replaced by scar tissue (Murthy 1999). However, it is possible for telangiectatic vessels to reappear at the margin of the cauterised area. Cautery causes sclerosis of the vessels and thickening of the mucosa, but in children with vestibulitis the bleeding often occurs from ulcerated nasal mucosa in the vestibule as the crusts break off, rather than from discrete vessels. Moreover, the itch resulting from crusting probably results in increased ‘picking’ of the nose, with resulting trauma and delay in healing, while toxins produced by bacteria colonising the nose may also contribute to further bleeding. As a result, cautery of such areas is likely to delay healing, and will not help to relieve vestibulitis. Despite its popularity, cautery of the septum also carries the risk of atrophy of the nasal mucosa which can lead to septal crusting and perforation (particularly in children), and can result in other adverse effects, including mucocutaneous reaction and tattooing of the septal mucosa (Mayall 1996; Murthy 1996). The drugs used to produce local anaesthesia preceding cautery, especially cocaine, carry well-established risks of adverse effects (Murthy 1999). In many countries the use of cocaine has been replaced by the use of less potentially toxic local anaesthetic and decongestant agents. The application of antiseptic nasal cream is less traumatic, but may also fail to relieve the vestibulitis because of habitual nose picking and recolonisation of the nose with bacteria (Ruddy 1991).

Why it is important to do this review

Treatment of recurrent epistaxis in children is somewhat simplified by the fact that the source of bleeding for the vast majority of cases is from the anterior septum, and by the fact that no specialised equipment is required for diagnosis and treatment. Most paediatric patients - unless actively bleeding - can therefore be effectively managed on an outpatient basis. Nevertheless, management continues to pose a problem for both general practitioners and otolaryngologists, in part because no single method of treatment has achieved universal acceptance. A systematic review of published clinical trials of interventions for recurrent epistaxis in children is therefore presented, using established meta-analytical techniques.

Objectives

To assess the effectiveness of different interventions for the management of recurrent idiopathic epistaxis in children.

Methods

Criteria for considering studies for this review

Types of studies
All identified randomised controlled trials which fulfilled the criteria outlined below. We also identified controlled clinical trials.

Types of participants
Children aged 16 and under diagnosed as suffering from recurrent idiopathic epistaxis.

Types of interventions
All surgical and medical interventions for the treatment of idiopathic epistaxis in children. Possible interventions included silver nitrate cautery, antiseptic nasal carrier cream, nasal saline spray, bland oils or ointments (e.g. petroleum jelly), tranexamic acid gel and fibrin sealant. Comparisons of interest were between any intervention versus any other or versus a placebo.

Types of outcome measures

Primary outcomes
Effectiveness in control of epistaxis - frequency and severity of episodes following treatment: whether epistaxis had stopped completely, decreased, remained the same or increased.

Secondary outcomes
Adverse and/or side effects.

Search methods for identification of studies
We conducted systematic searches for randomised controlled trials. There were no language, publication year or publication status restrictions. The date of the last search was 5 March 2012, following previous searches in 2007 and 2003.

Electronic searches
We searched the following databases from their inception for published, unpublished and ongoing trials: the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library 2012, Issue 2); PubMed; EMBASE; CINAHL; LILACS; KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; BIOSIS Previews; ISRCTN; ClinicalTrials.gov; ICTR and Google.

We modelled subject strategies for databases on the search strategy designed for CENTRAL. Where appropriate, we combined subject strategies with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the Cochrane Handbook for Systematic Reviews of Interventions (Handbook 2011)). Search strategies for major databases including CENTRAL are provided in Appendix 1.

Searching other resources
We scanned reference lists of identified studies for further trials. We searched The Cochrane Library, PubMed, TRIPdatabase and Google to retrieve existing systematic reviews possibly relevant to this systematic review, in order to search their reference lists for additional trials.

Data collection and analysis

Selection of studies
The two authors reviewed the full-text articles of the retrieved trials and applied the inclusion criteria independently. We resolved any differences in opinion about which studies to include in the review by discussion.

Data extraction and management
The two authors independently extracted data from the studies using standardised forms. We extracted data so as to allow an intention-to-treat analysis. Where data were missing, we wrote to the authors of the study requesting further information.

Assessment of risk of bias in included studies
The two authors undertook assessment of the risk of bias of the included trials independently, taking the following into consideration, as guided by the Cochrane Handbook for Systematic Reviews of Interventions (Handbook 2011):
- sequence generation;
- allocation concealment;
- blinding;
- incomplete outcome data;
- selective outcome reporting; and
- other sources of bias.

We used the Cochrane ‘Risk of bias’ tool in RevMan 5 (RevMan 2011), which involved describing each of these domains as reported in the trial and then assigning a judgement about the adequacy of each entry: low, high or unclear (or unknown) risk of bias.

Data synthesis

RESULTS

Description of studies
See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

Results of the search
The original searches in August 2003 retrieved 726 references, of which 717 were immediately considered unsuitable for inclusion. The majority of these considered epistaxis only as a side effect and the others were either review articles, descriptive studies or uncontrolled trials. Of the nine possibly relevant studies, two trials included adults only (Morra 1982; Tang 2001), and two trials that included both adults and children were excluded (after having...
contacted the authors), as paediatric data only proved impossible to extract (Murthy 1999; Vaiman 2002). We excluded two further trials as they were not randomised and so were not of sufficient methodological quality (Tarantino 1989; Ye 1997). Three trials satisfied all aspects of our inclusion criteria (Kubba 2001; Loughran 2004; Ruddy 1991). Searching the bibliographies of all relevant papers did not reveal any further trials. The methods, participants, interventions and outcomes of the included studies are listed in the table of Characteristics of included studies.

