EDITORIAL

Is there an ideal treatment option for hereditary hemorrhagic telangiectasia?

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Hereditary hemorrhagic telangiectasia (HHT) is an ***uncommon autosomal dominant disease*** with an incidence of 1 in 5000-8000 persons. It is a multisystem disorder that can affect: the nose, the lungs, the skin, the gastrointestinal tract, the liver, the brain.

Telangiectasias represent ***small dilated blood vessels*** located near the surface of the skin or the mucous membranes, measuring between 0.5 and 1 mm in diameter.

Epistaxis is the ***most common symptom of HHT***, its cause being the telangiectasias that develop on the nasal mucosa. The epistaxis appears because of the air passing through the nose that leads to dryness and rupture of the fragile blood vessels. Epistaxis is an important factor that ***reduces the quality of life in HHT patients.*** It has been observed that frequent episodes of epistaxis and abundant bleeding decreased patient's quality of life[1]. On the other hand, the patients with less than one episode of epistaxis per month are more active both at work and in the social life.

There is a wide variety of therapeutic options in case of HHT, starting with local treatment options, up to systemic medication and ending with surgical solutions. This may prove that, until now, none of them is perfect in trying to solve the therapeutic puzzle of the HHT patient.

The rationale for using **topical treatment** is due to the hypothesis that endonasal crusting and airflow lead to damage of endonasal telangiectasias and secondary bleeding. So, the humidification/ lubrication (e.g. humidifiers, vaseline, oestrogen containing ointment) of the nasal mucosa may prevent endonasal crusting and epistaxis.

The results of this local therapy vary very much in the literature and the identified problem is that ***their application may trigger epistaxis*** by the microtrauma produced.

Nasal packing in the treatment of HHT is used in ***managing acute epistaxis.*** Nasal packing with ***non-absorbable materials*** is ***to be avoided***, since it produces more trauma to the mucosa and further bleeding on pack removal.

New absorbable materials (sometimes embedded in procoagulant ointments) are used for severe or persistent epistaxis (e.g. Surgicel™, Nasopore™, Floseal™, RapidRhino™).

No positive long-term effects of any kind of materials used regarding the decrease in ***frequency/severity of epistaxis*** in HHT patients are reported.

Taking into consideration the **hormonal treatment**, Sadick et al.[2] showed promising results in topical ***estriol application*** on the nasal mucosa in ***association with plasma surgery*** – they flatten prominent nasal telangiectasia and induce squamous metaplasia of the nasal mucosa (6-month follow-up).

Oral oestrogens produce positive results regarding the loss of blood and the frequency of epistaxis[3]. But there are also some negative side effects: feminizing side effects (when used in high dozes), prothrombotic effects which are problematic in patients with HHT.

Tamoxifen administration is another hormonal therapy associated with HHT. Yaniv et al.[4] showed ***significant reduction in the frequency and severity of epistaxis***, with associated ***significant improvement in haemoglobin levels and quality of life.*** The treatment has also been associated with an ***increased rate of venous thromboembolism.***

In 1974, Sokoloff et al.[5] first described the **percutaneous therapeutic embolization** of the nasal blood circulation. Usually, it is performed distally at the level of the maxillary artery, but it can also be performed in the facial artery. The embolic material used is polyvinyl alcohol particles (PVA).

The results on ***short term are promising***, but there is ***no evidence of any long-term benefit*** (re-establishment of collateral supply?). Elden et al. reported a 100% success rate in case of 16 HHT 1 week after

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embolization, but with a long-term improvement of 30% and a long-term result of 17% in case of an elective embolization[6]. Fisher et al. treated 8 patients, 2 of them presenting long-term improvement with a decrease in their nosebleed episodes[7]. In another study, Layton et al. performed embolization on 12 patients with HHT and they reported that 58% of the patients needed surgery and/or re-embolization, in 25% a single procedure cure was performed and 17% continued to have severe epistaxis[8].

The poor long-term results and the ***possible life-threatening complications*** (risk of stroke/cerebral infarction[9]) transformed the percutaneous embolization in a ***therapeutic option in acute situations.*** It can be indicated in those cases when all modern medical and surgical treatment options have failed to reduce severe nosebleeds, in acute intractable epistaxis to create the opportunity for surgical procedures.

Antiangiogenic therapy – Bevacizumab. Recent studies reveal that in Rendu-Osler disease, because of certain genetic mutations of the vascular endothelium, there is an increase in vascular endothelial growth factor (VEGF) levels. Because VEGF may be responsible for the formation of telangiectasias, the administration of an anti-VEGF, named bevacizumab, may lead to a significant decrease in epistaxis occurrence.

And there are promising results for systemic therapy with some improvements in epistaxis or gastrointestinal bleedings.

But what about side effects? These include spontaneous gastrointestinal perforation, cytopaenia, hypertension, delayed wound healing, nasal septum perforation, weakness and haemorrhage[10]. To avoid these, local intranasal administration (spray or submucosal injections) was proposed, but this may lead to nasal septum perforation and consecutive epistaxis.

Argon Plasma Coagulation represents ***one of the main interventional techniques*** aiming to treat the recurrent epistaxis caused by telangiectasias. This procedure uses "argon gas to deliver plasma of evenly distributed thermal energy to a field of tissue adjacent to the probe"[11]. It seems to be a ***safe and efficient technique***, with reduction of the frequency and severity of epistaxis. But the treatment addresses the effects of the disease. If the causes are not treated, new lesions will inevitably form.

If it is successful, this treatment type can be repeated ad infinitum[2].

The one and only curative treatment known nowadays is the surgical closure of the nasal cavities using the technique of Young - the **Young Technique modified by Lund (Nasal closure)**[12]. This surgical procedure leads to serious consequences in terms of patients' quality of life, because the patients become permanent mouth breathers. The technique is reserved for: severe epistaxis, patients unresponsive to other treatments, patients with significant reduction in their quality of life and overall wellbeing.

If the procedure is reversed, nasal telangiectasias are still present and bleeding starts again.

CONCLUSIONS

Trying to answer the question...

"Is there an ideal treatment option for hereditary hemorrhagic telangiectasia?"

"I am not saying no, I am just saying not yet!"

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