Evaluating the effect of bleomycin injection in the head and neck hemangiomas and different types of low flow vascular malformation: cohort retrospective study

Original Article

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ABSTRACT

Introduction: Vascular anomalies are considered the most common form of congenital and neonatal dysmorphogenesis. They are classified into hemangiomas and vascular malformations (VMs) which are divided into high and low flow VMs which include venous, lymphatic, and combined lymphatico-venous malformations. Different treatment modalities for vascular anomalies including sclerotherapy, vessel embolization, surgical excision and a conjunction of these. Bleomycin developed as a cytotoxic antitumor agent Which has an antiproliferative effect. It has been become widely used for treatment of vascular anomalies because of its high sclerosing effect on vascular endothelium. **Objective:** to evaluate clinical and radiological effect of bleomycin injection for the treatment of head & neck hemangioma & different types of low flow vascular malformation. **Materials and Methods:** a retrospective study was done on 25 patients with different types of vascular anomalies and were treated by intralesional bleomycin injection at the Department craniomaxillofacial & plastic surgery at Alexandria university & Nile of hope hospital. Results: The clinical, radiographical and patient satisfaction outcomes were markedly improved. **Conclusions:** bleomycin injection into vascular lesion is a noninvasive modality for vascular malformations treatment with excellent results and low cost.

Key Words : Bleomycin injection, Low flow vascular malformation, Hemangioma, Head and neck.

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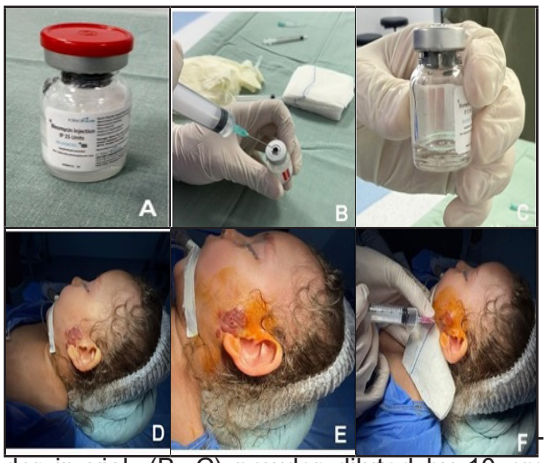
INTRODUCTION

Head and neck vascular anomalies are a complex group of lesions that challenge the maxillofacial physicians starting from understanding of the difference between its 2 main forms to its management. Based on the International Society for the Study of Vascular Anomalies (ISSVA) Mulliken and Glowacki[1] classified vascular anomalies into two categories as hemangiomas and vascular malformations (VMs)[1] which are further divided based on their flow into low flow VMs (LFVMs) including venous, lymphatic,combined i.e., venolymphatic and capillary malformation, or high flow including arterial malformation, arteriovenous malformation and arteriovenous fistula.[2,3]Venous and lymphatic malformations among other vascular lesions having incidence of 1:5000–10,000 and mainly occurs in head and neck regions by 40%. [4]Most of evidenced based studies confirmed that infantile hemangiomas have an incidence of 4–5%, but in the literature have an overall incidence of 3–10%.[5]Risk factors which concluded by a multicentric prospective study on infantile hemangiomas are Caucasian ethnicity, multiple gestations, prematurity, female gender, advanced maternal age and low birth weight.[6]Hemangiomas mainly present at birth and most diagnosed at 1 year old[7] while venous malformations usually present at birth which Slowly grow throughout life till diagnosed at second decade. Clinically, lesions of hemangioma presented as pink or violaceous oval or round plaques or exophytic masses associated with peripheral veins or surface telangiectasia ,[8] while venous malformation lesions presented as easily compressed pale-to-dark blue ill-defined masses[8] which have high response to infection, trauma or hormonal fluctuation.[7]Lymphatic malformations (LMs) develop at the onset of puberty during childhood although the presence of dysplastic vessels from birth, predominantly affecting females suggests a hormonal influence as estrogenic.[9] Occur usually in lymphatic-rich regions such as the axilla, groin, mediastinum, oral cavity and head and neck but it also can occur throughout the body. LMs sub divided into macrocystic, microcystic, or mixed, where Macrocystic LMs are large,cystic smooth lesions, lying either mostly superficially under subcutaneous tissue or normal skin or rarely at deep spaces as aerodigestive tract, retroperitoneum,[10] while microcystic LMs affecting usually mucosal surfaces or the skin,appear as firm, small,hemorrhagic or translucent vesicles that may appear like brawny edema.[11]There are many reported treatment modalities for VMs including copper needle treatment,sclerotherapy, vessel embolization, laser therapy, electrochemical therapy, surgical resection or conjugated treatment of these.Regarding percutaneous sclerotherapy is a safe and effective treatment to minimize bleeding during surgery and reduce the size of the lesion.[12] Sclerosing agents have been including bleomycin, sodium tetradecyl sulphate, absolute ethanol, sodium morrhuate, ethibloc and OK 432.[13-14] In 1966, Umezawa developed bleomycin as a antitumor cytotoxic drug.[15] Recently, bleomycin injection into the lesion has been shown to be an efficient noninvasive treatment for vascular lesions because of its apoptotic effect on immature cells that grow rapidly inducing degradation of DNA.[14,16] It has been become used widely because of its affordable price, availability, low side effects and elevated sclerosing effect on endothelium of blood vessels. The aim of this article is to evaluate the effect of bleomycin injection for the treatment of head & neck hemangioma & different types of low flow vascular malformation.