Update searches performed in October 2007 retrieved a further 933 references once duplicates were removed, of which 929 were considered unsuitable for inclusion. Four references were investigated further. Of these, Vyas 2006, a randomised controlled trial comparing Vaseline®, antiseptic cream (Naseptin®) and silver nitrate cautery in 205 children, satisfied all our inclusion criteria, but the paper is a conference abstract in which insufficient data are presented. Although contact was made with one of the co-authors (J Dempsit), he was able to provide neither additional data nor contact details for the study’s lead author. As a result, the study has therefore been placed in the Characteristics of studies awaiting classification section in the hope that data will be available for inclusion in a future update of this review. For the latest update of this review in 2012, further attempts to gain more information or contact the lead author were unsuccessful. The remaining three references proved to be: a follow-up study (Robertson 2007, published as a conference abstract) to an already included study (Kubba 2001), and two references to an ongoing study completed in 2008 (Kubba 2006); this has now been included in the latest update (Calder 2009). Perusal of Robertson 2007 suggests that this is not a report of a randomised controlled trial nor of the long-term effects of the original (randomised) interventions; rather, the children included in the original trial were the subjects of long-term follow-up to examine the effectiveness of the interventions they underwent at their eight-week clinic appointment in 2001, which were not randomly allocated (see below).

We again updated the searches in November 2009, July 2011 and March 2012, retrieving a total of 583 references. We removed 575 of these in first-level screening (i.e. removal of duplicates and clearly irrelevant references), leaving eight references for further consideration. An additional two studies met all inclusion criteria for the review (Calder 2009; Glynn 2011). The remaining studies were either in adults (Moumouidis 2006; Teker 2010; Troikaa 2010; Zhang 2008) or in patients with hereditary haemorrhagic telangiectasia (Geithoff 2010; Yaniv 2009).

A total of five studies are therefore now included in this review (Calder 2009; Glynn 2011; Kubba 2001; Loughran 2004; Ruddy 1991).

### Included studies

**Design**

Calder 2009 and Glynn 2011 were double-blind, randomised controlled trials. Kubba 2001 and Loughran 2004 were prospective, single-blind, randomised controlled trials. Ruddy 1991 was a quasi-randomised (i.e. by alternation) controlled trial.

**Sample sizes**

The included studies has the following sample sizes: Calder 2009 (109), Glynn 2011 (103), Kubba 2001 (103), Loughran 2004 (105) and Ruddy 1991 (48).

**Setting**


**Participants**

In Calder 2009, 109 of 261 children referred to the otolaryngology clinic of a children’s hospital with epistaxis were entered into the trial; 32 did not attend and a further 120 were unsuitable (allergy, refusal, no recent bleeds, no visible vessels, other). In Glynn 2011, 103 of 120 children (aged 3 to 16, mean eight years) referred to the otolaryngology department by accident and emergency or their family doctor for treatment of recurrent epistaxis were included in the study. Kubba 2001 recruited children (aged 3 to 13 years, median eight years) referred by their general practitioner (family doctor) to a children’s hospital otolaryngology clinic for recurrent epistaxis and Loughran 2004 recruited 105 children (aged 1 to 14 years, median nine years) referred by their general practitioner for recurrent epistaxis. In Ruddy 1991, children with at least one nosebleed in the last four weeks and a history of recurrent epistaxis were recruited. Only in the studies by Calder 2009 and Glynn 2011 was the presence of a visible vessel to cauterise one of the inclusion criteria. In Ruddy 1991 reference is made to “prominent vessels or other bleeding points” being present in participants but this is not clearly stated as an inclusion criterion.

**Interventions**

Calder 2009

The trial compared nasal cautery and antiseptic nasal cream to antiseptic cream alone in the management of paediatric epistaxis. Upon agreeing to participate patients were randomised using sequentially numbered, sealed, shuffled envelopes. Fifty-four were allocated to the treatment group (silver nitrate and antiseptic cream) and 55 to the control group (antiseptic cream). Pre-trial
duration of symptoms for all referred patients ranged from one month to nine years; the majority had symptoms for at least a year. The mean age was 7.4 (range 1 to 13 years) and frequency of bleeding ranged from six times a day to monthly. Both treatment and control groups underwent preparation of the nasal mucosa with lignocaine either as a spray (2%) or on a cotton wool pledget (4%); the treatment group then underwent nasal cautery with 75% silver nitrate to any visible vessels on the nasal septum whilst the control group underwent 'sham' cautery using the inactive end of the cautery stick. Both groups were asked to apply 0.5% neomycin + 0.1% chlorhexidine cream (Naseptin®) twice daily to the effected side for four weeks.

Glynn 2011

The trial compared the effectiveness of 75% versus 95% silver nitrate cautery for the management of idiopathic childhood epistaxis. Children were randomised prior to commencing the study using randomly allocated sealed envelopes: 50 (49 completing the trial) to group A treated with 75% silver nitrate and 53 (52 completing the trial) to group B treated with 95% silver nitrate. The frequency of epistaxis ranged from 4 to 20 episodes per month with a mean of five per month; there was no significant difference in the frequency and duration of epistaxis between the two groups. The pre-cautery anaesthesia and method of application was identical, taking care to avoid surrounding normal mucosa. Following cautery both groups were given a prescription for 0.5% neomycin + 0.1% chlorhexidine (Naseptin®) to apply to the cauterised site twice daily for two weeks. Initially children aged over six were asked to report pain on a visual analogue scale and parents asked to report pain on their children’s behalf if aged under six. Parents and children were also asked to maintain a diary of any further epistaxis until their follow-up appointment in two weeks and then eight weeks following cautery.

