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Main Article

Xylometazoline hydrochloride 0.1 per cent versus physiological saline in nasal surgical aftercare: a randomised, single-blinded, comparative clinical trial

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Abstract

Objectives: A variety of topical preparations are used for symptomatic relief following nasal surgery. The aim of this study was to compare the effect of two commonly used products on patient symptom scores following nasal surgery.

Design: Randomised, single-blinded, comparative clinical trial.

Setting: A single, secondary otorhinolaryngology centre.

Participants: One hundred and twenty patients undergoing septoplasty or functional endoscopic sinus surgery as an isolated procedure between November 2003 and January 2006. Patients undergoing additional nasal procedures were excluded, as were those requiring additional post-operative medications other than standardised analgesia.

Methods: Following nasal surgery, patients were randomised to receive either xylometazoline hydrochloride 0.1 per cent nasal spray or a sterile physiological saline aerosol.

Main outcome measures: Visual analogue scale symptom scores for nasal obstruction, rhinorrhoea, pain, loss of sense of smell and bleeding were assessed at day 10 post-operatively.

Results: Post-operative symptom scores were compared between treatment groups. Overall, median pain scores were significantly higher in the xylometazoline group ($p = 0.03$, chi-square test). When analysed by procedure, median pain scores were significantly higher in septoplasty patients using xylometazoline ($p = 0.019$, chi-square test).

Conclusion: There is no evidence to support the use of xylometazoline hydrochloride 0.1 per cent nasal spray over aerosolised physiological saline alone, following nasal surgery. Furthermore, there may be more pain associated with the post-operative use of xylometazoline.

Key words: Paranasal Sinuses; Otorhinolaryngologic Surgical Procedures; Postoperative Care; Xylometazoline; Saline

Background

Patients undergoing nasal surgery commonly experience a variety of symptoms in the post-operative period, including blockage, rhinorrhoea, pain, bleeding and reduced sense of smell. A variety of preparations are currently recommended for symptomatic relief in the post-operative period.[1,2] These include saline irrigations, steam inhalations, decongestants and intranasal steroid preparations. The intention of these interventions is to reduce nasal swelling, crusting and resultant symptoms.

There is currently little evidence in the literature to support the use of any particular preparation in nasal surgical aftercare.[3,4] Whilst the benefits of treating the nose to reduce swelling and crusting in the post-operative period would seem logical, it is not clear whether decongestants (with their potential side effects) confer any benefit on patients' symptoms, compared with simple saline solutions.

We conducted a randomised, single-blinded, comparative clinical trial of xylometazoline hydrochloride 0.1 per cent adult nasal spray versus a non-pharmacologically active, naturally occurring, isotonic sea water solution, in order to compare patients' symptom scores following nasal surgery.

We hypothesised that the use of xylometazoline hydrochloride (a decongestant) may provide additional benefit for those symptoms that we felt may be related to inflammatory vasodilation, i.e. blockage and bleeding.

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Method

Ethical considerations

Ethical approval was obtained from the Grampian local ethics department, and permission to carry out a study using a pharmaceutical product (i.e. xylometazoline hydrochloride 0.1 per cent) was obtained from the Medicines and Healthcare Regulatory Authority. Participation in the study was voluntary, and all patients attending for functional endoscopic sinus surgery (FESS) or septoplasty as an isolated procedure were included. A patient information sheet was provided and informed consent obtained from participants on admission to hospital.

Study design

A power calculation was performed to establish the required sample size.

In order to detect a difference in mean symptom scores on a visual analogue scale (VAS) of 10 mm or more, at a 5 per cent level of significance with 80 per cent power, a sample size of 60 patients was required in each arm of the trial (assuming a standard deviation of 19 mm).

The study was carried out at Aberdeen Royal Infirmary between November 2003 and January 2006. One hundred and thirty-one consecutive patients undergoing septoplasty or FESS as an isolated procedure were recruited in an in-patient setting. As per FESS exclusion criteria, any patients undergoing additional nasal procedures (such as turbinate reduction or intranasal polypectomy) were excluded. Patients who post-operatively required steroids or any other 'take home' medications other than standardised analgesia (i.e. 1 g paracetamol six-hourly) were also excluded.

Patients were randomised to receive either xylometazoline hydrochloride 0.1 per cent (Otrivine®; Novartis, Basel, Switzerland) adult nasal spray or sterile physiological saline aerosol (Sterimar®; Sofibel SAS, 92686 Levallois Perret cedex, France). Randomisation was performed by a Microsoft Access database generated by the National Health Service Grampian research and development department. This software program randomly allocated the patient's identity number to either the xylometazoline or physiological saline group.

