SOCIÉTÉ FRANÇAISE DE PHLEBOLOGIE

Investigation of foam sclerotherapy safety and of its possible alternative role to the thermal endovenous treatment of the saphenous vein insufficiency.

Enquête sur la sécurité de la sclérothérapie à la mousse et sur son possible rôle d'alternative aux traitements endoveineux thermiques de l'insuffisance veineuse saphénienne.

Tessari L.[1], Izzo M.[2], Cavezzi A.[3], Zini F.[4], Tessari M.[5], Ambrosino M.[6]

Summary

Before foam introduction, sclerotherapy effectiveness in saphenous reflux treatment was too small whenever compared to the other therapeutic options.

Conversely, nowadays in the international literature it's possible to find many evidences pointing out the overlapping outcomes obtained by a foam sclerotherapy treatment, in a mid-term comparison with the popular endovenous thermal techniques.

Foam safety investigations were performed both by means of electrophoresis analysis and of scintigraphic evaluation.

The results demonstrated how the drug is inactivated by the plasma proteins as soon as it gets into the blood stream and how no active drug is found in the cardio-pulmonary system.

Consequently, foam sclerotherapy side effects aetiology identification should not be focused on the drug or on the carrier (the gas) any longer.

Rather, new endothelial cathabolites like endothelin and histamine look like the most interesting target of future researches.

Résumé

Avant l'introduction de la mousse sclérosante, l'efficacité de la sclérothérapie dans le traitement du reflux saphène était trop faible en comparaison aux autres options thérapeutiques.

Inversement de nos jours, dans la littérature internationale, il est possible de trouver de nombreuses preuves qui mettent en évidence les résultats supérieurs obtenus à moyen terme par la sclérothérapie mousse, en comparaison avec les résultats obtenus avec techniques thermiques endoveineuse connues.

Des enquêtes sur la sécurité de la sclérothérapie à la mousse ont été réalisées à la fois par le biais de l'analyse d'électrophorèse et d'une évaluation scintigraphique.

Les résultats de ces études ont démontré comment le produit est inactivé par les protéines du plasma dès qu'il pénètre dans le courant sanguin, et qu'ainsi il ne se retrouve dans le système cardio- pulmonaire.

Par conséquent, désormais l'identification de l'étiologie des effets secondaires de la mousse ne doit pas être centrée sur le produit ou sur son support (le gaz).

Au contraire, de nouveaux catabolites endothéliaux comme l'endothéline et de l'histamine semblent devoir être à cible la plus prometteuse pour les recherches futures.

1. *Glauco Bassi Foundation, Trieste, Italy.*
2. *Math. Tech. Med., University of Ferrara, Italy.*
3. *Casa di Cura Stella Maris San Benedetto del Tronto, Italy.*
4. *Casa di Cura Città di Parma, Italy.*
5. *Tessari Studi, Peschiera del Garda (VR), Italy.*
6. *Centro Duomo Analisi- Nola, Italy.*

Lorenzo Tessari Lorenzo, Località Broglie 8 F, 37019 Peschiera du Garda (VR), Italy.
E-mail: lortes@icmnet.net, lorenzo.tessari@libero.it

Accepté le 10 mars 2014

In conclusion, considering that the foam sclerotherapy safety and effectiveness profiles are so competitive with the newest endovascular thermal devices, it becomes evident that the key point in the best therapeutic option is first of all an accurate echo-color-Doppler investigation, determining the exact reflux patterns.

Subsequently, the treatment choice should privilege the most effective, the cheapest and most minimally invasive technique. In this sense, foam sclerotherapy should always be taken into account.