Subjects and Methods

This was a clinical observational study including all available children diagnosed clinically and radiographically with hemangioma & low flow vascular malformations (lymphatic, venous and combined lympho-venous). This Cohort retrospective study of bleomycin injection was conducted in the interval between January 2022 till January 2025. Patients at this study were selected from the craniomaxillofacial & plastic surgery department at Alexandria university & Nile of hope hospital. Patients approval was obtained through a written consent for the use of intralesional bleomycin injection after explaining the possible side effects and detailed risks of the injection. Ethical approval was obtained from Committee of Alexandria University Faculty of Dentistry (IRB No. 001056 – IORG 0008839) prior to any research-related activities. All procedures performed in the study were conducted in accordance with the ethical standards given in the 1964 Declaration of Helsinki, as revised in 2013 and other ethical guidelines adopted by the Research Ethics Committee of Alexandria University Faculty of Dentistry. Total number of patients was 25 patients between 1m to 12 years old having hemangioma & low flow vascular malformations (lymphatic, venous and combined lympho-venous) on the basis of history and physical examination were included in this study.[17-19] Duplex ultrasound (DUS) was requested to assure diagnosis and exclude high flow

VMs from the study. Also exclude immunocompromised patients, patients with drug hypersensitivity to bleomycin & those with localized lesions that are accessible surgically, or with total vessel thrombosis or marked soft tissue component.[17]A standardized detailed sheet of case history recording the specific data of the patient including name, age, gender, weight, site of the lesion, size of the lesion, special investigations, allergy to any drug and past intervention for this lesion. The patients with hemangioma & low flow vascular malformations (lymphatic, venous, combined lympho-venous) were selected for bleomycin injection into the lesion. Serial photography and measurements taken before, during and after completion therapeutic session were recorded to document the response to treatment. The intervetion was performed in operating room under sedation anesthesia. Bleomycin powder (15 mg) was diluted in10 cm of normal saline. A dose of 1ml/kg was injected intralesional percutaneous or intra-oral puncture by 3 cm disposable sterilized plastic syringe in a radial fashion at each session (Figure 1). [20] At each session, a dose of 15 mg never exceeded. Well distributed injection was checked by blanching of the overlying skin during injection.[21] Injection, then application of pressure gauze for about 5–10 min, then application of pressure dressing. Patients were kept under observation for about 1 h to 2h then discharged and mild analgesia was prescribed. At least 3-4 weeks were maintained between each time of injection if needed.



der in vial. (B, C) powder diluted by 10 cm of saline. (D) 3 years old girl with low flow venous malformation at left preauricular area underwent sedation anesthesia. (E) field was disinfected by betadine. (F) injection was started of diluted bleomycin by dose 1mg/1kg/session in depth and radial fashion into the lesion after aspiration was done to avoid injection into blood vessels. Clinically, patient's follow-up was done every week as an outpatient, and parameters such as color, size and texture of the lesion were monitored after treatment at every week. Pre and post-injection serial photographs were taken for the evaluation of aesthetic appearance. Patients were followed for a period of 6–12 months. The results were documented based on a 4-point scale that was modified by Achauer et al.(22) and Hassan et al.(23) This scale took volume, colour and texture of the lesion after treatment into consideration, includes:

1. No response, where the size of the lesion not changed or enlarged.
2. Mild improvement, where less than 50% of lesions size decreased and appearance with mild improvement.
3. Marked improvement, where more than 51% of lesions size decreased and appearance with remarkable improvement less than 100%.
4. Cured, where complete disappearance of the lesions without recurrence for at least 6 months after last injection.