Patient assessment

Patients were recruited on the first post-operative morning, when the lead investigator supplied a patient information sheet and informed consent was obtained.

In addition to the patient information sheet, patients were given a simple, 100 mm visual analogue scale (VAS) scoring sheet with which to assess post-operative symptoms. The VAS scoring sheet consisted of five lines, one for each symptom in question (pain, bleeding, loss of sense of smell, rhinorrhoea ('running') and blockage). A clear explanation of how to complete the scoring sheet was given. For instance, 0 mm on the pain line corresponded to no discomfort at all, while 100 mm corresponded to the worst imaginable pain. The other symptoms (bleeding, loss of sense of smell, rhinorrhoea and nasal blockage) were described, and their scoring system was explained in a similar manner.

Patients were then randomised to receive either xylometazoline hydrochloride 0.1 per cent (Otrivine) adult nasal spray or a physiological sterile saline aerosol (Sterimar).

The physiological sterile saline aerosol contained 31.82 ml of sea water per 100 ml, plus monohydrated manganese salts in order to achieve a physiologically comparable concentration.

A clear explanation of how to use each product was given, including technique and dosing schedule. For the xylometazoline group, the dose was two puffs four times daily to both nostrils, as per the *British National Formulary*. For the physiological saline group, the dose was six times daily to both nostrils, encouraging patients to rinse from one side until saline ran through the contralateral nostril, as per the manufacturer's instructions. As pain scores were being recorded, analgesia was standardised to paracetamol 1 g six-hourly. The importance of compliance was explained to each patient at the time of recruitment. Paracetamol use was recorded on day 10.

On the 10th post-operative day, patients completed and returned the symptom assessment sheet judging their symptoms on that day. The symptom sheet was returned in a pre-paid envelope and was identifiable only by a number, which was retained in the randomisation program.

The visual analogue scores were measured by a second investigator blinded to the procedure performed and the treatment administered. The results were then cross-referenced with the randomisation log.

Statistical analysis

Data were entered into an Excel spreadsheet and then analysed using the Statistical Package for the Social Sciences version 14.0 software (SPSS Inc, Chicago, Illinois, USA). Medians of the visual analogue scores were compared using the median test, because the score distributions' shapes were not normal and differed to some degree between the treatment groups.

Results

One hundred and thirty-one patients were recruited between November 2003 and January 2006 (Figure 1). Despite telephone reminders to complete and return the symptom scoring sheets on day 10, only 120 scoring sheets were returned. The eleven patients who did not return their scoring sheets were excluded from further analysis (Figure 1).

The 120 patients included in the analysis comprised 77 men and 43 women, with a mean age of 43.1 years (range 16–73 years). Forty-seven patients underwent FESS and 73 patients underwent septoplasty. A statistically significantly greater proportion of men underwent septoplasty compared with FESS (56 men *vs* 17 women and 21 men *vs* 26 women, respectively) ($p = 0.001$, chi-square test). There was also a statistically significant difference in patients' mean ages, comparing the septoplasty (40.3 years) and FESS (47.6 years) groups ($p = 0.008$, *t*-test). We felt

