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Comparative evaluation of bleomycin and sterol in the management of low flow vascular malformations in the head and neck region

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Abstract

Introduction: Vascular malformations in any location usually have a devastating aesthetic effect in addition to that of being associated with pain and bleeding. Sclerotherapy has been used as an effective therapeutic modality for the management of the vascular malformations. This prospective study was intended to evaluate and compare the efficacy of bleomycin and Sterol in the management of low flow vascular malformations in the head and neck region.

Materials and Methodology: The study was carried out among 60 patients within the age group ranging from 8 months – 55 years. All the patients were diagnosed with vascular malformations both clinically as well as by Doppler study. The stipulated period that was adopted for this study was between June 2019 to April 2022. After fulfilling the inclusion criteria, cases were randomly assigned into two groups of eight each. Group 1 were administered bleomycin 8 mg, freshly prepared in 2 ml normal saline and 2% lidocaine 2 ml. Group 2 were administered 1 ml of 3% sodium tetra-decyl sulphate and 2 ml of 2% lidocaine.

Results: The effectiveness of bleomycin was found to be superior to STS, when used as Intralesional Sclerotherapy agent. Most of the vascular lesions of group 1 resolved after first dose giving a cure rate of 93.75%. and only one patient required a second injection of bleomycin to obtain cure, after 3 weeks with no recurrence was observed. Group 2 patients were not cured following first intralesional injection of STS except for the small sized lesions. All the cases required 4-6, a mean of five injections to obtain cure. Ten patients out of 16 reported back with recurrence within 2 years. Six patients in group 2 came under the category of effective, giving an overall effective response rate of 37.5% and the drug was ineffective in of 62.5% cases.

Conclusion: Sclerotherapy with direct intralesional injection of bleomycin was found to be superior to STS and found that there was no recurrence rate in bleomycin group when compared to STS group. However, 3% Sterol solution is relatively simple, safe and effective management for managing head and neck vascular malformations that can be done as an in-office procedure. Smaller lesions have a more favourable response.

Keywords: Vascular malformations, sclerotherapy, bleomycin

Introduction

Vascular malformations are one of the most common congenital and neonatal abnormalities and the most common location predilection is reportedly being head and neck region (60%)^[1]. Mulliken JB and Glowacki J have broadly classified these pathological conditions into haemangioma and vascular malformation^[2]. Based on the various researches available, haemangiomas usually predominant during the first few months of life but the vascular malformations are always present at birth. After the initial rapid proliferation during first two years of life, haemangiomas usually regress in a slow and steady manner whereas vascular malformations do not reduce overtime. Waner M and Suen JY in their study have classified vascular malformations into slow flow (capillary, lymphatic and venous) and fast flow (arterial, arteriovenous fistula and arteriovenous malformation)^[3].

The first developed anti-neoplastic antibiotic developed was bleomycin and later it was known to possess sclerosing effect. The mechanism of action that commonly involves include damage to endothelial cells with a nonspecific inflammatory reaction and occlusion of blood vessels.

Intralesional bleomycin injections have been demonstrated to be an effective alternative in the management of haemangiomas and lesions of vascular malformation^[4]. Sodium tetradecyl sulphate, 3% STS (Sterol)^[5], has been most commonly used as sclerosing agent since its introduction in the year 1946. STS is used commonly in the management of small varicose veins of the legs, as well as venous and lymphatic malformations^[6]. The mechanism of action of STS is to ensure maximum endothelial damage with reduced thrombus formation which could ultimately leads to fibrosis of the lesion^[5] and results in shrinkage. The vascular luminal obliteration may or may not be permanent as such.

Low flow vascular lesions such as venous malformations are basically comprised of large, irregular, deep dermal and subcutaneous blood-filled channels that usually impose a purplish discoloration to the skin above the lesion. Majority of the asymptomatic swellings are typically soft, poorly defined and are readily blanching while compression giving them a characteristic like “worm-bag” sensation. They have been no palpable thrill or audible & recordable bruit. The lesion might expand overtime and darken with crying, when agitated or when kept in a dependent position. Some of the lesions might increase in size with compression of the ipsilateral jugular vein. The usual valsalva manoeuvre might also increase the size of the lesion. The venous malformations are usually present at birth though not all are clinically visible and their growth may become fastened when the patient undergoes puberty or pregnancy with attendant hormonal variations. Low flow vascular anomalies most commonly localised in masseter, skin, lips, oral mucosa and mandible. Mandibular lesions may pose with loosening of teeth or bleeding of gums. Some lesions might also occur within orbit causing exophthalmos and vision changes.