Kubba 2001

The trial compared the effectiveness of antiseptic cream, 0.5% neomycin + 0.1% chlorhexidine (Naseptin®), with no treatment for childhood recurrent epistaxis. Participants were randomised by referral letter into two groups: 51 to the treatment group (47 completing the trial) and 52 to the control group (41 completing the trial). The frequency of pre-trial bleeds ranged from 1 to 90 per month (mean = 9) over a period of between 2 and 96 months (mean = 20). The treatment group was instructed to apply the cream to both nostrils twice daily for four weeks, and all participants were sent an epistaxis diary to complete.

Loughran 2004

The trial aimed to determine if topical nasal petroleum jelly (Vaseline®) was effective in the treatment of recurrent epistaxis in childhood. Participants were randomised by referral letter into two groups: 52 to the treatment group and 53 to the control group. The pre-trial duration of symptoms was between 2 and 84 months (median = 12), with bleeds lasting between 2 and 120 minutes (median = 5). The treatment group was instructed to apply petroleum jelly twice a day bilaterally for four weeks, to monitor any bleeds during a further four-week period, and to attend an eight-week outpatient appointment. The control group was given an eight-week outpatient appointment and instructed to monitor the number of bleeds during the preceding four weeks.

Ruddy 1991

The trial compared antiseptic nasal carrier cream, 0.5% neomycin + 0.1% chlorhexidine (Naseptin®), and silver nitrate cautery (under local anaesthetic) for the treatment of recurrent epistaxis in children. Participants were randomised into two equal treatment groups: Group 1 (24 children) was instructed to apply Naseptin® cream to both nostrils twice daily for four weeks; Group 2 (24 children) received a single treatment of cautery with 75% silver nitrate on a stick under local anaesthetic (cocaine 5%) to prominent vessels or other bleeding points. All participants were instructed to keep a note of the number of nosebleeds occurring in the four-week period immediately following completion of the four-week course of treatment.

Outcomes

Calder 2009

Following treatment both groups were called for an eight-week appointment and assessed by a researcher blind to the original treatment allocation. At eight weeks there were eight patients each in the treatment and control group lost to follow-up. Five patients in the treatment group and two in the control group admitted to discontinuing Naseptin® use prior to four weeks duration, but were still included in the analysis. In total 93 of 109 patients were considered to have completed the trial, 46 in the treatment group and 47 in the control.

Glynn 2011

At follow-up the diaries were reviewed and parents asked if their children had required any pain relief on the day of their cauterisation. Any patients that failed to attend outpatients were contacted by telephone and offered another appointment; information regarding further epistaxis was taken over the telephone if they failed to attend. One hundred and one patients attended for the two-week follow-up appointment and 93 for the eight-week follow-up appointment; the remaining eight were successfully contacted by telephone. Two patients failed to attend either appointment or be contactable via telephone (one from Group A and one from Group B). The main outcome measure was taken to be the number of children with complete resolution of epistaxis at follow-up appointment.

Kubba 2001

Both groups were called for an eight-week appointment at the otolaryngology clinic (for history, examination, tests when appropriate and nasal cautery if necessary). For those who failed to attend (n = 30) an attempt was made to collect data by telephone: this was successful in five cases in the treatment group and 10 cases in the control group. The main outcome measure was the number of children with complete resolution of their complaint (i.e. no
nosebleeds) during the four weeks immediately following completion of the four-week course of treatment.

Loughran 2004

The outcome measure was the proportion of children in each group without nosebleeds during the four weeks immediately following completion of the four-week course of treatment.

Ruddy 1991

The treatment outcomes were defined as follows: complete success (no bleeding in last four weeks); partial success (50% reduction in number of bleeds in last four weeks); and failure (less than 50% reduction in number of bleeds in last four weeks).

Excluded studies

We excluded 13 studies from the review. Reasons for exclusion are shown in the Characteristics of excluded studies table.

Risk of bias in included studies

Two authors subjected all included studies to a critical review of their methodology using the Cochrane 'Risk of bias' tool and graded them for their overall risk of bias according to the stated criteria, with scores of included studies ranging from low risk (Glynn 2011; Loughran 2004), to unclear risk (Calder 2009; Kubba 2001) and high risk (Ruddy 1991) of bias. Four studies described adequate randomisation, concealment and blinding procedures (Calder 2009; Glynn 2011; Kubba 2001; Loughran 2004), two were double-blind (Calder 2009; Glynn 2011) (participants and outcomes assessors) and two were single-blind (Kubba 2001; Loughran 2004) (outcome assessors only). All these trials also conducted power calculations in order to establish sufficient sample size from the outset. One trial was later found to have insufficient power following losses to follow-up and inaccurate estimates for results of patients within the control arm (Calder 2009).

Methodological quality was reduced in Kubba 2001 by substantial losses to follow-up (14.5% of all participants; 9% of treatment group, 21% of control group) and by no intention-to-treat analysis being undertaken.

In Ruddy 1991, no blinding or method of allocation concealment was described. There was also no randomisation method given, but when contacted one of the authors (David Proops) recalled that alternating patients were randomised at presentation, making this a quasi-randomised trial. No power calculations for correct sample sizes were apparently made, with the result that the sample size was too small to give the results of the trial sufficient weight (24 participants in each group, when by our calculations there should have been at least 53 per group for 80% power).

Effects of interventions

Primary outcome measure: effectiveness in control of epistaxis

We assessed each included study with regards to the primary outcome of efficacy in epistaxis control; relating to frequency and severity and if episodes of epistaxis increased, remained, decreased or ceased completely.