Also, the patient or the parents filled in questionnaire based on their satisfaction related to pain, over all symptoms and self-confidence which is similar to PRO questionnaire of Abdelaty et al (17) but it was more simplified by measuring satisfaction on only 3 domains and not 6 domains excluded daily activities, movement and health perception as they were not affected at the present studied patients. Each domain is measured before and after 12 weeks the procedure by given a grade from 1 to 5, corresponds to reference

- d_1 very dissatisfied
- d_2 refers to dissatisfied
- d_3 refers to neutral
- d_4 refers to satisfied
- d_5 refers to very satisfied

Radiographically,[24,25] After 12 weeks of the procedure Duplex US was done and compared with the preoperative one in the same region to estimate the improvement. The outcome was classified as:
1-GradeI: total or near total obliteration of the vascular space.
2-Grade II: decrease of the size of the lesion, the number of vascular spaces, or partial obliteration (increased echogenicity).
3-Grade III: nothing is changed

Statistical Analysis

Data was analyzed using IBM SPSS version 23 for Windows, Armonk, NY,USA. Qualitative variables were summarized using frequency and percentage while quantitative variables were presented using mean, medina, standard deviation,minimum and maximum. Pearson Chi Square test and the Wilcoxon Signed Rank test were used for data comparisons.All tests were two tailed and the significance level was set at p value<0.05.

Results

This retrospective study was conducted in the interval between January 2022 till January 2025 on all available patients (25) at the Department craniomaxillofacial & plastic surgery at Alexandria university (by 15 patient) & Nile of hope hospital (by 10 patient), included 16 females and 9 males. Their ages ranged from 6 months to 12 years (mean, 5.44 years). They were diagnosed by vascular lesion types where 10 patients (mean, 40%) with hemangiomas, 6 patients with low flow venous malformation (mean, 24%), 4 with lymphatic malformation (mean, 16%) and 5 patients with veno-lymphatic malformation (mean, 20%). Table 1 Diagnosis was based on clinical presentation and radiographically where all 25 patients (mean, 100%) provided basically doppler ultrasound (DUS) on affected area used as reference to original size of lesion to be compared with post operative DUS to detect any improvement in the lesion size, 4 patients (mean, 16%) with CT, 12 patients (mean, 48%) with MRI, 5 patients (mean, 20%) with CTA, only 1 patient (mean, 4%) with FNAC and 2 patients (mean, 8%) with MRA. Table 1. There were a wide variety of the lesion site where 5 patients (mean, 20%) affected at forehead area, 2 patients (mean, 8%) at temporal area, 5 patients (mean, 20%) at parotid area, 1 patient (mean, 4%) at Eyebrow, 1 patient (mean, 4%) at eyelid, 4 patients (mean, 16%) at nose, 1 patient (mean, 4%) at orbital area, 6 patients (mean, 24%) at cheeks, 4 patients (mean, 16%) at nose, 8 patients (mean, 32 %) at lip, 1 patient (mean, 4%) at commissure, 2 patients (mean, 8%) at preauricular area, , 1 patient (mean, 4%) at chin, 1 patient (mean, 4%) at periorbital, 1 patient (mean, 4%) at submandibular area, 1 patient (mean, 4%) at tongue and 1 patient (mean, 4%) at palate. Table 1

Table 1: Demographic data and characteristics of the study sample

Variables		N= 25 ptients
Age in years	Mean ±SD	5.44 ±3.53
Gender: n (%)	Males	9 (36%)
	Females	16 (64%)
Pre-operative radiograph: n (%)	US	25 (100%)
	CT	4 (16%)
	MRI	12 (48%)
	CTA	5 (20%)
	FNAC	1 (4%)
	MRA	2 (8%)
Lesion type: n (%)	Hemangioma	10 (40%)
	Low flow venous malformation	6 (24%)
	Lymphatic malformation	4 (16%)
	Veno-lymphatic malformation	5 (20%)
Site: n (%)	Forehead	5 (20%)
	Parotid	5 (20%)
	Eyebrow	1 (4%)
	Eyelid	1 (4%)
	Nose	4 (16%)
	Orbital	1 (4%)
	Cheek	6 (24%)
	Lip	8 (32%)
	Commissure	1 (4%)
	Preauricular	2 (8%)
	Parapharyngeal	1 (4%)
	Chin	1 (4%)
	Temporal	2 (8%)
	Periorbital	1 (4%)
	Sub-mandibular	1 (4%)
	Tongue	1 (4%)
	Palatal	1 (4)%

They were treated as inpatient and analyzed prospectively with percutaneous bleomycin injection ranging between 1 – 15 times (mean, 5.36) under sedation anesthesia with a period between each time ranging from 1 month to 12 months (mean, 3.38) for needed cases.