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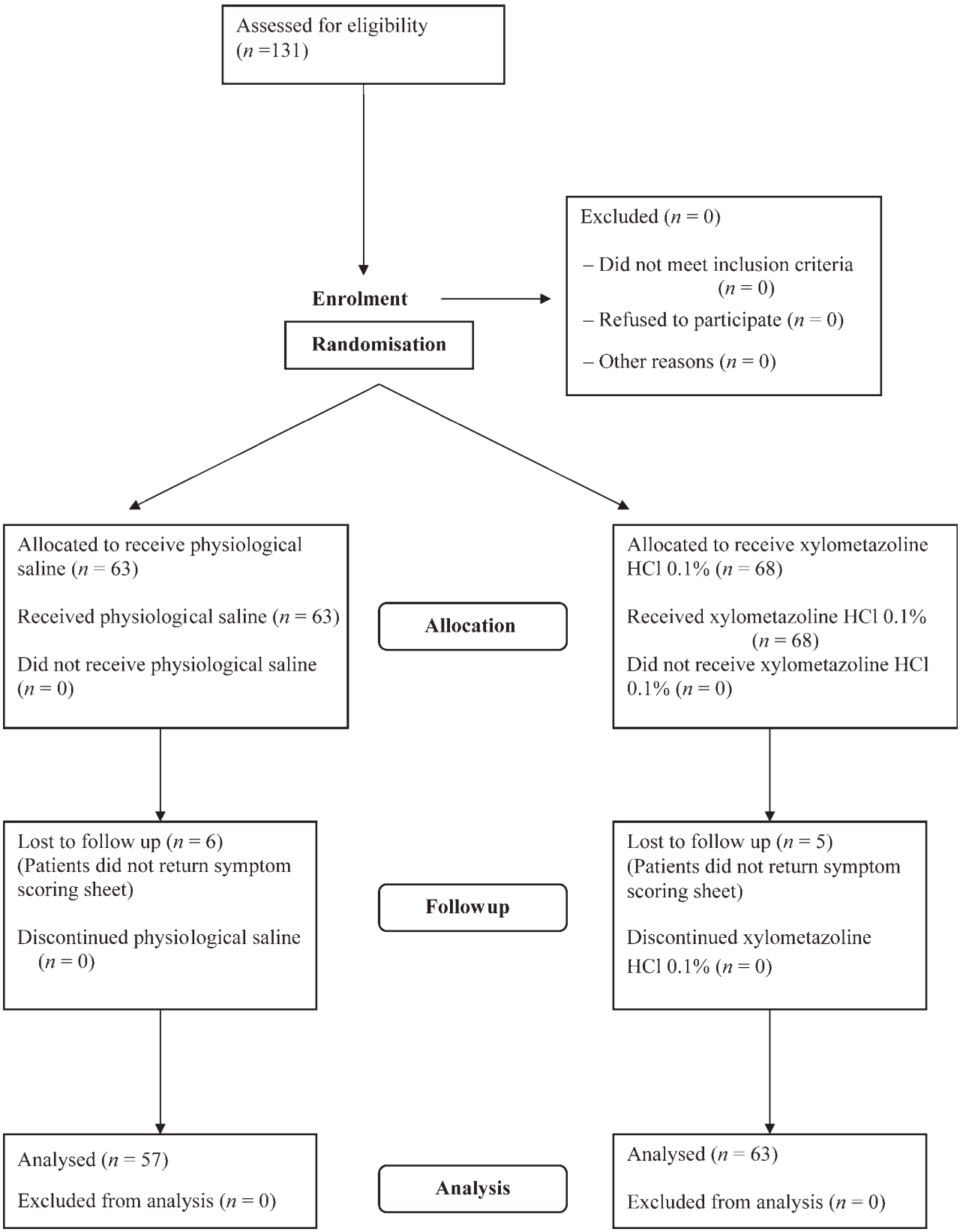

FIG. 1
Flow chart showing patient enrolment, randomisation, allocation, follow up and analysis.

these findings reflected the fact that younger patients were more likely to require septal surgery as a consequence of trauma. However, it is important to note that the ratio of men to women was similar in the xylometazoline and physiological saline groups (Table I).

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TABLE I

XYLOMETAZOLINE AND PHYSIOLOGICAL SALINE GROUPS: DEMOGRAPHIC DATA

Characteristic	Xylometazoline*	Saline†
Age ± SD (mean; years)	44.8 (15.5)	41.3 (14.1)
Procedure (*n*)		
Septoplasty	39	34
FESS	24	23
Male:female (*n*)		
Septoplasty	30:9	26:8
FESS	8:16	13:10
Total	38:25	39:18

*$n = 63$; †$n = 57$. SD = standard deviation; FESS = functional endoscopic sinus surgery

Sixty-three patients received xylometazoline post-operatively and 57 received physiological saline. In the xylometazoline group, 24 had undergone FESS and 39 septoplasty. In the physiological saline group, 34 patients had undergone septoplasty and 23 FESS (Table I).

All the patients in the study recorded using 1 g paracetamol six-hourly, as instructed at the time of recruitment.

Symptom scores for the two treatment groups were analysed, comparing post-operative nasal obstruction, rhinorrhoea, pain, loss of sense of smell and bleeding.

Overall, median pain scores were statistically significantly higher with xylometazoline compared with physiological saline ($p = 0.030$, chi-square test) (Table II). When we considered separately patients undergoing FESS or septoplasty, median pain scores were higher in the xylometazoline group for both procedures, but this difference was only statistically significant in septoplasty patients ($p = 0.019$, chi-square test) (Figures 2 and 3).

There were no statistically significant differences noted for the other symptoms, either overall or adjusting for procedure performed (Table II and Figures 2–4).

None of the patients using either xylometazoline or physiological saline required any additional 'rescue' analgesia.

The 11 patients who did not return their symptom score sheets were followed up by telephone. Four were not contactable, five had lost their symptom score sheets and the remaining two patients no longer wished to take part in the study.