Calder 2009

This study compared the effectiveness of silver nitrate cautery and Naseptin® against Naseptin® cream alone for the treatment of recurrent epistaxis in children. The primary outcome measure was no bleeding in the four weeks following completion of treatment. The authors used an intention-to-treat analysis and reported no significant differences between the two groups (21 of 46 treatment and 14 of 47 control, P = 0.114). They also assessed difference in severity or frequency of bleeds: 42 (91.3%) of 46 in the treatment group compared to 33 (70.2%) of 47 had an improvement in these symptoms, which was statistically significant (P = 0.01). This study suggests that nasal cautery combined with Naseptin® is superior to Naseptin® alone in the treatment of recurrent idiopathic epistaxis when vessels are visible. This study was, however, underpowered by the authors own admission, making the results less meaningful.

Glynn 2011

This study compared the effectiveness of 75% silver nitrate (group A) with 95% silver nitrate (group B). In group A, 43 (88%) of 49 children had complete resolution of epistaxis; three underwent repeat cauteryisation with the same concentration stick. At eight weeks, 48 (98%) of 49 had complete resolution; the one child without resolution was subsequently diagnosed with von Willebrand’s disease. In group B initial follow-up showed resolution of epistaxis in 34 (65%) of 52 cases; six were re-cauterised with the same concentration stick. At eight weeks complete resolution had occurred in 47 (90%) of 52 children. One of these five children was subsequently diagnosed with von Willebrand’s disease. The authors noted a statistically significant difference between groups A and B at two weeks (P = 0.01) but not at eight weeks (P = 0.12). This study suggests that nasal cautery with 75% silver nitrate is more effective at controlling recurrent epistaxis compared to 95% silver nitrate in the short term when followed up with Naseptin® cream, but there is little difference in the long term.

Loughran 2004

Loughran’s study presented a comparison between petroleum jelly (Vaseline®) and no treatment. In the treatment group, 37/51 (73%) had post-treatment bleeds, compared with 35/53 (66%) in the control group, with no statistically significant difference between the groups (P = 0.47). Petroleum jelly was found to be no more effective than no treatment for the control of recurrent childhood epistaxis.

Kubba 2001

This study compared the effectiveness of antiseptic nasal carrier cream (Naseptin®) with no treatment. Data were available on the number of participants who had no bleeds in the four weeks following completion of treatment (i.e. the four weeks preceding the
eight-week clinic review), but there were a significant number of participants who were lost to follow-up: 15 (four in the treatment group, 11 in the control group) out of a group of 103 (14.5%). Complete data were available for 88 (85.5%) participants: 21/47 (45%) in the treatment group (five of whom did not receive treatment as intended) with post-treatment bleeds, compared with 29/41 (71%) in the control group, giving a statistically significant difference in favour of Naseptin® (P = 0.01). From this per-protocol (i.e. complete case) analysis, the authors concluded that their study showed a significant short-term benefit in the use of antiseptic cream when compared to no treatment: "This equates to a relative risk reduction of 47%* (95% confidence interval 9% to 69%), and an absolute risk reduction of 26% for persistent bleeding (95% confidence interval 12% to 40%), giving a number needed to treat of 3.8 (95% confidence interval 2.5% to 8.5%)."

(Kubba 2001, p.47) (*By our calculations this should read 37%). However, an intention-to-treat analysis provided the following results: 21/51 (41%) in the treatment group with post-treatment bleeds, compared with 29/52 (56%) in the control group with post-treatment bleeds, with no statistically significant difference between the groups (P = 0.14). Two different sensitivity analyses confirm this result: i) a best-case scenario for both groups (i.e. assuming that all those lost to follow-up failed to attend the clinic because they had no post-treatment bleeds) gave an identical result to that of the intention-to-treat analysis; ii) a best-case scenario for no treatment (i.e. assuming that everyone lost from the treatment group had post-treatment bleeds, but everyone lost from the control group was clear of bleeds) gave 25/51 (49%) with bleeds in the treatment group, compared with 29/52 (56%) in the control group with post-treatment bleeds, with no statistically significant difference between the groups (P = 0.49). Thus, as the authors themselves stated: "A large proportion (29%) of the children referred did not attend for their appointment...If failure to attend is more common in those whose symptoms have settled, it would tend to bias our results away from showing a significant difference."

Our intention-to-treat and sensitivity analyses show that in this trial there was no statistically significant difference between Naseptin® and no treatment.

Ruddy 1991

This study compared antiseptic nasal carrier cream (Naseptin®) with silver nitrate cautery. In the Naseptin® group, 11/24 (45%) participants experienced post-treatment bleeds compared with 9/24 (38%) in the cautery group, with no statistically significant difference between treatments (P = 0.56). Three participants - one in the Naseptin® group, two in the cautery group - were lost to follow-up. This suggests that antiseptic nasal cream alone may be as effective as silver nitrate cautery alone in the treatment of recurrent epistaxis in childhood.

Secondary outcome measures: adverse or side effects of treatment

The secondary outcome measures related to adverse or side effects of the treatment; we also assessed these according to the review protocol.

Calder 2009

There was a single adverse event reported of a child developing a rash, who stopped taking the Naseptin® cream. There were no adverse effects of nasal cautery except for transient discomfort.

Glynn 2011

Pain scores in group A ranged from 0 to 5 with a mean of 1 and in group B from 1 to 9 with a mean of 5. This was considered statistically significant (P = 0.001). At two weeks an eschar was visible in two (4%) of 49 patients in group A and 15 (29%) of 52 in group B; these disappeared at eight weeks in both groups. There were no cases of tattooing or septal perforation in either group, but there was a case of a small adhesion between the nasal septum and inferior turbinate in group B.

The study suggests that nasal cautery with 75% silver nitrate is less painful and has fewer side effects than 95% silver nitrate in the short term.

Loughran 2004

No data were available on the severity of post-treatment bleeds or adverse and/or side effects.

Kubba 2001

No data were available on the severity of post-treatment bleeds or adverse and/or side effects.