Table 2. Patients' follow up was done for 12 months.

Variables		N= 25 patients
Number of injections	Mean ±SD	5.36 ±3.62
	Min – Max	1 – 15
Time between each injection (months)	Mean ±SD	3.38 ±3.52
	Min – Max	1 – 12

Clinical outcome based on pre & post photos of the lesion revealed that one patient (mean, 4%)

provement,3 patients (mean, 12%) had marked improvement, and 13 patients (mean, 52%) were totally cured. Table 3

Table 3: Clinical improvement and postoperative DUS

Clinical improvement: n (%)	No response	1 (4%)
	Mild improvement	3 (12%)
	Marked improvement	13 (52%)
	Cured	13 (52%)
Postoperative DUS: n (%)	Grade I	16 (64%)
	Grade II	9 (36%)

Clinical outcomes in relation with each type of vascular lesions, showed that 6 patients (mean, 60%) with hemangiomas had improved outcome, 3 patients (mean, 30%) were totally cured and only 1 patient (mean, 10%) had no change, while patients with low flow venous malformation were totally cured except for only 1 case showed mild improvement, 2 patients with lymphatic malformation (50%) were improved and the other 2 cases (50%) were totally cured, and 2 patients with veno-lymphatic malformation (40%) were improved while other 3 cases (60%) were totally cured. Table 4

Table 4: Association between clinical improvement and lesion type

Lesion type	Clinical improvement		
	No rsponse	Improved	Cured
Hemangioma	1 (10%)	6 (60%)	3 (30%)
Low flow venous malformation	0 (0%)	1 (16.7%)	5 (83.3%)
Lymphatic malformation	0 (0%)	2 (50%)	2 (50%)
Veno-lymphatic malformation	0 (0%)	2 (40%)	3 (60%)
p value[1]	0.508		

p value[1]: Pearson Chi Square test

Clinical marked improvements and complete cure showing in the following (Figures 2-7)

Figure (2): (A, B, C, D) Showing 7 years old girl presented with a left, periorbital, cheek, upper lip, commissure and intra-oral buccal low flow venous malformation. (E, F, G, H) showing marked clinical improvement after 13 bleomycin injections during 12 months with check heamangioma has no change, while 8 patients (mean, 32%) had mild im

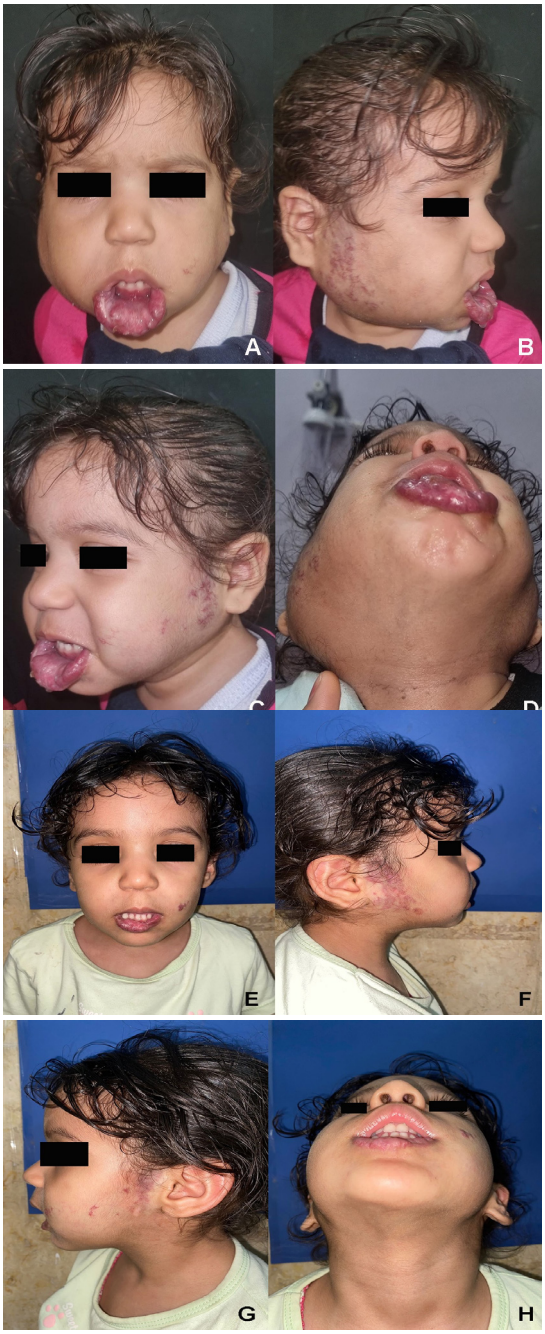
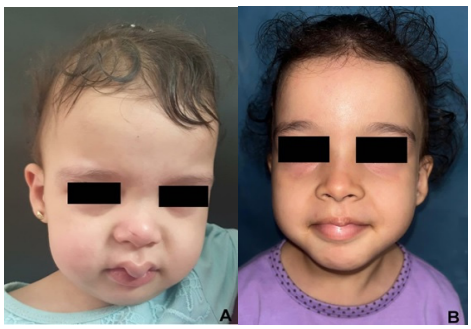