Keywords: *foam sclerotherapy, safety, endovenous treatment, chronic venous disease therapy.*

En conclusion, en considérant que les profils « sécurité et efficacité » de la sclérothérapie à la mousse sont devenus très largement compétitifs avec les derniers appareils thermiques endovasculaires, il devient évident de noter que le point clé du choix de la meilleure option thérapeutique repose :

- *D'abord sur l'enquête précise écho-Doppler couleur, pour déterminer exactement les motifs de reflux.*
- *Ensuite, il faut privilégier la solution la plus efficace, la plus économique et la technique la plus mini-invasive. En ce sens, la sclérothérapie à la mousse doit toujours être prise en compte.*

Mots-clés : sclérothérapie à la mousse, sécurité, traitement endoveineux, traitement de la maladie veineuse chronique.

Introduction

Nowadays, the most interesting innovation in sclerotherapy is the sclerosing foam use, to be obtained by the transformation of a detergent sclerosing agent in mini- (or micro-) bubble foam. In this way it is possible to enhance the sclerosing effect by providing a longer contact of the drug with the endothelium without any blood interference.

In December 1999, in Paris, Tessari presented the Tourbillon Method (Tessari method).

Aim of this work is to fulfil the demand of creating sclerosing foam in a feasible, instantaneous, easy-to-use and cost-effective way. Moreover, the obtained foam must maintain along a sufficient time its typical features (adhesiveness, compactness, durability, echo visibility).

The present work offers also a description production method addressed to obtain the following foam properties: density, stability, sterility, standardization and reproducibility.

Secondary endpoint of the present study is to assess foam sclerotherapy safety profile, pointing out the difference among drug and carrier-derived complication causes.

In particular the safety profile investigation is addressed to demonstrate:

1) if bubbles and drug are linked or separated in their pathway within the blood stream
2) the possible changes in the bubble propagation following various therapeutic procedures (such as limb elevation, immobility after the injections, etc.)
3) if labelling the sclerosant drug with technetium (Pertecnetato 99mTCO4-) may be a correct procedure to highlight the pathway and propagation of the sclerosant drug in foam sclerotherapy.

Methods

The foam is obtained by two disposable syringes and a peculiar sterile three-way tap, mixing sterile air and STSP (purified sodium tetradecylsulphate) or other tensioactive sclerosing agents. In this way it is possible to obtain dense foam in a few seconds that can be injected easily.

The obtained and not used foam can be left into the sterile syringe and used again in the same patient and in the same session. Several factors may influence the bubble size (syringes volume, strength in mixing etc). In our daily practice we prefer 3 and 5 ml syringes with a ratio drug/air of 1:4 -1:5, with ten complete passages and 2-3 ml of foam per session.

Concerning the safety profile, a first echocardiography investigation has been performed on one patient: the arrival time of the bubbles and their persistence modalities and the time within the atrium (after a standardised injection of sclerosant foam) have been monitored and calculated in different intervals.

– 4 mls of foam (Tessari method) of Polidocanol 0,5 % + CO_2 O_2 have been injected in the left great saphenous vein and in a right posterior calf tributary;

– in another case, 4 ml of sclerosant foam (Tessari method) of Polidocanol 0.5 % + air have been injected in a left posterior calf tributary. Bubbles movement related to limb elevation, immobilisation-mobilisation has been assessed.

A second investigation has been performed to assess the possibility to label the sclerosant drug, the microbubble and the technetium (Pertecnetato 99mTCO4-).

The same patient has been investigated in different sessions, in order to detect the pulmonary transit and the captation of the labelled marker within his target organs (thyroid, salivary gland, kidneys, stomach, etc.).

In particular, the following assessments have been performed:

– Pathway of FREE 99mTCO4-
– Pathway of 99mTCO4- within sclerosant foam made by Polidocanol 2 % + air
– Pathway of 99mTCO4- within sclerosant foam made by Polidocanol 2 % + CO_2 O_2
– Pathway of 99mTCO4- within sclerosant foam made by Sodium Tetradecylsulfate 1 % + CO_2 O_2
– The pathway of 99mTCO4- within sclerosant foam made with Sodium Tetradecylsulfate 1 % + air

Results

The three main outcomes of our studies are summarised below:

1) By means of echocardiography it is not possible to highlight any link between drug and bubbles.
2) Elevation of the limb and post-injection limb immobility, significantly influence the passage of the microbubbles in the blood stream / heart propagation.
3) The labelling of the sclerosant drug with Pertecnetate 99mTCO4- is not an adequate procedure to highlight the pathway of the sclerosant drug in foam sclerotherapy.