Ruddy 1991

No data were available on the severity of post-treatment bleeds. All children undergoing silver nitrate cautery reported that it was a painful experience, despite the use of cocaine 5% for local anaesthesia. Participants using Naseptin® occasionally complained of an unpleasant taste or smell.

DISCUSSION

No result from any of the five included trials showed any single treatment to be significantly better than either any other treatment or no treatment for recurrent idiopathic epistaxis in children upon completion of the trials.

The quality of three of the five studies was not high. Two studies had small sample sizes (Calder 2009; Ruddy 1991) and another had significant losses to follow-up (Kubba 2001). In the two trials of high methodological quality Vaseline® was no better than no treatment (Loughran 2004) and 75% silver nitrate cautery with Naseptin®, whilst better than 95% silver nitrate cautery with Naseptin® at two weeks, was no better at eight weeks (Glynn 2011), therefore neither showed a significant difference between interventions upon completion of the studies.

A major weakness in all trials was the follow-up period of four (Calder 2009; Kubba 2001; Loughran 2004; Ruddy 1991) and eight weeks (Glynn 2011). We believe this is an insufficient period
over which to evaluate the effectiveness of treatment of a recurrent and (generally) episodic condition.

It should be noted that both Kubba 2001 and Loughran 2004 adopted a rather unusual methodological approach to study enrolment. The trials were both undertaken in a hospital setting in which participants were randomised and admitted to the trials on receipt of a referral letter from a general practitioner (i.e. from primary care). This process took place prior to the patients (or carers) having given consent to the patients’ participation in the trial, or indeed before they even knew a trial was being undertaken. Loughran states that there were both advantages and disadvantages to this approach: “The advantage is that it allowed the normal outpatient wait to act as a natural observation period for the control arm. It would have been difficult to get ethical or parental approval to assess a child and then send them away without treatment.” This statement (which also appears, worded slightly differently, in Kubba 2001) is questionable, however. If, in the study setting in question, it was “normal” to wait eight weeks for an outpatient appointment (and hence an eight-week treatment delay was usual and acceptable), then it would not have been unethical for patients to be sent away without treatment. Instead, some might question the concept of enrolling people in a trial without their prior knowledge and consent.

Furthermore, this enrolment method, as Loughran concedes, has its own problems: “The disadvantages are that occasionally the referral letter is misleading or even incorrect in its assumptions, and the fact that compliance rates may be higher if patients are initially seen at the clinic and the trial fully explained, and the chance to ask questions is given.” Relying on a referral letter to assess the eligibility of patients means that no proper history is taken - as stated above, this is an important issue in the treatment of recurrent idiopathic epistaxis, as other causes for the condition should be ruled out before treatment is given. As a result, both trials had to exclude participants (five in Kubba 2001, one in Loughran 2004), although Kubba 2001 failed to record the reason for these exclusions.

The most notable results came from Ruddy 1991 and Glynn 2011. Ruddy 1991 was the trial of lowest quality, which suggested that antiseptic cream may be as effective as silver nitrate cauter (a procedure generally perceived by participants in the trial as painful and unpleasant). However, this was a small study with low power. Glynn 2011 noted that 75% silver nitrate cauter with Naseptin® was more effective than 95% silver nitrate cauter and Naseptin® at two weeks (Glynn 2011). Furthermore, it was better tolerated in terms of adverse outcomes, making 75% silver nitrate preferable to 95% silver nitrate during nasal cauterisation for paediatric idiopathic epistaxis.

A U T H O R S ’ C O N C L U S I O N S

Implications for practice
The optimal management of children with recurrent idiopathic epistaxis remains unknown, however if chemical cauter is utilised 75% silver nitrate is preferable to 95% silver nitrate as it is more effective in the short term and less painful. Overall there appear to be no serious adverse effects associated with any of the treatments evaluated, although children receiving silver nitrate cauter commonly report the experience as painful (despite the use of local anaesthetic).

Implications for research
High-quality randomised controlled trials are needed to assess the relative merits of not only antiseptic cream and silver nitrate cauter, but also of other interventions currently in use for the treatment of idiopathic paediatric epistaxis (for example, nasal sprays, antifibrinolytic agents and bland oils or ointments). Some children with recurrent troublesome epistaxis undergo bipolar diathermy cauterisation under general anaesthesia; the merits of this, compared to alternatives, should also be evaluated. These studies should compare different interventions either with placebo or no treatment, be of sufficient quality and size, and have a follow-up period of at least a year. Data on the natural resolution rate of (severe) recurrent idiopathic epistaxis in children would also be helpful.

A C K N O W L E D G E M E N T S

We wish to thank Dr. Maroeska Rovers for her statistical advice.
References to studies included in this review

Calder 2009  {published data only}

Glynn 2011  {published data only}

Kubba 2001  {published data only}

Loughran 2004  {published data only}

Ruddy 1991  {published data only}

References to studies excluded from this review

Geisthoff 2010  {published data only}

Mathiasen 2005  {published data only}

Morra 1982  {published data only}

Moumoulidis 2006  {published data only}

Murphy 1999  {published data only}

Tang 2001  {published data only}

Tarantino 1989  {published data only}

Teker 2010  {published data only}

Troika 2010  {published data only}
Vaiman 2002 {published data only}

Yaniv 2009 {published data only}

Ye 1997 {published data only}

Zhang 2008 {published data only}

References to studies awaiting assessment

Vyas 2006 {published data only}


Additional references

Amin 2007

Barelli 1977

Beran 1986

**Murthy 1996**

**Nunez 1990**

**Petruson 1974**

**Petruson 1979**

**RevMan 2011**

**Sengupta 2010**

**Tibbelin 1995**

**Watkinson 1997**

**Wurman 1992**

**References to other published versions of this review**

**Burton 2004**

* Indicates the major publication for the study
### Characteristics of included studies [ordered by study ID]