TABLE II

XYLOMETAZOLINE AND PHYSIOLOGICAL SALINE GROUPS: VAS SCORES FOR POST-OPERATIVE SYMPTOMS

Symptom	Xylometazoline*	Saline†	*p*
Pain	22 (5–35)	10 (5–22)	0.03
'Running'	11 (4–30)	10 (4–19)	0.72
Loss of sense of smell	39 (17–64)	41 (13–79)	1.00
Bleeding	5 (0–18)	4 (1–17)	0.86
Blockage	42 (13–72)	40 (19–67)	0.72

Data are shown as median (interquartile range, median test). *$n = 63$; †$n = 57$. VAS = visual analogue scale

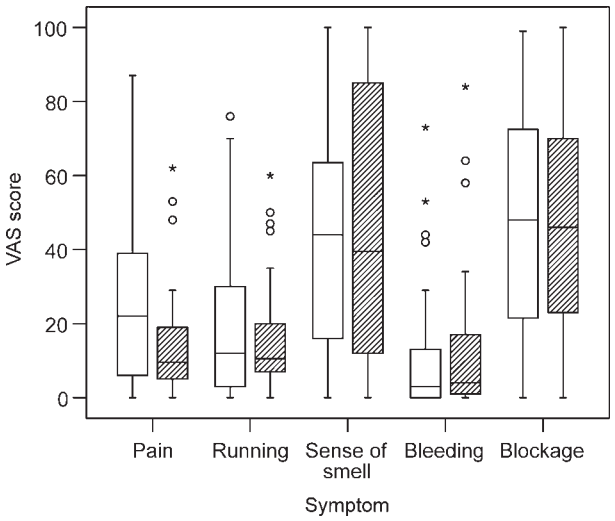

FIG. 2

Box plots of visual analogue scale (VAS) scores for the different symptoms, in septoplasty patients treated with xylometazoline HCl 0.1% (white boxes) or physiological saline (shaded boxes). Outliers (o) and extreme values (*) are indicated.

No adverse events were reported relating to the use of either of the trial products.

Discussion

Background

Symptoms following nasal surgery are common, including nasal obstruction, rhinorrhoea, pain, bleeding and hyposmia. These are related to post-operative inflammation, swelling and mucociliary dysfunction as a result of the surgery and underlying mucosal pathology. It has been suggested that intranasal saline irrigation may serve to improve mucociliary

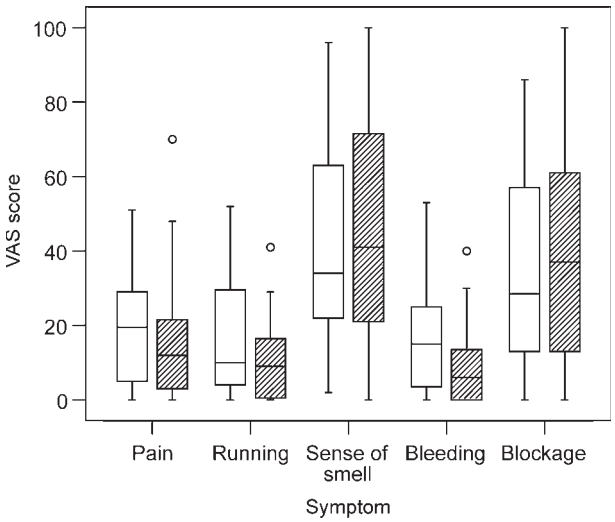

FIG. 3

Box plots of visual analogue scale (VAS) scores for the different symptoms, in functional endoscopic sinus surgery patients treated with xylometazoline HCl 0.1% (white boxes) or physiological saline (shaded boxes). Outliers (o) and extreme values (*) are indicated.

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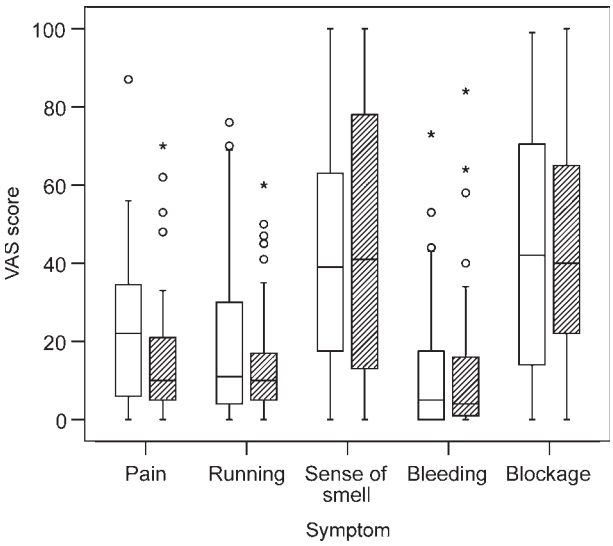

