Original Article

Comparing bleomycin and sodium tetradecyl sulfate for treatment of low flow craniomaxillofacial venous malformations

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Objective: To compare the efficacy of bleomycin versus sodium tetradecyl sulfate for the treatment of low flow craniomaxillofacial venous malformations in the Pakistani population.

Methodology: This study utilized a randomized controlled trial design and was conducted at the Department of Oral & Maxillofacial Surgery, Allama Iqbal Medical College/Jinnah Hospital, Lahore, over six months. Patients who underwent sclerotherapy were given prophylactic antihistamine medication before the procedure. Patients with abnormal values in specific blood tests were excluded. Two groups were formed: Group A received a combination of xylocaine with adrenaline and bleomycin, while Group B received sodium tetradecyl sulfate. Outcome was assessed in both groups.

Results: The study enrolled participants with an age range of 8 to 40 years. The duration of symptoms varied from 8 to 24 months. The size of the lesions ranged from 6×10mm to 40×40mm. The study population consisted of 43.2% male patients and 56.8% female patients. Statistical analysis using the chi-square test revealed a significant association between treatment efficacy and the two groups, with a p-value of 0.020.

Conclusion: This study compares the efficacy of Bleomycin and Sodium Tetradecyl Sulfate (STS) in treating low-flow craniomaxillofacial venous malformations, with Bleomycin demonstrating a higher response rate, particularly in facial and oral cavity lesions. The findings support sclerotherapy as an effective minimally invasive treatment.

Keywords: Bleomycin, craniomaxillofacial venous malformations, intralesional sclerotherapy, sodium tetradecyl sulfate.

INTRODUCTION

Craniomaxillofacial venous malformations (CVM) encompassed a spectrum of vascular abnormalities affecting the head and neck region.[1] These involve anomalous structures within the blood vessels, including veins, arteries, lymphatics, or capillaries.[1,2] CVMs are classified into two major categories based on their hemodynamic characteristics[3] high flow and low flow lesions.[3,4] While high flow lesions were associated with arterial feeders and a risk of hemorrhage, low flow lesions predominantly consisted of venous channels and posed challenges due to their chronic nature and potential for progressive growth.[5]

The management of low flow CVMs typically involved a multidisciplinary approach, with treatment options ranging from observation and compression therapy to more invasive interventions such as surgery and embolization.[1,5,6] In recent years, sclerotherapy had emerged as a minimally invasive therapeutic modality for the treatment of these lesions.[7] Sclerotherapy involves the injection of a sclerosing agent into the malformation, leading to endothelial damage, thrombosis, and subsequent lesion regression.[8]

Among the various sclerosing agents available, bleomycin and sodium tetradecyl sulfate (STS) had shown promise in the treatment of low flow CVMs.[7] Bleomycin, an antineoplastic agent had been utilized in the management of various vascular anomalies, including venous malformations. On the other hand, STS, a detergent-like substance, had been widely used as a sclerosing agent for the treatment of venous diseases.[9] Given the potential efficacy of bleomycin and STS in the treatment of low flow CVMs, it was crucial to compare their effectiveness and determine the optimal treatment approach.[10] This study aimed to conduct a comparative analysis of bleomycin and STS in the management of low flow CVMs, with a specific focus on evaluating their therapeutic outcomes and identifying the agent with superior efficacy.

METHODOLOGY

This study employed a randomized controlled trial design conducted in the Department of Oral & Maxillofacial Surgery at Allama Iqbal Medical College/Jinnah Hospital in Lahore from January 25, 2021, to July 26, 2021. Approval from the Ethical Review Board of Allama Iqbal Medical College/Jinnah Hospital, was obtained (Ref. No. 49th/ERB, dated 15/05/2019). An informed consent was

taken from all participants.

The sample size for the study was determined based on a previous study by Bajpai et al, with a total of 74 participants 37 in Group A and 37 in Group B).[11] The sample size ratio between Group B (STS) and Group A (Bleomycin) was assumed to be 1, with a 5% level of significance and 80% power of the study. The effectiveness of bleomycin in Group A was estimated to be 87.5%, while STS in Group B was estimated to be 62.5%. Non-probability consecutive sampling technique was used.

Patients aged 8 to 40 years both males and females, with low-flow vascular lesions diagnosed as venous malformations through the Doppler study were included in the study. The size of the lesions ranged from 6×10mm to 40×40mm, measured by ultrasonography. Exclusion criteria consisted of immunocompromised patients, pregnant women, previously treated patients, patients with lesion recurrence, abnormal values in specific blood tests (Hb, Platelet count, PT, APTT, INR), and patients taking antihypertensive medications.

Sclerotherapy sessions were performed at two-week intervals, with randomization achieved through a lottery method. Prophylactic antihistamine medication (cetirizine 10mg) was administered one hour before the procedure. The injections were given by a single operator under strict aseptic conditions. Group A received 4ml of 2% xylocaine with adrenaline and 8mg of freshly prepared bleomycin in 2ml of normal saline, while Group B received 1ml of 3% (30mg) STS prepared in 4ml of 2% xylocaine with adrenaline. Up to five injections were given if necessary. The size of the lesion was measured and compared after the 10th week.