**Calder 2009**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>Randomised, double-blind</td>
</tr>
</tbody>
</table>
| **Participants**                                      | Setting: children’s hospital  
Country: Scotland  
Mean age: 7.4 years  
% female: 36.7  
Number randomised: 109  
Lost to follow-up: 16 (8 from treatment group and 8 from control group)                                                                 |
| **Interventions**                                     | One-off application of 75% AgNO₃ and then Naseptin® twice daily for 4 weeks versus 'sham' cautery and Naseptin® twice daily for 4 weeks  
8-week trial: 4-week treatment, 4-week follow-up                                                                                                 |
| **Outcomes**                                          | Episodes of epistaxis in weeks 5 to 8 of the trial                                                                                                                                                     |
| **Notes**                                             | Overall risk of bias unclear                                                                                                                                                                           |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias)        | Low risk           | “Those who agreed to participate were randomly allocated with sequentially numbered, sealed, shuffled envelopes that contained the instructions "treatment" or "control."  
The allocation was carried out by the principal investigator who opened the envelopes once the patient had agreed to participate” |
| Allocation concealment (selection bias)            | Unclear risk       | “The allocation was carried out by the principal investigator who opened the envelopes once the patient had agreed to participate”                                           |
| Blinding (performance bias and detection bias)     | Unclear risk       | Patient blinding was undertaken by using 'sham cautery', however on a number of occasions (≤ 15), older patients/parents noticed the wrong side of the applicator was being used  
Assessor blinding was undertaken by using different surgeons to assess the outcomes from those in the enrolment clinic; the assessors were unaware of the treatment given.  
This, however, was compromised on 3 occasions, twice when the patients informed the assessor of their treatment and once when information was sought as a patient had worsening bleeding |
Calder 2009  (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>16 patients lost to follow-up, 8 from each arm of the study</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>The majority of patients were followed up approximately 2 months after initial treatment, however those that did not attend their appointment were seen or telephoned up to 2 months later. It is known that prolonged follow-up can result in spontaneous resolution of symptoms or recurrence after initially successful treatment</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Intention-to-treat analysis utilised. Estimates (made using 2 previous studies) for resolution in the control arm were lower than expected; post hoc power analysis showed that the study was underpowered</td>
</tr>
</tbody>
</table>

Glynn 2011

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised, double-blind</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Setting: National Children's Hospital</td>
</tr>
<tr>
<td></td>
<td>Mean age: 8 years</td>
</tr>
<tr>
<td></td>
<td>Number randomised: 103</td>
</tr>
<tr>
<td>Interventions</td>
<td>75% silver nitrate and Naseptin® twice daily for 2 weeks versus 95% silver nitrate and Naseptin® twice daily for 2 weeks</td>
</tr>
<tr>
<td></td>
<td>8-week trial: initial treatment then follow-up at 2 weeks and follow-up at 8 weeks</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Episodes of epistaxis in 2 weeks following treatment and 8 weeks following treatment</td>
</tr>
<tr>
<td>Notes</td>
<td>Overall risk of bias low</td>
</tr>
</tbody>
</table>

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>200 opaque envelopes were numbered sequentially, a random number table was then used to generate the group assignment. If the last digit of the number was from 0 to 4 it was to group A, and if the last digit from 5 to 9 it was group B; these were placed inside the envelopes and sealed</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>As eligible children entered the trial sequential envelopes were opened to give the group assignment after parents had given consent</td>
</tr>
</tbody>
</table>
**Glynn 2011** (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>Low risk</td>
<td>All silver nitrate sticks were removed from packaging and placed in a bag labelled A and B, neither the patients or the doctors were aware of the concentration used until after completion of the study. To maintain blinding subsequent follow-up was carried out by a doctor who did not carry out the cauterisation</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>2 patients lost to follow-up, 1 in each arm of the study</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>-</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>An intention-to-treat analysis was used</td>
</tr>
</tbody>
</table>

**Kubba 2001**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised, single-blind</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Setting: hospital</td>
</tr>
<tr>
<td></td>
<td>Country: UK</td>
</tr>
<tr>
<td></td>
<td>Median age: 8</td>
</tr>
<tr>
<td></td>
<td>% female: 47</td>
</tr>
<tr>
<td></td>
<td>Number randomised: 103 participants</td>
</tr>
<tr>
<td></td>
<td>Lost to follow up: 15 participants</td>
</tr>
<tr>
<td>Interventions</td>
<td>Naseptin® antiseptic cream (0.5% neomycin and 0.1% chlorhexidine) versus no treatment</td>
</tr>
<tr>
<td></td>
<td>8-week trial: 4-week treatment, 4-week follow-up</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Episodes of epistaxis during 4 weeks following 4-week treatment</td>
</tr>
<tr>
<td>Notes</td>
<td>Overall risk of bias unclear</td>
</tr>
</tbody>
</table>

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>&quot;Randomisation was done at the time of receiving the referral letter. A computer-generated random list of treatment options was produced, and these were placed into separate sealed opaque envelopes, shuffled and then numbered sequentially&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>See above</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>Unclear risk</td>
<td>Single-blind study. The medical assessors were unaware of the treatment provided and assessment was carried out by different team members to those that performed the ran-</td>
</tr>
</tbody>
</table>
domination, they were also instructed not to ask about the treatment used until all data had been gathered and recorded. However, the authors admit that during assessment it may have become clear as to whether the patient was receiving treatment or not, but the assessors were happy that blinding was maintained in the majority of cases.

