Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER470
Topic:	FloSeal use in the treatment of epistaxis
Summary of findings:	FloSeal is a bioresorbable topical haemostatic agent which can be used in the treatment of epistaxis (nosebleeds) if first aid treatments do not work. This can avoid the requirement for packing and subsequent hospital stays for people who require hospital interventions for the treatment of epistaxis. HTW researchers identified one guideline on the treatment of epistaxis. Two systematic reviews/ meta-analysis, one additional brief literature review and eight individual studies which assessed FloSeal alongside other methods of treating epistaxis were also identified. Overall, some evidence was found to support the use of FloSeal in treating anterior epistaxis, but mixed evidence was found in the use of FloSeal for treating posterior epistaxis and more research may be needed in this area. Economic analyses considering the US and Canadian healthcare systems suggest that FloSeal may be cost-effective when compared to packing in the treatment of epistaxis. However, these studies are only partially applicable to the UK NHS perspective.

Introduction and aims

Epistaxis is bleeding from the nose, caused by damage to the blood vessels of the nasal mucosa. It is a common condition, with around 60% of the UK population having experienced it during their lifetime. Occurrence peaks in incidence from ages 2-10 years of age, and in those over 45. Epistaxis can be anterior, originating towards the front of the nose and resulting in bleeding out of the nostrils, or posterior, originating towards the back of the nose near the throat which can result in blood going down the throat. Posterior epistaxis is more likely to require medical attention.

Medical attention for a nosebleed is only sought in a small proportion of instances (around 6% of cases). According to data submitted by the Topic Proposer of hospital admissions across England, around 10,000 people are admitted to hospital each year for epistaxis, at a cost to the NHS of over £12 million (Dallimore, 2022). Patel and Fowell (2013) state there an average of 1440 admissions for epistaxis in Wales per year. Those who require medical attention include people who are haemodynamically compromised or for whom first aid treatments (pressure to the nose) does not work. At that point, NICE Clinical Knowledge Summary (CKS, 2022) recommend performing nasal cautery or packing as the next line of treatment. When using packing, a 48-hour period of hospitalisation for observation is required and the packing is removed once the condition resolves, which can cause re-bleeding. Treatment options which minimise the use of packing and subsequent hospitalisation would therefore reduce the number of inpatient stays for people with acute epistaxis.

FloSeal is a topical haemostatic agent, which uses a paste-like mixture of thrombin and gelatin to promote haemostasis and clotting at the site of a bleed. It can be used in several indications, but this report is focused on its use in the treatment of epistaxis. It is bioresorbable, and as such does not need removing in the same way that packing does. There are similar bioresorbable technologies available, for example Nasopore which is a foam packing/ dressing, Surgicel which is made from oxidized regenerated cellulose and Surgiflo, which is another gelatin/ thrombin matrix, but these are not specifically covered within this report.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of FloSeal in the treatment of epistaxis in the hospital setting.

Evidence overview

No Heath Technology Assessments reviewing the use of FloSeal or other topical haemostatic agents were identified.

Secondary Evidence

HTW identified one systematic review (Iqbal et al, 2017), one systematic review and meta-analysis (Milinis et al, 2021) and a clinical trial combined with a literature review (Wakelam et al, 2017) assessing the use of FloSeal and other haemostatic agents in the treatment of epistaxis.

Milinis et al (2021) reviewed the evidence around dissolvable intranasal haemostatic agents and identified 12 studies, eight of which related to a gelatin-thrombin matrix (six reporting FloSeal, and two reporting Surgicel). The meta-analysis favoured dissolvable haemostatic agents over packing in short-term control of bleeding (risk ratio 1.20; 95% confidence interval 1.05 to 1.37; P=0.007). The authors noted that there was only one study reporting 30-day control and this did not show a statistically significant difference between packing and haemostatic agents. Milinis et al (2021) noted that in most studies, successful short-term haemostasis was reported in 80%-100% of patients, but this was substantially reduced in one study (Khan et al, 2015) where it was only

achieved in 14% of patients (described further below). Patient discomfort was assessed in two studies, lower discomfort levels were reported during insertion and treatment/ removal (visual analogue scale [VAS] 2.4/10 vs 7.8/10, p=0.022 and VAS 0.5/10 vs. 4.5/10, p=0.002, respectively), when using FloSeal compared to nasal packs. Additionally, patient satisfaction was higher (VAS 9.1/10 vs 1.2/10, p<0.001) when FloSeal was used compared to nasal packs. The authors reported heterogeneity in outcome measures and inclusion criteria, and a moderate to high risk of bias in all studies.

Iqbal et al (2017) had a wider remit and reviewed both non-dissolvable and dissolvable packs. They identified 27 articles overall, nine of which reviewed dissolvable packs (including FloSeal). There were no complications reported, and the evidence identified suggested there was no need to admit patients who were treatment via dissolvable packs into hospital, but one study did suggest an observation period of one hour prior to discharge. The authors found some evidence supporting use of FloSeal in anterior epistaxis, but less robust evidence supporting its use in posterior epistaxis. There was some heterogeneity and bias amongst studies noted. Iqbal et al (2017) also noted that FloSeal could be applied by appropriately trained non-specialist staff.