Discussion

The everyday and worldwide use of echo-color-Doppler has brought great innovation in the haemodynamic interpretation of the lower limb venous drainage.

The same use of passive and active manoeuvres to elicit the reflux has pointed out as in almost the 50% of cases a valve incompetence actually shows a dissociation, having discrepancy among one test positivity (like the hyper-pressure Valsalva one) and the other one negativity (like the compression/relaxation for example).

In this context, it is important to think about the fact that the various tests used to diagnose valvular incontinence are not equal.

An adequate sonographic investigation of the venous reflux pattern allows the precise identification of the leaking points, so making it possible to adopt a mini-invasive approach, tailored on every single patients haemodynamic features.

Foam sclerotherapy has demonstrated to provide highly competitive results, in a standardized and reproducible way.

Moreover, foam sclerotherapy have demonstrated an extremely high safety profile, where the possible rare complications are mainly linked neither to the carrier (the bubble) nor to the drug (inactivation by plasma proteins).

In conclusion there is an urgent need to produce an intense literature answering to two main topics:

1) If the foam sclerotherapy complication is not linked to the drug or to the carrier, could it be linked to those endothelial cathabolytes that are released after the sclerotherapy session (endothelin, histamine-like)?
1) “CUI PRODEST?” a therapeutic option selection based on new technological innovations that do not take into account the advancement in the haemodynamics knowledge and the effectiveness and safety of the already existing therapeutic tool, like foam sclerotherapy?

References

1. Bassi G. Année Académique 2047. Rapport sur la Médecine. Phlébologie 1980; 33, 1: 207-9.
2. Escribano J.M., et al. Durability of Reflux-elimination by a minimal invasive CHIVA. Procedure on patients with Varicose Veins. A 3-years prospective case study. Eur. J. Vasc. Endovasc. Surg. 2003; 25:159-63.
3. Criado E., et al. Haemodynamic surgery for varicose veins: Rationale and anatomic and haemodynamic basis. Phlebology 2003; 18.
4. Cappelli M., Turchi A., Molino Lova R., Ermini S., Bono G. Nuovi concetti nell’emodinamica del ritorno venoso dell’arto inferiore nella Varicosi. Ospedali d’Italia - Chirurgia 1995; 47: 13-36.
5. Cappelli M., Molino Lova R., Ermini S. La Correzione emodinamica della syndrome varicose. In La Chirurgia Conservativa del Sistema Venoso Superficiale. Paolo Zamboni Ed. C.E.L.I Faenza 1996; Cap. 5.
6. Cappelli M., Molino Lova R., Ermini S., Turchi A., Bono G., Bahnini A., Franceschi C. Ambulatory Conservative Hemodynamic Management of Varicose Veins: Critical Analysis of Results at 3 Years. Florence-Italy and Paris-France. Ann. Vasc. Surg. 2000; 14: 376-84.
7. Cappelli M., Molino Lova R., Ermini S., Zamboni P. Hemodynamics of the saphenous-femoral junction. Patterns of reflux and their clinical implications. Int. Angiol. 2004; 23,1: 25-8.
8. Cappelli M., Molino Lova R., Ermini S., Zamboni P. Relationship between the calibre of the greater saphenous vein and the competence, or absence/incompetence of femoral valve in subject with incompetence of the sapheno-femoral junction. Abstract. 5th Meeting EVF, Varsavia. June 2004.
9. Tessari L. Empleo de esclerosantes en forma de microespumas en la terapéutica de los grandes ejes venosos superficiales. Lecture at the 2nd International Course Subdiaphragmatic Chronic Venous Insufficiency: abdomino pelvic and lower limbs. Madrid Octubre 2004.