Incomplete outcome data (attrition bias)
All outcomes
High risk
Methodological quality was reduced by substantial losses to follow-up (14.5% of all participants; 9% treatment group, 21% of control group)

Selective reporting (reporting bias)
Unclear risk
-

Other bias
Unclear risk
Intention-to-treat analysis not undertaken

Loughran 2004

Methods
Randomised, single-blind

Participants
Setting: hospital
Country: UK
Median age: 9 years
% female: 35
Number randomised: 105 participants
Lost to follow-up: 0

Interventions
Vaseline® petroleum jelly versus no treatment
8-week trial: 4-week treatment, 4-week follow-up

Outcomes
Episodes of epistaxis during 4 weeks following 4-week treatment

Notes
Overall risk of bias low

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>&quot;Randomisation was performed using a computer generated random list, which was placed in sealed envelopes, shuffled and sequentially numbered.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>See above</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>Unclear risk</td>
<td>Single-blind study. “The member of the medical staff who reviewed the patients in the clinic was blinded to the randomisation and specifically avoided asking questions about the treatment used until the end of the assessment.” The authors admit that it may have been evident despite</td>
</tr>
</tbody>
</table>
the assessors best efforts to conceal which arm of the study the patient belonged to. Patients were aware of their presence in the treatment and control group as there was no placebo available; it is unclear whether the patient outcomes were influenced by this.

| Incomplete outcome data (attrition bias) | Low risk | No losses to follow-up |
| Selective reporting (reporting bias) | Unclear risk | The completion rate of epistaxis diaries was low, therefore the parent’s and child’s reports of the presence of nosebleeds in the preceding 4 weeks was utilised as it was the only method available |
| Other bias | Low risk | An intention-to-treat analysis was used |

**Ruddy 1991**

| Methods | Alternation, not blind |
| Participants | Setting: hospital  
Country: UK  
Age: 3 to 14 years  
% female: not known  
Number included: 48 participants  
Lost to follow-up: 3 |
| Interventions | Naseptin® antiseptic cream versus silver nitrate cautery  
8-week trial: 4-week treatment, 4-week follow-up |
| Outcomes | Episodes of epistaxis during 4 weeks following 4-week treatment |
| Notes | Overall risk of bias high |

**Risk of bias**

| Bias | Authors’ judgement | Support for judgement |
| Random sequence generation (selection bias) | High risk | No methods were mentioned within the paper, however upon contacting one of the authors they recalled alternating the patients to different treatment groups, making this a quasi-randomised study |
| Allocation concealment (selection bias) | Unclear risk | See above |
| Blinding (performance bias and detection bias) All outcomes | High risk | No blinding was used. “Neither double nor single blinding was possible because it was obvious to both surgeons and patients what technique was administered.” |
Incomplete outcome data (attrition bias)

All outcomes | Unclear risk
--- | ---
3 patients were lost to follow-up, 1 from the group treated with Naseptin® and 2 from the group treated with silver nitrate cautery. Given there were no power calculations for this study, our calculations that 53 participants were required per group for 80% power suggests the study was underpowered prior to these losses, making the impact unclear

Selective reporting (reporting bias)

Unclear risk

- Other bias

High risk

No power calculations for correct sample sizes were apparently made, with the result that the sample size was too small

AgNO₃: silver nitrate

### Characteristics of excluded studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geisthoff 2010</td>
<td>ALLOCATION Randomised controlled trial PARTICIPANTS Patients with hereditary haemorrhagic telangiectasia and minimum age 18 years to be included in study</td>
</tr>
<tr>
<td>Mathiason 2005</td>
<td>ALLOCATION Randomised, double-blind PARTICIPANTS Adults (aged 30 to 90 years)</td>
</tr>
<tr>
<td>Morra 1982</td>
<td>ALLOCATION Randomised, double-blind PARTICIPANTS Adults (aged 14 to 82 years)</td>
</tr>
<tr>
<td>Moumoulidis 2006</td>
<td>ALLOCATION Randomised, single-blind PARTICIPANTS Adults (aged 16 and over)</td>
</tr>
<tr>
<td>Murthy 1999</td>
<td>ALLOCATION Randomised, not blind PARTICIPANTS Adults and children combined. Author contacted: raw data no longer available; impossible to extract paediatric data</td>
</tr>
<tr>
<td>Study</td>
<td>ALLOCATION</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Tang 2001</td>
<td>Unclear</td>
</tr>
<tr>
<td>Tarantino 1989</td>
<td>Quasi-randomised (alternation), no allocation concealment, blinding unclear</td>
</tr>
<tr>
<td>Teker 2010</td>
<td>Randomised, non-blind</td>
</tr>
<tr>
<td>Troikaa 2010</td>
<td>Unclear</td>
</tr>
<tr>
<td>Vaiman 2002</td>
<td>Randomised, allocation concealed, double-blind</td>
</tr>
<tr>
<td>Yaniv 2009</td>
<td>Randomised, double-blind, placebo-controlled trial</td>
</tr>
<tr>
<td>Ye 1997</td>
<td>No randomisation, allocation concealment or blinding reported. Author contacted, but failed to respond</td>
</tr>
<tr>
<td>Zhang 2008</td>
<td>Randomised, blinding unclear</td>
</tr>
</tbody>
</table>

### Characteristics of studies awaiting assessment [ordered by study ID]

**Vyas 2006**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised (method of randomisation/allocation unavailable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Setting: hospital</td>
</tr>
<tr>
<td></td>
<td>Country: UK</td>
</tr>
<tr>
<td></td>
<td>Median age: unknown</td>
</tr>
<tr>
<td></td>
<td>% female: unknown</td>
</tr>
</tbody>
</table>
| Interventions | Number randomised: 205 participants  
Lost to follow-up: unknown |
|---------------|-----------------------------------|
| 1. Vaseline® only | 2. Naseptin® only  
3. Silver nitrate cautery only  
4. Silver nitrate cautery and Naseptin® |
| Outcomes | Episodes of epistaxis in 2 and 6 months following treatment |
| Notes | Full details of study unavailable, no statistical analysis can be undertaken |
## Appendices

