European Journal of Molecular & Clinical Medicine

ISSN: 2515-8260, Volume 10, Issue 02, 2023

Original Research

Outcomes Of Intralesional Bleomycin For The Management Of Cutaneous Low Flow Venous Malformations

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ABSTRACT

Background: Venous malformations are a type of vascular malformation with abnormally developed vein, venules and venous capillaries bunching together to produce soft cystic reducible masses containing venous blood. They account for about two third of vascular malformations. It may involve skin, mucosa or any other part of the body. The aim of this study was to evaluate the efficacy and safety of intralesional bleomycin sclerotherapy in low flow venous malformations.

Materials and Methods: During 2019- 2022, 213 patients with cutaneous venous malformations were treated with bleomycin sclerotherapy at a tertiary care hospital. The diagnosis of venous malformation was made on the basis of clinical history and physical examination and confirmed by doppler ultrasonographic examination Only patients with low flow venous malformations were treated with intralesional bleomycin sclerotherapy**.**

Results: All were treated with intralesional bleomycin (0.1 I.U/ kg body weight) on an outpatient basis. Complete resolution (grade 4) was observed in 76(35.6%) patients and almost complete resolution (grade 3) with very minimal residual lesion or pigmentation was seen in 89(41.7%) patients thus producing a complete or near complete response in 77.3% patients.

Conclusion: Intralesional bleomycin sclerotherapy is an excellent treatment modality for the management of low flow venous malformations with very low procedural morbidity.

Keywords: venous malformations, bleomycin, sclerotherapy, intralesional.

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INTRODUCTION

Venous malformations are a type of vascular malformation with abnormally developed veins, venules and venous capillaries bunching together to produce soft cystic reducible masses containing venous blood. They account for about two third of vascular malformations. It may involve skin, mucosa or any other part of the body

Venous malformations are mostly found in children and gradually increase in size with age. Bluish or purplish discoloration of skin with cystic reducible mass is the most common presentation. Cosmetic disfiguration, pain, bleeding, ulceration and compression of surrounding structures are the most common symptoms

A doppler ultrasonography is very useful investigation to differentiate high flow and low flow vascular malformations. A CT angiography may be required in large vascular malformations.

Traditionally Surgical excision offers complete cure but excessive bleeding, cosmetic disfigurement, risk of damage to surrounding structures like nerves, vessels etc, often makes

complete excision difficult if not impossible. Additionally added risk of regional or general anaesthesia are always there.
Intralesional sclerotherapy offers excellent alternative with no or minimal complication and can be done as out patient procedure. Over the years many sclerosing agents have been tried with varying success and safety profile. Sodium Morrhuate though produces thrombosis and occlusion of vascular channels but may lead to hematoma and skin ulceration.
Ethanol though easily available but skin necrosis, neuropathy, excruciating pain limits its use.
Bleomycin a widely used anti-cancer drug produces local fibrosis and this property has been used to treat venous malformation.

MATERIALS & METHODS

During 2019- 2022 213 patients with cutaneous venous malformations were treated with bleomycin sclerotherapy at a tertiary care hospital.
The diagnosis of venous malformation was made on the basis of clinical history and physical examination and confirmed by doppler ultrasonographic examination
Only patients with low flow venous malformations were treated with intralesional bleomycin sclerotherapy. A written informed consent was taken from all patients, after explaining possible risks and complications.
Measurements of all lesions were done before every procedure in longer and shorter axis. The longer axis was taken as reference and comparison. The amount of bleomycin injected was kept low at 0.1 IU/kg body weight. Complete aspiration of interstitial fluid intralesional bleomycin injected.
Patient remained in observation for about one hour and was subsequently discharged
Monthly sessions were taken and lesion measured before each session. Response to treatment i.e, reduction in size, any adverse reaction of previous session like pain, inflammation, ulceration, infection etc. were observed and meticulously recorded. Serial photographic evidence was also kept. The response to treatment was classified into 4 grades according to the percentage decrease in size post treatment.

RESULTS

Out of 213 patients, 103 were male and 110 were females. Median age of patients was 17 years and the patients ranged between 3 years to 48 years. All were treated with intralesional bleomycin (0.1 I.U/ kg body weight) on an outpatient basis between March 2019 to march 2022.

Table 1: Grades of response as percentage reduction in size

Grade	Percentage Reduction
1	<50%
2	50%-75%
3	76%-99%
4	100%

Most common site of vascular malformations was over the limbs (97 patients) followed by neck(33 patients), face (32patients), abdomen(16 patients), chest (10patients) and one patient had lesion over the vulva. Almost all the patients complained of deformity that included discoloration and swelling. Pain was prominent in 73 patients and 3 patients had had at least

one episode of bleeding. One school going teenager complained of bullying at school due the lesion over his face.