Figure (3): (A, B, C, D) Showing 3 years old girl presented with bilateral Parotid, cheeks & lower lip hemangioma. (E, F, G, H) showing marked clinical improvement after 15 bleomycin injections during 12 months

Figure (4): (A) Showing 2 years old girl presented with hemangioma at right temporal, right side of forehead, right eyebrow, upper eyelid & nose. (B) showing complete cure after 9 bleomycin injections through 10 months.



Figure(5): (A)Showing 4 years old girl presented with hemangioma at upper lip.(B) showing complete cure after 3 bleomycin injections through 3 months

Figure (6): (A) Showing 9 years old girl presented with veno-lymphatic malformation at the left parotid area. (B) showing complete cure after 3 bleomycin injections through 3 months

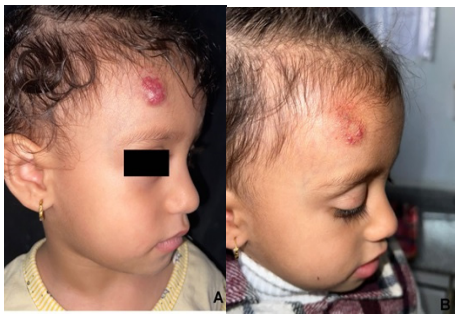


Figure (7): (A) Showing 2 years old girl presented with hemangioma at the right-side forehead. (B) showing clinical improvement

after 4 bleomycin injections through 5 months. Radiographical outcomes based on post DUS compared with pre injection, revealed complete obliteration in 16 patients (mean, 64%) and reduction in lesion size in 9 patients (mean, 36%). Table 3 Subjective outcome filled in survey based on patient and parent satisfaction related to pain, over all symptoms and self-confidence filled in questionnaire. Results revealed that mean pain score before injection was 1.80 with SD ±0.76 that markedly decreased after injection to mean 4.44 with SD ±0.71 and this was statistically significant as p value=<0.001*. Table 5

Table 5: Comparison of satisfaction of patients regarding subjective improvement domains

	Pain		Overall symptoms		Self Confidence	
	Before	After	Before	After	Before	After
Mean ±SD	1.80 ±0.76	4.44 ±0.71	1.80 ±0.76	4.44 ±0.71	1.60 ±0.71	4.48 ±0.71
Median	2.00	5.00	2.00	5.00	1.00	5.00
Min – Max	1.00 – 3.00	3.00 – 5.00	1.00 – 3.00	3.00 – 5.00	1.00 – 3.00	3.00 – 5.00
p value[1]	<0.001*		<0.001*		<0.001*	

Statistically significant at p value<0.05, p value1: Wilcoxon Signed Rank test Regarding over all symptoms, mean value before treatment was 1.80 with SD ±0.76 that markedly decreased after treatment with mean value 4.44 with SD ±0.71. and this was statistically significant as p value=<0.001. self-confidence mean value before treatment was 1.60 with SD ±0.71 that markedly decreased after treatment with mean value 4.48 with SD ±0.71. and this was statistically significant as p value=<0.001*. Table 5