### Appendix 1. Search strategies

<table>
<thead>
<tr>
<th>CENTRAL</th>
<th>PubMed</th>
<th>EMBASE (Ovid)</th>
<th>CINAHL (EBSCO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. EPISTAXIS single term</td>
<td>#1 &quot;Epistaxis&quot; [Mesh] OR epistax* [tiab] OR nosebleed* [tiab] OR rhinorrhag* [tiab] OR rhinorrhaeg* [tiab]</td>
<td>1 &quot;epistaxis/ 2 (epistax* or nosebleed* or rhinorrhag* or rhinorrhaeg*).tw. 3 exp &quot;nose/ 4 (nose or nasal).ti. 5 exp &quot;bleeding/ 6 (hemorrhag* or haemorrhag* or bleed* or bloodloss or (blood and loss*)).ti. 7 4 or 3 8 6 or 5 9 8 and 7 10 1 or 9 or 2</td>
<td>S1 (MH &quot;Epistaxis&quot;) S2 TI epistax* or nosebleed* or rhinorrhag* or rhinorrhaeg* S3 (MM &quot;Nose&quot;) S4 TI nose or nasal S5 S3 or S4 S6 (MH &quot;Hemorrhage&quot;) S7 TI (hemorrhag* or haemorrhag* or bleed* or bloodloss) or TI (blood AND loss*) S8 S6 or S7 S9 S5 and S8 S10 S1 or S2 or S9</td>
</tr>
<tr>
<td>(MeSH term)</td>
<td>#2 &quot;nose&quot; [Mesh] OR nose [tiab] OR nasal [tiab]</td>
<td>#4 #1 OR (#2 AND #3)</td>
<td></td>
</tr>
<tr>
<td>2. epistax*</td>
<td>#3 &quot;hemorrhage&quot; [Mesh] OR hemorrhag* [tiab] OR haemorrhag* [tiab] OR bleed* [tiab] OR bloodloss* [tiab]</td>
<td>#5 #9 OR #12</td>
<td></td>
</tr>
<tr>
<td>3. rhinorrhag* OR rhinorrhaeg*</td>
<td>#5 #9 OR #12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. NOSE single term (MeSH term)</td>
<td>#6 #1 OR #2 OR #3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. nose OR nasal*</td>
<td>10. #4 OR #5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. HEMORRHAGE explode all trees (MeSH term)</td>
<td>11. #6 OR #7 OR #8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. bleed* OR hemorrhag* OR haemorrhag*</td>
<td>12. #10 AND #11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. bloodloss* OR (blood NEAR loss*)</td>
<td>13. #9 OR #12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Cochrane ENT Disorders Group Trials Register

- #1 TI=(epistax* or nosebleed* or rhinorrhag* or rhinorrhaeg*)
- #2 TI=(nose or nasal).ti.
- #3 TI=(hemorrhag* or haemorrhag* or bleed* or bloodloss or (blood and loss*)).ti.
- #4 #2 AND #3
- #5 #1 OR #4

### CAB Abstracts (Ovid)

- 1 epistaxis/ 2 (epistax* or nosebleed* or rhinorrhag* or rhinorrhaeg*).tw. 3 (nose or nasal).ti. 4 (hemorrhag* or haemorrhag* or bleed* or bloodloss or (blood and loss*)).ti. 5 3 AND 4 6 1 OR 2 OR 5

### ICTRP

- epistaxis OR nosebleed* OR rhinorrhag* OR rhinorrhaeg* OR nose AND bleed* OR nose AND hemorrhag* OR nose AND haemorrhag* OR nose AND blood*
WHAT'S NEW

Last assessed as up-to-date: 5 March 2012.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 March 2012</td>
<td>New citation required and conclusions have changed</td>
<td>Two further studies are included in the review (Calder 2009; Glynn 2011). We made a small change to the conclusions with regard to silver nitrate nasal cautery. We have used the Cochrane ‘Risk of bias’ tool to assess the quality of studies.</td>
</tr>
<tr>
<td>5 March 2012</td>
<td>New search has been performed</td>
<td>New searches (November 2009, July 2011 and March 2012).</td>
</tr>
</tbody>
</table>

HISTORY

Review first published: Issue 1, 2004

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 October 2008</td>
<td>Amended</td>
<td>Converted to new review format.</td>
</tr>
<tr>
<td>13 November 2007</td>
<td>New search has been performed</td>
<td>The review was updated. The search strategy was run on all databases in October 2007. We found one new potential study, but this was still ongoing and will be included in a future update of the review.</td>
</tr>
</tbody>
</table>

CONTRIBUTIONS OF AUTHORS

Ali Qureishi: lead author, study selection, data extraction, quality assessment, data analysis and interpretation and writing of review.

Martin Burton: design of review, study selection, quality assessment, analysis and interpretation of data. Clinical, methodological and editorial input and advice.

DECLARATIONS OF INTEREST

None known.
SOURCES OF SUPPORT

Internal sources
• None, Not specified.

External sources
• None, Not specified.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW
In the 2012 update we have adopted the Cochrane 'Risk of bias' tool for the assessment of study quality, as guided by the Cochrane Handbook for Systematic Reviews of Interventions (Handbook 2011).

INDEX TERMS

Medical Subject Headings (MeSH)
Administration, Intranasal; Chlorhexidine [therapeutic use]; Drug Combinations; Emollients [therapeutic use]; Epistaxis [*drug therapy]; Neomycin [therapeutic use]; Petrolatum [therapeutic use]; Randomized Controlled Trials as Topic; Recurrence; Silver Nitrate [therapeutic use]

MeSH check words
Adolescent; Child; Child, Preschool; Humans; Infant