Size of the lesion in longest dimension varied from 2.1cm to 15.6 cm with a median size of 6.7cm.

Table 2: No. of sessions undertaken for the study group

No. of sessions required	No. of cases	%age
2	31	14.55%
3	97	45.53%
4	67	31.45%
5	17	7.98%
6	1	0.46%

The no. of monthly sessions required ranged from 2 to 6 with majority of patients requiring 3 or 4 sessions. Only one patient was administered 6 doses but the patient was lot to follow up.(Table 2)

In our study the dose administered intralesionally in each session was very low (0.1 IU/kg body weight) with mean cumulative dose of 33 IU and the maximum cumulative dose not exceeding 54 IU

Table 3: Response rate with respect to grades of resolution

Grade of response	No. of cases	%age
Grade 1(<50%)	5	2.3%
Grade 2(50-75%)	43	20.1%
Grade3(76-99%)	89	41.7%
Grade 4(100%)	76	35.6%

The response was carefully measured and graded before each session. Out of 213 patients 76(35.6%) had complete response and no residual lesion. Almost complete resolution (grade 3) with very minimal residual lesion or pigmentation was seen in 89(41.7%) patients thus producing a complete or near complete response in 77.3% patients. Moderate resolution (grade 2) was seen in 43(20.1%) patients. Only 5 (2.3%) patients had minimal resolution (grade 1) but no patient had any worsening or any major complication.(Table 3)

Table 4: Various complications recorded and their frequency

Complication	No. Of cases	Percentage
Transient rash	9	4.22%
Bullae	7	3.28%
Local pigmentation	12	5.63%
Ulceration	5	2.34%

Most of the patients had no post session complications and were discharged after 1 hour of observation. No major complication like anaphylaxis, haemorrhage or abscess formation was noted. Very few patients developed minor complications which resolved with symptomatic treatment with in a few days (Table 4).

DISCUSSION

Low flow venous malformations can be treated by sclerotherapy, surgical excision, erradiation, cryotherapy and laser therapy. Small superficial venous malformations are amenable to laser therapy. Surgical excision though required rarely, is associated with high morbidity, cosmetic deformity, functional impairment and high recurrence.

Intralesional Bleomycin sclerotherapy is an outpatient minimally invasive treatment modality widely used for low flow venous malformations confirmed by doppler ultrasonography.

The mechanism of action of bleomycin is snipping of DNS chain during S-phase of cell cycle thus disturbing the cell proliferation and its sclerosing character effects the vascular endothelium.[1,2,3,4] It is this sclerosing effect that leads to resolution of hemangiomas/AVMs.

Bleomycin is administered intravenously in treatment of various malignancies. Pulmonary fibrosis is the most severe complication of intravenous bleomycin therapy. The risk of pulmonary fibrosis is significant when the cumulative dose exceeds 450mg (450 IU). In our study the dose administered intralesionally in each session was very low 0.1 IU/kg body weight with mean cumulative dose of 33 IU and the maximum cumulative dose not exceeding 50 IU. We had intentionally kept the maximum cumulative dose to very low so as to avoid any long term side effects. An informed consent was taken from all the participants before each session and therapy sessions stopped as soon as the patient was satisfied with the outcome and achieved desired resolution. Out of 213 patients 76(35.6%) had complete response and no residual lesion. Almost complete resolution (grade 3) with very minimal residual lesion or pigmentation was seen in 89(41.7%) patients thus producing a complete or near complete response in 77.3% patients. Moderate resolution (grade 2) was seen in 43(20.1%) patients. Only 5 (2.3%) patients had minimal resolution (grade 1) but no patient had any worsening or any major complication.(Table 3)

Alakaily et al[5] performed sclerotherapy under ultrasound guidance and prescribed oral dexamethasone. Hout et al[6] and Yamaki et al[7] performed sclerotherapy under ultrasound guidance to avoid intravenous administration and hence minimise complications. Our study did not involve any steroid treatment and was done without ultrasound guidance. The results of our study were comparable and no major complication was reported and only transient minor local side effects were observed in a very small number of patients.

CONCLUSION

Intralesional bleomycin sclerotherapy shows excellent results in the treatment of low flow venous malformations. The treatment can be done on an outpatient basis with very low morbidity thus avoiding the complications and morbidity associated with surgical treatment.

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