Therefore, this prospective study were intended to compare and evaluate the efficacy of bleomycin vs Sterol in the management of low flow vascular malformations in the head and neck region.

Materials and Methodology

After seeking permission from the institutional ethical committee, patients within the age group ranging from 8 years– 40 years with a provisional diagnosis of low vascular malformations diagnosed as venous malformation clinically and by Doppler study were taken from the out-patient Department of Oral and Maxillofacial Surgery GDC Srinagar Dental College and Hospital were screened. The stipulated period that was adopted for this study was between June 2019 to April 2022. The cases were randomly divided into two groups of 16 each, and categorized as,

Group 1 - Bleomycin 8 mg, freshly prepared in 2 ml normal saline and 2% lidocaine 2 ml.

Group 2 - 1 ml of 3% sodium tetra-decyl sulphate and 2 ml of

2% lidocaine Descriptive statistics and parameters like frequencies and percent ages were employed in order to accurately elaborate the experience with regard to the sclerotherapy procedure with bleomycin and Sterol. Values are presented as number (%), mean \pm SD or median (range).

Results

Group 1 patients who received an intralesional injection of bleomycin found that in 15 patients the lesion disappeared, the color of the skin overlying the lesion became normal which before gave a bluish hue and size on palpation regressed considerably within 3 weeks of first dose of drug administration. There was no recurrence of the lesion in the time period in which patients were observed (2-3 years). These fifteen patients came under the category of cured. Giving a response rate of 93.75%. Only one patient in group 1 required a second injection of bleomycin to obtain cure, after 3 weeks as the response obtained by first dose was very minimal and a considerable. (Table 1).

Group 2 patients who received STS was not cured following first intralesional injection of STS except for the small sized lesions. All the cases required 4-6, a mean of five injections to obtain cure. It was found that small lesions cured completely whereas lesions with wider diameter showed no resolution on application of STS. Ten patients out of 16 reported back with recurrence within 2 years. Six patients in group 2 came under the category of effective, giving an overall effective response rate of 37.5% and the drug was ineffective in of 62.5% cases.

Complications that were encountered in group 2 included cutaneous blister and ulcer formation, at injection site in two cases and scarring in one patient. Erythema appeared on skin overlying the lesion and injection site in three patients which persisted for 2-3 days. No other significant systemic or local complications were encountered.

In this study, neither gender nor age was associated to be a predisposing factor for a poor result in Sclerotherapy. Those patients who had fulfilled the inclusion criterion, the mean age group was ranged between 8 years to 40 years with 19.0 ± 1.4 . The major adverse effects that were encountered in this study using these drugs were reportedly pain, oedema after injection which was promptly managed by analgesics as well as intramuscular injection of dexamethasone. And in almost 11.7% of the patients developed superficial ulceration which was healed without any adverse events and one patient developed ecchymosis after injection. The lesions that are developed mostly involved the following locations lips, cheek, buccal mucosa, tongue, combined lesions of labial and buccal mucosa, combined lesions of buccal mucosa and tongue and left parotid region. The size of the vascular malformations mostly ranges from 1-9 cms at its widest diameter with an average size of 3.4 cms.

Table 1: The efficiency of sclerotherapy in the management of vascular malformations

Parameters	Group -1 (n = 16)	Group - 2 (n = 16)
Male	9 (56.25%)	10 (62.5%)
Female	7 (43.75%)	6 (37.5)
Treatment response Complete resolution No resolution	15 (93.75%) 1 (6.25%)	6 (37.5%) 10 (62.5%)

Discussion

The size, location, surgeon preference and their comfort largely determine the effectiveness of managing vascular malformations. Small Venous malformations can possibly be completely removed. However, complete surgical removal of an extensive oral or facial venous malformation is scarcely

possible without minimising the function or causing additional disfigurement and/or severe hemorrhage.⁷The various other treatment modalities quite possibly includes the use of Nd: YAG laser therapy. The major disadvantage of this treatment is reportedly its limited use for superficial cutaneous lesions and the potential risk of jeopardizing the

intimate vital structures in the face.

