NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Cyanoacrylate glue occlusion for varicose veins

Varicose veins in the legs are swollen and enlarged veins. They develop when the small valves inside a vein stop working properly, allowing blood to pool in the vein. This can cause pain, aching and swelling in the legs, and skin problems including inflammatory dermatitis and ulceration. In cyanoacrylate glue occlusion, medical glue is injected into the affected vein to close it and prevent blood pooling in the vein.

The National Institute for Health and Care Excellence (NICE) is examining cyanoacrylate glue occlusion for varicose veins and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about cyanoacrylate glue occlusion for varicose veins.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.
- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the Interventional Procedures Programme manual, which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 19th March 2015

Target date for publication of guidance: 24 June 2015

1 Provisional recommendations

1.1 Current evidence on the safety and efficacy of cyanoacrylate glue occlusion for varicose veins is limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to undertake cyanoacrylate glue occlusion for varicose veins should take the following actions.

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for the public ***[[URL to be added at publication]]*** is recommended.
- Audit [URL to audit tool to be added at publication] and review clinical outcomes of all patients having cyanoacrylate glue occlusion for varicose veins (see section 7.1).

1.3 Patient selection should be carried out by clinicians who can offer a range of treatment options in addition to cyanoacrylate glue occlusion.

1.4 This procedure should only be carried out by clinicians with specific training in this technique.

1.5 NICE may update the guidance on publication of further evidence.

2 Indications and current treatments

2.1 Varicose veins are a sign of underlying venous insufficiency and affect 20–30% of adults. Most people with varicose veins have no symptoms but venous insufficiency may cause fatigue, heaviness, aching, throbbing, itching and cramps in the legs. Chronic venous insufficiency can lead to skin discoloration, inflammatory dermatitis and ulceration. Great saphenous vein insufficiency is the most common form of venous insufficiency in people presenting with symptoms.

2.2 Most varicose veins do not cause serious health problems, so treatment is not usually needed on medical grounds. If symptoms are severe, the main treatment options include endothermal ablation, ultrasound-guided foam sclerotherapy, and surgery (usually stripping and ligation of the great and small saphenous veins, and phlebectomies). Conservative treatments such as compression hosiery (support stockings or tights) may be used if interventional treatment is unsuitable.

3 The procedure

3.1 Cyanoacrylate glue occlusion aims to close varicose veins by adherence then fibrosis of the lumen, without the need for tumescent anaesthesia (infusion of a large volume of dilute local anaesthetic around and along the entire length of the vein). The need for post-operative compression therapy is also reduced.

3.2 The procedure is done using local anaesthesia. An introducer sheath is inserted into the distal great saphenous vein in the affected leg and, using ultrasound guidance, a delivery catheter is advanced into position just before the sapheno-femoral junction. The proximal vein is compressed and a measured dose of cyanoacrylate glue is delivered through the tip of the catheter to seal the vein. The catheter is withdrawn in stages and the steps repeated to close the vein (that is, proximal vein compression and further measured doses) using ultrasound imaging to monitor progress. The procedure may also be done in a similar fashion for the small saphenous vein.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

4.1 A randomised controlled trial of 222 patients with varicose veins treated by cyanoacrylate glue occlusion or radiofrequency ablation reported closure rates of 100% and 86% respectively at 1-month follow-up ($p<0.01$; absolute numbers not reported). A case series of 38 patients treated by cyanoacrylate glue occlusion reported complete closure of the great saphenous vein in 100% (38/38) of patients at 48-hour follow-up (diagnosed by duplex ultrasound imaging). The closure rates at 12- and 24-month follow-up were 92%; there were 2 partial recanalisations and 1 complete recanalisation. A case series of 70 patients reported that 93% (63/68) of patients were free from recanalisation at 12-month follow-up. A case series of 65 saphenous vein procedures (43 great saphenous veins and 22 small saphenous veins) reported a closure rate of 99% at 3-month follow-up (absolute numbers not reported). A case series of 10 vein procedures (8 great saphenous veins and 2 anterior accessory saphenous veins) reported that all 8 great

saphenous veins were closed at follow-up (3–6 months); in 1 patient with double anterior accessory saphenous vein insufficiency, 1 side was only partially closed 3 days after the procedure and it had totally recanalised by 2-month follow-up. A case report of a patient who was being treated with an anticoagulant at the time of the procedure reported complete closure of the great saphenous vein at 8 weeks but extensive recanalisation was seen at 6-month follow-up.