Post-operative analgesic medication (Flurbiprofen 100mg BID) and Omeprazole 20mg BID were administered for two days. Patients were observed for approximately one hour before discharge, with pressure packing applied for one hour. Outcomes were assessed using the Weidong Shou standards and a blinded radiologist evaluated the scans.[10]

Statistical Analysis: The data were analyzed using SPSS ver. 22.0. Stratification was performed to control for effect modifiers such as age, gender, duration and site of lesion, size of lesion, and number of injections. The post-stratification chi-square test was used to compare sclerotherapy outcomes between the two groups. Statistical significance was set at a $p \leq 0.05$.

Table 1: Demographic details.

	Minimum	Maximum	Mean	SD
Age	8	40	24.58	8.826
Duration of symptoms (months)	8	24	16.19	4.920
Number of injections for sclerotherapy	1	5	3.22	1.808

RESULTS

From a cohort of 74 patients, the age range observed was 8 to 40 years having, with a mean age of 24.58±8.826 years (Table 1). The duration of symptoms varied from 8 to 24 months, with a mean duration of 16.19±4.920 months.

Table 2: Stratification of outcome in both groups with regards to gender.

Gender	Group	Efficacy		Total	p-value
		Yes	No		
Male	Group A	16	1	17	0.061
	Group B	8	7	15	
Female	Group A	15	5	20	0.426
	Group B	14	8	22	
Total		53	21	74	

Table 3: Stratification of efficacy in both groups with regards to site of lesion.

Site of lesion	Group	Efficacy		Total	p-value
		Yes	No		
Face	Group A	10	0	10	0.025
	Group B	6	4	10	
Maxilla	Group A	7	1	8	0.919
	Group B	6	1	7	
Mandible	Group A	2	2	4	0.679
	Group B	5	3	8	
Oral cavity	Group A	12	3	15	0.020
	Group B	5	7	12	
Total		53	21	74	

The number of injections for sclerotherapy ranged from 1 to 5, with a mean of 3.22±1.808 injections. The size of the lesions ranged from 6 x 10mm to 40×40mm. Among

the patients, 32 (43.2%) were male, and 42 (56.8%) were female (Table 2). The distribution of lesion sites was as follows: 20 (27%) in the face, 15 (20.3%) in the maxilla, 12 (16.2%) in the mandible, and 27 (36.5%) in the oral cavity (Table 3). Efficacy was observed in 53 (71.6%) patients, while 21 (28.4%) patients did not show efficacy (Table 4). A significant association between efficacy and treatment groups was found using the chi-square test (p=0.020). No significant association was found between efficacy and gender in both treatment groups.

Table 4: Efficacy of drugs.

		Efficacy		X^2	p value
		No	Yes		
Group A (Bleomycin)	Count	6	31	5.38	0.020
	% within group A	16.2%	83.8%		
	% within efficacy	28.6%	58.5%		
Group B (Sodium Tetradecyl Sulfate	Count	15	22		
	% within group B	40.5%	59.5%		
	% within efficacy	71.4%	41.5%		

DISCUSSION

In a study, the efficacy of Bleomycin in treating venous malformations was investigated in a diverse patient population. Their results demonstrated a response rate of 85% in patients below the age of 18 and 75% in patients above the age of 18.[9]

These findings suggest that Bleomycin is effective in both pediatric and adult populations. Regarding the efficacy of Sodium Tetradecyl Sulfate (STS) in different age groups, another study evaluated the treatment outcomes of venous malformations using STS. They reported a response rate of 70% in patients below the age of 18 and 60% in patients above 18.[12] These findings indicate that STS can be effective in both pediatric and adult patients. Based on the available literature, our study aligns with previous research, demonstrating that both Bleomycin and STS effectively treat low-flow craniomaxillofacial venous malformations across different age groups.[11,12]

In our present study, the minimum duration of symptoms for low-flow craniomaxillofacial venous malformations was 8 months. In comparison, the maximum duration was 24 months, with a mean and standard deviation of 16.19± 4.920 months. To compare these findings with existing literature, we reviewed studies focusing on the duration of symptoms in patients with similar venous malformations. One study investigated the duration of symptoms in a cohort of patients with venous malformations. They reported a range of symptom duration from 6 to 36 months, with a mean duration of 20 months.[13] This study's findings suggest that our results align with the reported duration of symptoms in the literature. Overall, our study's findings regarding the duration of symptoms in low-flow craniomaxillofacial venous malformations are consistent with previous literature, indicating a range of 6 to 36 months and a mean duration of approximately 15 to 20 months. This consistency strengthens the validity of our study and adds to the growing body of evidence in this field.

One of the limitations of our study is the relatively small sample size. The limited number of participants in our Pakistani cohort might restrict the generalizability of the findings to a larger population. Future studies with larger sample sizes would be beneficial in providing more robust evidence. Despite its contributions, our study has a notable gap in the lack of long-term follow-up and evaluation of treatment outcomes. Assessing the efficacy and durability of treatment responses over an extended period is essential in understanding the true effectiveness of the interventions employed.

CONCLUSION

This study highlights the comparative efficacy of Bleomycin and Sodium Tetradecyl Sulfate (STS) in the treatment of low-flow craniomaxillofacial venous malformations within the Pakistani population. Both agents demonstrated significant therapeutic benefits; however, Bleomycin showed a higher response rate, particularly in facial and oral cavity lesions. The findings align with existing literature, supporting the efficacy of sclerotherapy as a minimally invasive treatment for venous malformations. Despite its smaller sample size and limited follow-up, this study underscores the potential of Bleomycin as a superior option for managing these challenging conditions.

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