Wakelam et al (2017) reported the outcomes of three studies which used FloSeal, again noting that a good level of patient satisfaction was identified in the literature. They found that no complications were reported and that there were lower re-bleed rates. The authors noted that FloSeal was less effective in treating posterior bleeds according both to the included literature, and their own trial results, in which it failed within the one patient included who had a posterior bleed, who subsequently required surgical intervention.

Primary Evidence

HTW identified seven individual studies, five of which had been included in the above reviews (Wakelam et al, 2017; Khan et al, 2015; Lau et al, 2016; Cote et al, 2010; Mathiasen et al, 2005) and two had not (Lee et al, 2019 and Murray et al, 2018). One additional case-study was identified from the secondary evidence references (Kilty et al, 2013).

Lee et al (2019) performed a prospective trial in two centres. People with anterior epistaxis who also had hereditary hemorrhagic telangiectasia were treated with FloSeal, and seven patients were included in their final analysis. They found FloSeal was well-tolerated and improved clinical assessment scores of the nasal cavity at one-month, but it did not improve epistaxis severity score.

Murray et al (2018) performed a randomised controlled trial in two centres with people referred for persistent epistaxis, randomising between FloSeal and packing. They found no difference in initial haemostasis (76.9% vs. 84.6%, p = 1.000), haemostasis at 48 hours (76.9% vs. 69.2%, p=1.000), requirement for admission (15.4% vs. 46.1%, p = 0.202) or 30-day re-presentation rates (15.4% vs. 46.1%, p=0.202). However, they found that pain during treatment and removal was reduced, and that FloSeal provided a cost saving.

Lau et al (2016) noted a success rate of 75% for FloSeal (v 85% for packing, no statistically significant difference) with similar levels of re-admission. Their reported success rates are in line with Murray et al (2018) as reported above, Cote et al (2010), who noted 80% success rate, and Wakelam et al (2017) who reported a 90% success rate. Mathiasen et al (2005) reported a statistically significant improvement in success rate when treating anterior epistaxis compared to packing (9.9% vs. 7.7%, p<.001). Khan et al (2015) noted an overall success rate of only 14%, with a much higher success rate when treating anterior epistaxis; FloSeal worked in 66% of three anterior bleed cases and 9% of 36 posterior bleed cases (posterior bleed fail rate was statistically

significant, p<0.001). This is in contrast to Kilty et al (2013) who treated patients with posterior epistaxis only and had a success rate of 80% with Floseal.

Mathiason et al (2005) reported that re-bleed rates within seven days were 14% with FloSeal and 40% with nasal packing, and at removal of the pack, 63% patients experienced a re-bleed (compared to no FloSeal patients, p<0.001). In addition, it was reported that fewer in-person ENT consultations were requested in people treated with FloSeal compared to nasal packing (8.6% vs. 31.0%, p<0.05) (Mathieson et al, 2005).

Studies also reported on length of stay in FloSeal groups. Lau et al, 2016 noted a general trend in shorter stays but noted this was not statistically significant. Wakelam et al (2017) reported stays were only 2.75 hours, but no comparative duration of stay for other treatment options was provided.

Economic evidence

HTW identified two economic analyses of FloSeal (Le et al, 2018; Murray et al, 2018), and one brief cost summary within a trial (Kilty et al, 2013).

Le et al (2018) performed a cost-utility analysis of FloSeal using a Markov model over a lifetime horizon from the perspective of the Canadian healthcare system. They found that FloSeal had higher costs (CAD6,527 vs. CAD$4,460) but greater quality adjusted life years (QALYs) than packing (8.183 vs. 7.915). The resulting incremental cost effectiveness ratio (ICER) of CAD$7,718 per QALY is below thresholds typically applied in Canada. suggesting that, despite a greater upfront cost than packing, FloSeal was cost-effective.

Murray et al (2018) performed an economic evaluation from a societal perspective and presented results to show the perspectives of a single-payer health system. They found that there was a mean cost-saving of CAD$1568, and CAD$2233 from a wider societal perspective. They noted that these cost savings were maintained even if the cost of FloSeal increased four-fold. FloSeal was estimated to be both cheaper and more effective compared with nasal packing. It was reported to be the dominant strategy, with an ICER of –CAD$11,891 per re-bleed avoided (95% CI: -CAD$37,658 to +CAD$473).

Kilty et al (2013) state that institutional per-case costs of treating patients with posterior epistaxis were $522 with Floseal, $2,697 with endoscopic surgery, $4,222 with posterior packing and $5,010 with embolisation.

Areas of uncertainty

There was mixed evidence for the treatment of posterior epistaxis, which is more likely to need hospital treatment than anterior epistaxis. More evidence is needed in this setting.