Discussion

Head and neck vascular anomalies are challenging in their management. They have different types including hemangiomas, LVMFs (including venous, lymphatic and veno-lymphatic) and HVMFs and have high rate of incidence such as the Venous and lymphatic malformations with incidence of 1:5000–10,000(4) and the infantile hemangiomas with an overall incidence of 3–10%.(5) Mostly they present at birth either diagnosed at 1 year old as hemangioma(7) or diagnosed at second decade as venous malformations, while lymphatic malformations develop during childhood at the onset of puberty. Patients usually complaining of pain if lesions causing pressure on nearby nerve or superimposed by infection, facial deformity affecting child self-confidence and complaints related to the site of lesion as difficult in swallowing associated with LFVM at oropharyngeal area. Treatment modalities for VMs including laser therapy, vessel embolization, electrochemical therapy, copper needle treatment, surgical excision, sclerotherapy by bleomycin, sodium morrhuate, sodium tetradecyl sulphate, ethibloc, OK 432, absolute ethanol or combined treatment of these.[13-14] Bleomycin was developed by Umezawa in 1966 as a cytotoxic antitumor drug. (15) Recently, used as sclerosing agent injected into the hemangiomas and LFVMs as shown to be an effective nonsurgical treatment because of its apoptotic effect.[14,16] It has been become used widely because of its affordable price, high availability, low side effects and high sclerosing effect on endothelium of blood vessels. In the literature, there is deficiency in studies clarifying bleomycin objective (clinical and radiographical) and subjective outcomes on different types vascular malformations including hemangiomas, venous, lymphatic and venolymphatic malformations. So, in our study we tend to show bleomycin effect on each type of vascular lesions clinically, radiographically and subjectively. The patients in the this study were children with vascular malformations (n = 25), out of which 9 males and 16 females In this study Lips and cheeks were the most common affected sites. This was with agreement of the study of Jan et al [26] that had the commonest sites were oral cavity, lips and tongue. The number of injections of bleomycin rquired in this study ranged from 1 - 15 which was in contrast to the study of Hassan et al that had a maximum number of 6 injections, [23] As in our study 15 patients out of 25 had vascular lesions at multiple sites at head region and as we should not exceed 1mg / 1kg / session so rquired more sessions of injection. The present study reported complete cureand marked improvement in 64% of patients who did not need any surgery. This is in agreement with the study published by Hassan et al.[23] which recorded complete cure and marked improvement in 71% of cases that did not

need any surgery with accepted appearance. In the present study mild improvement was recorded in 8 patients (32%) where residual lesions that are seen during clinical follow up or at duplex US not treated as no painor function limitation were reported. This is in contrast to Jan et al [26] where only 2 patients (6.66%) with mild improvement that underwent for surgery after reduction in the size of the lesion and vascularity done by the bleomycin injection, this allowed aesthetic closure at a later date. Vascular malformations are considered a chronic disease with low rate of improvement in long term the procedure with patients and know their expectations and the achievable improvement.[27]Bleomycin injection percutaneously causes vascular endothelium destruction, causing sclerosing effect. In this study, the injection was repeated every 1 to 3 months as this duration was found to be consistent with the expected changes in the hemangiomas, low flow VM, lymphatic and venolymphatic malformation. Only in 4 cases, time between injections was exceeded the previous period due to poor follow up from parents. Bleomycin injection has been used to treat hemangiomas, lymphatic venous and venolymphatic malformation with a success rate of 90%, 100%, 100% and 100% respectively,[12,19] Hyperpigmentation was only complication encountered in present study in 4 patients (16%) that layer referred to dermatologist to deal with it. Although systemic bleomycin treatment has the potential to cause pulmonary fibrosis, there are no cases in the literature have been reported when bleomycin was used as a sclerosing agent as this complication can be avoided or reduced, if the dose / session is maintained under 1 mg/kg per session.[28] In present study, the dosage per session was maintained at 1 mg/kg and the interval between injections was ranged between 1-3 months except for 4 cases time between injection was exceeded due to poor follow up from parents. The recommended dose for bleomycin injection into the lesion is 1 mg/kg/dose and a dose of 15 mg at each session is never exceeded. In this study Duplex US was the basic radiology with all the patients, either requested upon examination or found with them already done before they came for examination, used in confirming diagnosis, differentiating low-flow from high-flow lesions and post operative assessment of lesion size. Despite Some authors have described the MRI is the most accurate radiology in the assessment of the reduction in the size of lesion however it is high cost, needs contrast, and general anesthesia in children. (29) Beside DUS, some patients had another radiological investigation who was requested by physicians before they came for examination as MRI, CT-angio, MRA, FNAC and conventional CT. Radiographic outcome showed, in this study by comparing between pre and post change in lesion size with DUS, 16 patients (64%) showed complete obliteration of lesion, and 9 patients (36%) showed marked decrease in lesion size where all cases of VMs were completely cured, while patients with hemangiomas showed 50% complete recovery and 50% marked improvement. LMFs showed better response to bleomycin than VLMs where 3 patients out of 4 (75%) with LMFs were completely cured while only 3 patients out of 5 with VLMFs (60%) were completely cured. This is in agreement with the study of Nevesny et al, where the MRI-detected size reduction was 50% or more for 64% of the VMs and 87% of the LMs. [27]There are 2 options for treatment of lymphatic malformation either sclerotherapy or surgical excision. The treatment choice depends on the physician, preference of the child's family, the lesion type and site. The definitive treatment for LMs is surgical excision, however it may be not easy as the lesion has thin-walled and infiltrative nature that often do not respect tissue planes leading to a high possibility of complications (12%–23%) like injury of vital organs and nerves, bleeding, infection, scar formation, and recurrence rate ranging from 15 to 53%.[30,31]This study showed a significant statistical difference in patients and parent satisfaction filled in questionnaire in all cases before and after bleomycin injection regarding pain, over all symptoms and self-confidence. This is contrast with Horbach et al retrospectively who assessed the long-term PRO in 77 patients who had bleomycin injection where only about 49% of the involved patients reported a degree of improvement in their satisfaction and life quality. [32] A possible explanation for this could be that the patients' expectations exceeded the outcomes that could realistically be achieved. Subjective outcome based on patient and parent satisfaction related to pain, over all symptoms and self-confidence filled in questionnaire which is similar to PRO questionnaire of Abdelaty et al(17) but it was more