4.2 The randomised controlled trial of 222 patients reported an improvement in the Venous Clinical Severity Score of approximately 3.5 points from baseline at 3-month follow-up ($p<0.01$), with no differences between the 2 treatment groups (cyanoacrylate glue occlusion or radiofrequency ablation). The case series of 38 patients treated by cyanoacrylate glue occlusion reported an improvement in the mean Venous Clinical Severity Score from 6.1 at baseline to 1.5 at 12-month follow-up (n=36, $p<0.001$). At 6- and 24-month follow-up, 84% and 65% of legs respectively had no oedema, compared with 39% of legs before treatment (absolute numbers not reported). Before treatment, all legs showed clinically relevant varicosities. At 12-month follow-up, 50% (18/36) of legs were free from varicosities and 25% (9/36) had only limited varicosities. At 24-month follow-up, 35% of legs were free from varicosities and 65% had only limited varicosities (absolute numbers not reported). In the same study, the proportion of patients free from pain increased from 13% at baseline to 84% at 6-month follow-up and 64% at 24-month follow-up (absolute numbers not reported). The case series of 70 patients reported an improvement in the mean Venous Clinical Severity Score from 4.3 at baseline to 1.1 at 12-month follow-up ($p<0.0001$).

4.3 The specialist advisers listed key efficacy outcomes as complete closure of great/small saphenous vein (on duplex ultrasound),

absence of long-term recanalisation, improvement in leg symptoms, improvement in quality of life and patient satisfaction.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

5.1 Thread-like thrombus extensions across the sapheno-femoral junction were reported in 21% (8/38) of patients in a case series of 38 patients (seen on ultrasound imaging at the 48-hour follow-up). At 6-month follow-up, all thrombus extensions had resolved without clinical sequelae. Thrombus extension into the common femoral vein was reported in 1 patient in a case series of 70 patients; this resolved without progression.

5.2 Phlebitis was reported in 16% (6/38) of patients in the case series of 38 patients; the patients had mild pain and erythema, which persisted for an average of 6 days. Superficial thrombophlebitis that resolved spontaneously was reported in 1 patient in the same case series. A mild phlebitic reaction was reported in 11% (8/70) of patients in the case series of 70 patients, with a median duration of 6.5 days. Self-limited thrombophlebitis was reported after 40% (4/10) of procedures in a case series of 10 veins. 'Mild' phlebitis in the treatment zone was reported in 6% (6/108) of patients treated by cyanoacrylate glue occlusion in a randomised controlled trial of 222 patients. 'Moderate' phlebitis not in the treatment zone was reported in 1 patient treated by cyanoacrylate glue occlusion in the same study and 'mild' superficial vein thrombophlebitis was reported in 3% (3/108) of patients.

5.3 Low-grade cellulitis that resolved with oral antibiotics was reported in 1 patient in the case series of 38 patients. Moderate access site

infection was reported in 1 patient treated by cyanoacrylate glue occlusion in the randomised controlled trial of 222 patients.

5.4 A postoperative erysipeloid-phlebitic skin reaction was reported after 15% (10/65) of procedures in the case series of 65 patients; all resolved quickly after conservative compression therapy. A hypersensitivity reaction was reported in 1 patient in the case series of 10 veins; the patient had simultaneous occlusion of both incompetent anterior accessory saphenous veins and the reaction was thought to be caused by subcutaneous delivery of the adhesive.

5.5 Hyperpigmentation was reported in 1 patient in the case series of 38 patients: this was still visible at 12-month follow-up.

5.6 Moderate and mild paraesthesia were each reported in 1 patient treated by cyanoacrylate glue occlusion in the randomised controlled trial of 222 patients.

5.7 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers described the following anecdotal adverse events: nerve injury (no other details provided); and inadvertent injection into the subcutaneous space, muscle or perivenous space. They considered that the following were theoretical adverse events: embolisation of glue to the lungs; cerebrovascular complications giving rise to transient or permanent neurological sequelae; deep vein thrombosis; scarring; ulceration; haematoma; and pain.

6 Committee comments

6.1 The committee noted that cyanoacrylate glue occlusion for varicose veins has the theoretical benefit of allowing people to have

outpatient treatment for varicose veins, without the use of tumescent anaesthesia or compression hosiery.

6.2 The committee noted that the published evidence is relatively small and that rare or uncommon risks may not yet be apparent.

7 Further information

7.1 This guidance requires that clinicians undertaking the procedure make special arrangements for audit. NICE has identified relevant audit criteria and is developing an audit tool (which is for use at local discretion), which will be available when the guidance is published.

7.2 For related NICE guidance, see the NICE website.

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