Sclerotherapy is adopted to be a safe and effective treatment modality with reportedly minimal morbidity. There are many other agents that were administered for sclerotherapy: sodium morrhuate, bleomycin, ethanolamine Oleate, ethanol, hypertonic saline and various combinations of these medications^[8]. The most common adverse effects were skin necrosis and ulceration, hypersensitivity, and swelling. Sodium tetra-decyl sulphate (STS) is a widely used sclerosing agent which has been commercially available in Canada and Europe for many years and is primarily used in the management of varicose veins. STS has been authenticated and approved by the US Food and Drug Administration (FDA) for sclerotherapy of varicose veins. In this study, clinical experience with the use of STS 3% solution intended to elucidate STS as a minimally invasive, safe and effective management of head and neck vascular malformations. The responses that were observed to this therapy were majorly very satisfactory in 93.75% of the treated bleomycin patients who showed good to complete response. The ideal response to STS injection was showed clearly in venous malformations smaller than 2.5 cm due to the undeniable fact that the efficacy of the sclerosis majorly depends on the caliber of the vessels and the blood flow through them. On the other hand, the lower efficacy of sclerotherapy of larger caliber or faster flow lesions was observed as a result of less sclerosant agent making in direct contact with the endothelial cells of the lesional walls^[9]. Stimson *et al.*, in their study had used 3% STS foam to treat 12 patients who had venous malformations in the head and neck. They observed that a single modality of treatment might be adequate for small lesions, but the injections may be safely repeated until a satisfactory result is extracted in large lesions. The patients in this study research were effectively managed in an office setting without any radiological guidance.

Similarly, Khandpur *et al.*, observed that 90-100% regression in the size of lesions by direct intralesional injection of 3% STS without radiological guidance into venous malformations and lymphatic anomalies. The findings of this case series showed excellent to good results in 61.6% of the patients, and moderate to mild results in 30.8% of the patients with direct percutaneous and per mucosal intralesional injections of the 3% STS solution. In this series, one patient who was previously treated by intralesional steroid injections observed no response to therapy and these results were advertently comparable to those results which were obtained from the use of a foam technique (Tessari's method) in which the sclerosing agent foam was formed using a three-way stopcock and two syringes which thereby mixing air with liquid sodium tetradecyl sulphate to create a foam^[10, 11]. The adequate formulation was observed to be one-part sclerosant solution to four parts air. The major objective of this method was to verify the safety, feasibility and efficacy of different doses and concentrations of a sclerosing drug. The concentrations that were predominantly used ranged from 0.1 to 3% of STS depending upon the caliber of the veins, with the larger caliber lesion, the higher concentration of STS was employed. The major advantage of this method included minimal extravasation of sclerosant foam making it less harmful than the liquid solutions. Tessari's foaming method had been originally used for sclerotherapy of varicose veins of lower limbs thereby increased hydrostatic pressure might increase extravasation of the sclerosant agent^[12]. Foaming minimises the extravasation related adverse effects and provides sclerosant rich procedure resulting in severe intimal damage.

Follow up of the patients was promptly scheduled every 2 weeks and the repeated injections were scheduled after 4 weeks in those patients reported with unsatisfactory results. Four of the patients in this series had two or more repeated injections. The results were carefully monitored by clinical observation, documented and compared by serial photographs as well as clinical measurements. Unknowingly, the continuity of treatment usually varied among patients due to limited availability of the sclerosant agent, poor patient compliance with the regular follow up and the patient's satisfaction with satisfiable results. In the present study, the reported side effects were mild in nature and healed spontaneously. In this study, no serious complications were reported like facial nerve palsy and blindness that have been reported earlier by other researchers.¹³ Post injection inflammatory reactions and pain were recorded in all patients. One patient reported with a small ulceration at the injection site and another patient developed ecchymosis. Soft-tissue swelling generally increases in the region of the vascular malformation that are immediately after the injections. Moreover, necrosis and inflammation that were induced by the sclerosis usually subsided with fibrous tissue formation, and thereby progressive reduction in the lesion size^[14, 15].

Conclusion

To conclude, sclerotherapy with direct intralesional injection of bleomycin was found to be superior to STS and found that there was no recurrence rate in bleomycin group when compared to STS group. However, 3% Sterol solution is relatively simple, safe and effective management for managing head and neck vascular malformations that can be done as an in-office procedure. Smaller lesions have a more favourable response. In the near future, further controlled studies are needed to be performed to assess the overall efficacy of STS in the management of venous malformations of the head and neck, as well as long term follow-up to observe positive results.

Conflict of Interest

Not available

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Not available

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