simplified by measuring satisfaction on only 3 parameters and not 6 parameters excluded daily activities, movement and health perception as they were not affected at the present studied patients. There is no standardized PRO survey for vascular malformations. In Abdelatyet al study, A more simple form of Short Form 36-item Health Survey (SF-36) questionnaire was used, which is a universal tool validated previously to evaluate the health status in multiple medical conditions.[33] There are 2 limitations of this study, first, the effect of bleomycin sclerotherapy was more in the LM group than in the VM group so further research is needed to understand why. Second limitation is that postintervention MRI was not the standard radiology done before and after injection to asses the lesion changes; but, duplex US showed satisfying results with affordable price.

Conclusion

Objective (clinical, radiographical) and subjective satisfactory results were achieved after intralesional bleomycin injection for hemangiomas, and different types of low flow vascular malformations with no complication. It is a non-surgical modality for treatment of vascular malformations with excellent results and low cost that should be taken into consideration before thinking about surgery to avoid scar formation especially in lesions present at esthetic areas and decrease the risk of massive bleeding. Although it is simple to administer, however does require multiple sedation anesthesia, and completion of treatment may take a few months.

References

[1]Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: A classification based on endothelial characteristics. Plast Reconstr Surg 1982: 69: 412 422.

[2]Churojana A. Bleomycin: An effective drug for intralesional injection treatment of vascular anomalies. Pharm Pharmacol Int J 2020: 8: 38 40.

[3]Mohan AT, Adams S, Adams K, Hudson DA. Intralesional bleomycin injection in management of low flow vascular malformations in children. J Plast Surg Hand Surg 2015: 49: 116 120.

[4]Callahan AB, Yoon MK. Infantile hemangiomas: a review. Saudi J Ophthalmol 2012;26:283-291

[5]Syed NM. Vascular lesions of head and neck: a literature review. Indian J Dent Sci 2016: 8:176-182.

[6]Schwartz SR, Blei F, Ceisler E. Risk factors for amblyopia in children with capillary hemangiomas of the eyelid and orbit. J AAPOS 2006: 10: 262-268.

[7]Fonseca RJ, Turvey RD, Timothy A, Marciani RD, Turvey TA. Surgical pathology, In: Textbook of oral and max illofacial surgery. vol 5. Saunders, Philadelphia, 2000.

[8]Steiner JE, Drolet BA. Classification of Vascular Anomalies: An Update. Semin Intervent Radiol 2017: 34: 225-232.

[9]Rockson SG. Lymphedema. Am J Med 2001:110: 288-295.

[10]Defnet AM, Bagrodia N, Hernandez SL, Gwilliam N, Kandel JJ. Pediatric lymphatic malformations: evolving understanding and therapeutic options. Pediatr Surg Int 2016: 32:425-433.

[11]Elluru RG, Balakrishnan K, Padua HM. Lymphatic malformations: diagnosis and management. Semin Pediatr Surg 2014: 23: 178-185.

[12]Bilici S, Avci V, Öztaş T, Asena M, Çelik K. The treatment of lymphangiomas with bleomycin in childhood: A retrospective observational study. Haydarpasa Numune Med J 2019: 59: 315 319.

[13]Erikci VS. Intralesional bleomycin sclerotherapy in children with lymphangiomas: A review article. Ann Plast Reconstr Surg 2020: 4: 1069.