FIG. 4
Box plots of visual analogue scale (VAS) scores for the different symptoms, in all patients treated with xylometazoline HCl 0.1% (white boxes) or physiological saline (shaded boxes). Outliers (o) and extreme values (*) are indicated.

clearance by increasing the ciliary beat frequency.[5,6] Additionally, patients often find intranasal saline irrigation useful in softening crusting after nasal surgery,[2] although uncertainty exists as to whether hypertonic or normal saline is best.[5–9]

After nasal surgery, it is widespread current practice to give patients a variety of preparations intended to combat symptoms and promote mucosal healing. These range from simple saline irrigations to intranasal or oral steroids. There is currently little evidence in the literature to support the preferential use of any one product or method of instillation over another.

Synopsis of key findings

The current study was a single-blinded, randomised, comparative clinical trial of the use of xylometazoline hydrochloride 0.1 per cent versus physiological saline following nasal surgery, comparing patients' symptom scores. We hypothesised that the use of a decongestant may provide additional benefit for those symptoms we felt may be related to inflammatory vasodilation, i.e. blockage and bleeding. We found no difference in median scores for either of these symptoms. Additionally, there was a significantly higher median pain score associated with the use of xylometazoline, particularly in those who had undergone septoplasty.

Based on our findings, there is no clear evidence to support the use of xylometazoline hydrochloride 0.1 per cent rather than simple physiological aerosolised saline, in order to control post-operative nasal symptoms.

Economic considerations

If the results of the current study are analysed from an economic standpoint, topical decongestants are relatively cheap, with xylometazoline hydrochloride 0.1 per cent (Otrivine adult nasal spray) costing £1.91 for 10 ml, whereas physiological sea water micro-spray (Sterimar) costs £5.99 for a 100 ml canister from commercial pharmacies. As physiological sea water microspray is a medical device rather than a medicinal product, many hospital pharmacies do not routinely stock it, and this should be taken into account when considering the economic impact on the health service. The cost is therefore borne by the patient, and this may have a negative effect in terms of patient compliance, with some patients being unable to afford the treatment.

- **A variety of topical preparations are used for symptomatic relief following nasal surgery. The aim of this study was to compare the effect of two commonly used products on patient symptom scores following nasal surgery**
- **Patients were randomised to receive either xylometazoline hydrochloride 0.1% nasal spray or sterile physiological saline aerosol, following nasal surgery**
- **There was no evidence to support the use of xylometazoline over physiological saline alone after nasal surgery**
- **Additionally, there may be more pain associated with the post-operative use of xylometazoline**

Another important consideration when prescribing post-operative intranasal preparations is potential side effects. Xylometazoline hydrochloride 0.1 per cent has the potential to cause rhinitis medicamentosa if abused. Some patients often continue decongestants, despite warnings, as they find them the only effective symptomatic relief. This is not a problem with saline irrigations, which can be used safely long-term with no significant side effects other than a degree of local irritation.

Study limitations

The authors recognise the limitations of not having a blinded, placebo arm of the trial.

The authors also recognise the limitation of a 'one-off' assessment of post-operative nasal symptoms on day 10. Currently, very little is known about the decay in pain and the use of post-operative analgesia following nasal surgery.[10–12] One recent study has suggested that patients take approximately nine to 10 days to recover from nasal surgery.[10]

Although the use of a pain diary may have yielded more information in this area, the authors felt that this may have reduced patient compliance, which may have impacted on the power of the study. Consequently, a single assessment of post-operative nasal symptoms on day 10 was used.

Patients using additional post-operative analgesics or topical nasal preparations were excluded from the study, as the authors felt that this may affect

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patients' VAS scores. Therefore, in an attempt to standardise post-operative treatment, it is recognised and accepted that this study population differs from that of the general population undergoing either septoplasty or FESS.

Unfortunately, it was not possible to standardise either the surgical technique or the extent of the surgery carried out, and the authors accept that this may have led to some variability in symptom-reporting between patients.

Conclusion

There is no evidence to support the use of xylometazoline hydrochloride 0.1 per cent over physiological aerosolised saline alone after nasal surgery. Additionally, there may be more pain associated with the use of xylometazoline hydrochloride 0.1 per cent post-operatively.

Further research is required to compare saline irrigation to other commonly prescribed post-operative medications, in order to establish if any additional benefit is obtained.

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