First-line treatments for epistaxis in the UK include nasal cautery, and there was limited evidence comparing FloSeal against this method. Further research may be required in this area.

Economic analysis performed to date considered Canadian and American settings and therefore is only partially applicable to the UK setting. Economic analysis considering the perspective of the UK NHS would be required to fully demonstrate cost effectiveness.

Literature search results

Health technology assessments and guidance

National Institute for Health and Care Excellence. (2022). Epistaxis (nosebleeds): Scenario: Acute epistaxis. Clinical Knowledge Summaries. Available at: https://cks.nice.org.uk/topics/epistaxis-nosebleeds/management/acute-epistaxis/ [Accessed 05/05/2023)

Evidence reviews and economic evaluations

Iqbal I, Jones G, Dawe N et al. (2017). Intranasal packs and haemostatic agents for the management of adult epistaxis: Systematic review. The Journal of Laryngology & Otology. 131(12): 1065-1092. https://doi.org/10.1017/S0022215117002055

Le A, Thavorn K, Lasso A, et al. (2018). Economic evaluation of floseal compared to nasal packing for the management of anterior epistaxis. Laryngoscope. 128(8): 1778-1782. https://doi.org/10.1002/lary.27081

Milinis K, Swords C, Hardman JC et al. (2021). Dissolvable intranasal haemostatic agents for acute epistaxis: A systematic review and meta-analysis. Clinical Otolaryngology. 46(3): 485-495. https://doi.org/10.1111/coa.13717

Wakelam OC, Dimitriadis PA, Stephens J. (2016). The use of FloSeal haemostatic sealant in the management of epistaxis: a prospective clinical study and literature review. The Annals of The Royal College of Surgeons of England. 99(1):28-30. https://doi.org/10.1308/rcsann.2016.0224

Individual studies

Côté D, Barber B, Diamond C, Wright E. (2010). FloSeal hemostatic matrix in persistent epistaxis: prospective clinical trial. Journal of Otolaryngology - Head & Neck Surgery. 39(3):304-8. PMID: 20470677.

Khan MK, Reda El Badawey M, Powell J, Idris M. (2015). The utility of FloSeal haemostatic agent in the management of epistaxis. The Journal of Laryngology & Otology. 129(4):353-7. https://doi.org/10.1017/S0022215115000663

Lee JM, Wu V, Faughnan ME et al. (2019). Prospective pilot study of Floseal® for the treatment of anterior epistaxis in patients with hereditary hemorrhagic telangiectasia (HHT). Journal of Otolaryngology - Head & Neck Surgery. 48(1):48. https://doi.org/10.1186/s40463-019-0379-y

Lau AS, Upile NS, Lazarova L, Swift AC (2016). Evaluating the use of Floseal haemostatic matrix in the treatment of epistaxis: a prospective, control-matched longitudinal study. European Archives of Oto-Rhino-Laryngology. 273(9):2579-84. https://doi.org/10.1007/s00405-016-3948-y

Mathiasen RA & Cruz RM. (2005). Prospective, randomized, controlled clinical trial of a novel matrix hemostatic sealant in patients with acute anterior epistaxis. Laryngoscope. 115(5):899-902. https://doi.org/10.1097/01.MLG.0000160528.50017.3C

Murray S, Mendez A, Hopkins A et al. (2018). Management of Persistent Epistaxis Using Floseal Hemostatic Matrix vs. traditional nasal packing: a prospective randomized control trial. Journal of Otolaryngology - Head & Neck Surgery. 47(1):3. https://doi.org/10.1186/s40463-017-0248-5

Ongoing research

Not searched

Other

Reverse citation

Kilty SJ, Al-Hairy, M, Al-Matairi D et al. (2013). Prospective clinical trial of gelatin-thrombin matrix as first line treatment of posterior epistaxis. The Laryngoscope. 124(1):38-42. https://doi.org/10.1002/lary.24240

Background information

Patel A, Fowell C. (2013). Epistaxis. InnovAiT. 6(5):269-274. doi:10.1177/1755738012467443

Provided by TP

Dallimore, A. (2022). HES Data: Epistaxis with procedure cost and bed days, England NHS Trusts. Vantage download from NHS Digital.

Date of search:	April 2023
Concepts used:	Bioresorbable, Epistaxis, FloSeal, Nosebleed, Topical haemostatic agent
HTW topic categorisation:	Blood and immune system; Ear, nose and throat

Proposed research question and evidence selection criteria (if selected)

Proposed research question	The clinical and cost-effectiveness of FloSeal in the treatment of acute epistaxis.

	Included	Excluded
Population	People presenting at A&E with epistaxis, or those who develop epistaxis in ENT departments and wards	Recurrent epistaxis
Intervention	FloSeal	
Comparison/ comparators	Nasal pressure, tranexamic acid, packing, cauterising	
Outcomes	Tolerability and side effects Haemostatic success Re-bleed rates Hospital admission rates and duration of stay Requirement for further treatment (e.g. packing)	
Study design		