[14]Regmi D, Bista M, Shrestha S, Shrestha D, Mahato NB. Comparative study on efficacy of intralesional bleomycin injection in head and neck lymphangioma and vascular malformation. J Clin Diagn Res 2017: 11: MC04 6.

[15]Umezawa H. Recent study on biochemistry and action of bleomycin. In Carter SK, Crook ST, Umezawa H, eds: Bleomycin: Current Status and New Development. New York: Academic Press NY 1978: 15 20.

[16]Horbach SE, Rigter IM, Smitt JH, Reekers JA, Spuls PI, van der Horst CM. Intralesional bleomycin injections for vascular. Plast Reconstr Surg 2016: 137: 244-256.

[17]Abdelaty MH, Badran AI, Aborahma AM, Elheniedy MA, Kamhawy AH. Intralesional injection of bleomycin in the management of low flow vascular malformations: Results and factors affecting the outcome. J Vasc Surg Venous Lymphat Disord 2024: 12: 101694.

[18]Alqahtani SS, Ibrahim AH, Hader HA, Al Dumairy MA. Successful intralesional bleomycin injections for the management of a huge life-threatening cervical lymphangioma in a 3-day-old neonate. Ann Pediatr Surg 2018 : 14: 92-94.

[19]Muir T, Kirsten M, Fourie P, Dippenaar N, Ionescu GO. Intralesional bleomycin injection (IBI) treatment for haemangiomas and congenital vascular malformations. Pediatr Surg Int 2004: 19: 766-773.

[20]Poole S. Bleomycin sulphate dosing nomenclature. Aust J Hosp Pharm 1998;: 28: 211-211.

[21]Upadhyaya VD, Bhatnagar A, Kumar B, Neyaz Z, Kishore JS, Sthapak E. Is multiple session of intralesional bleomycin mandatory for complete resolution of macrocystic lymphatic malformation? Indian J Plast Surg 2018: 51: 60 65.

[22]Achauer BM, Chang CJ, Vander Kam VM. Management of hemangioma of infancy: Review of 245 patients. Plast Reconstr Surg 1997: 99: 1301 1308.

[23]Hassan Y, Osman AK, Altyeb A. Non-invasive management of hemangioma and vascular malformation using intralesional bleomycin injection. Ann Plast Surg 2013: 70: 70 73.

[24]Dubois J, Soulez G, Oliva VL, Berthiaume MJ, Lapierre C, Therasse E. Soft-tissue venous malformations in adult patients: imaging and therapeutic issues. Radiographics 2001: 21:1519-1531.

[25]Bertino F, Braithwaite KA, Hawkins CM, Gill AE, Briones MA, Swerdlin R, et al. Congenital Limb Overgrowth Syndromes Associated with Vascular Anomalies. Radiographics 2019: 39: 491-515.

[26]Jan I, Shah A, Beigh SH. Therapeutic effects of intralesional bleomycin sclerotherapy for non-invasive management of low flow vascular malformations - A prospective clinical study. Ann Maxillofac Surg 2022: 12: 151-156.

[27]Nevesny F, Chevallier O, Falvo N, Guillen K, Malakhia A, Pellegrinelli J, et al. Bleomycin for Percutaneous Sclerotherapy of Venous and LymphaticMalformations: A Retrospective Study of Safety, Efficacy and Mid-Term Outcomes in 26 Patients. J Clin Med 2021: 10: 1302.

[28]Pawar NM, Singh AP, Gupta AK, Chaturvedi V, Barolia DK. Comparison of intralesional bleomycin with/without doxycycline in the primary management of pediatric lymphangiomas. Formos J Surg 2021: 54: 177 182.

[29]Vollherbst DF, Gebhart P, Kargus S, Burger A, Kühle R, Günther P, et al. Image-guided percutaneous sclerotherapy of venous malformations of the head and neck:-clinical and MR-based volumetric mid-term outcome. PLoS One 2020: 15: e0241347.

[30]Okada A, Kubota A, Fukuzawa M, Imura K, Kamata S. Injection of bleomycin as a primary therapy of cystic lymphangioma. J Pediatr Surg 1992: 27: 440-443.

[31]Charabi B, Bretlau P, Bille M, Holmelund M. Cystic hygroma of the head and neck-a long-term follow-up of 44 cases. Acta Otolaryngol Suppl 2000;543:248-250.

[32]Horbach SER, van de Ven JS, Nieuwkerk PT, Spuls PI, van der Horst C, Reekers JA. Patient-reported outcomes of bleomycin sclerotherapy for low-flow vascular malformations and predictors of improvement. Cardiovasc Intervent Radiol 2018: 41: 1494-1504.

[33]Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992: 30: 473-483.