

## Efficacy of Sodium Tetradecyl Sulphate for the Treatment of Venous Malformation of The Head and Neck

Komal Akram, Uzair Bin Akhtar, Shoaib Younus\*, Omer Sefvan Janjua\*\*, Rubbab Zahra\*\*\*, Sana Babar\*\*

Department of Dentistry, Sharif Medical and Dental College, Lahore Pakistan, \*Institute of Dentistry, Combined Military Hospital Lahore/ National University of Medical Sciences (NUMS) Pakistan, \*\*Department of Dentistry, Faisalabad Medical University, Faisalabad Pakistan, \*\*\*Department of Dentistry, Avicenna Medical and Dental College, Lahore Pakistan,

### ABSTRACT

**Objective:** To assess the efficacy of Sodium Tetradecyl Sulphate for the treatment of venous malformations of the head and neck region.

**Study Design:** A prospective clinical study.

**Place and Duration of Study:** Oral and Maxillofacial Surgery department of Sharif Medical and Dental College Lahore, Pakistan from Apr 2021- Apr 2022.

**Methodology:** All the patients who met the inclusion criteria and were willing to take part in the study were enrolled. Pre-operative demographic data, clinical examination findings were noted in the specially designed proforma. The diagnosis was confirmed using doppler ultrasonography. 0.5-2ml of 3% STS was injected in the lesions transcutaneously or transmucosally depending on the location after aspiration and till blanching of the lesion occurred. Cases were followed up for 04 weeks and pre-op and post-op results were assessed independently by a consultant using the Achauer's scale.

**Results:** Total 22 patients were enrolled. Mean age in the study was 17+11.93 years. Male to female ratio was 1:2.1. Buccal mucosa and the tongue were the most common sites, involved in 7(31.8%) cases. Complete and partial resolution was obtained in 14(63.6%) 22 cases. There were no post op complaints in majority of the patients. Post op pain, ulceration and sloughing was reported by 2(9.1%) of the patients.

**Conclusion:** The results of the study show that 3% STS was effective in reducing the size of the lesion to approximately 50% to the original size. Overall efficacy was found to be 63.6% with minimum morbidity and side effects.

**Keywords:** Head and Neck, Sclerotherapy, Venous malformations.

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### INTRODUCTION

Vascular tumors and vascular malformations (VMs) are two categories of pathologies that are currently included in the classifications of the International Society for the Study of Vascular Anomalies (ISSVA).<sup>1,2</sup> Hemangiomas as well as potentially aggressive & malignant proliferative endothelial lesions are examples of vascular tumors. Venous malformations, Capillary malformations, Arteriovenous malformations (AV), Lymphatic malformations, and Arteriovenous fistulae are among some examples of the abnormal vasculature that constitute VMs. They are also categorized in accordance to the kind of flow, such as increased or decreased flow.<sup>2</sup>

The hallmark of vascular malformations (VM) is a tiny, non-proliferating endothelium wall encircled by only a thin layer of smooth muscles. Usually, such

lesions do not involute and continue to grow proportionate to body size, frequently achieving vast volumes.<sup>3</sup> Hemangiomas seem to be aggressive, proliferating tumors that have a distinctive pattern of development that starts out quickly after birth and then slows down.<sup>3</sup> Even though the incidental finding of propranolol's pharmacological efficacy for the treatment of juvenile hemangiomas changed the therapy of such lesions, the overall results and benefits to patients of VM treated with propranolol therapy, are not encouraging.<sup>4</sup>

The most frequent vascular malformations include venous malformations (VMs), which emerge because of mistakes in venous formation. The head and neck area accounts for almost 40% of VM cases.<sup>5,6</sup> that makes therapy challenging, particularly in this anatomically fragile region. Such deformities are genetic defects which do not regress naturally but instead increase proportionately to the size of the body.<sup>7,8</sup> Yet, these lesions can quickly increase in adolescence, pregnancies, infections, trauma, and hemorrhage.<sup>7,8</sup>

**Correspondence:** Dr. Komal Akram, Department of Dentistry, Sharif Medical and Dental College, Lahore Pakistan

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VMs can range between a single cutaneous varicosity or small squishy masses to complicated lesions that invade several tissue planes. These are quick to replenish and have softer, fragile, non-pulsatile mass. Symptoms of VM can range from bluish to reddish skin discolorations, discomfort, swelling, infections, ulcers, bleeding, breathing and speaking difficulties depending on its size as well as site.<sup>8,9</sup> VMs can be treated in several ways, such as surgery, sclerotherapy, laser treatment, and cryotherapy.<sup>5,6</sup> Head and neck VMs may significantly affect both esthetic appearance and function. In addition to being a social problem for several individuals, peri-oral lesions may cause hemorrhage and pain in everyday tasks like eating or talking.

One of the first choice and the least traumatic therapy to decrease the size of a lesion is sclerotherapy (intralesional), this corresponds to the intralesional delivery of a sclerosant and has a documented success of 83% in studies.<sup>7-10</sup> Numerous substances, such as hypertonic saline Sodium Tetradecyl Sulphate (STS), nitrogen, bleomycin, warm water, OK-32 & ethanol are used as sclerosing agent.<sup>6</sup> Such compounds obliterate the vascular endothelial, causing thrombosis and swelling that leads to fibrosis and eventually the remission of the lesion.<sup>10</sup>

From 1946, STS, has been employed extensively as a sclerosing drug. Smaller leg varicose veins, in addition to venous & lymphatic abnormalities, are frequently treated with STS.

The rationale of the current study was to determine the efficacy of 3% STS for the treatment of oro-facial VMs. There are only a few local studies on the subject therefore we believe that this study will expand the local database on the subject and will be helpful in guiding the clinicians who have to treat these lesions in the head and neck region. The mechanism of action of STS is by causing endothelial impairment with little thrombus development, which results in scarring of the lesion and regression of the abnormal arteries.<sup>1</sup>

The goal of the present study was to evaluate the effectiveness of 3% STS in treating oro-facial VMs. There aren't many regional analyses on the topic, so we think this project will add to the local body of knowledge and be useful in directing surgeons who must manage such lesions within head and neck area.

### **METHODOLOGY**

This clinical study was conducted from Apr 2021-Apr 2022 at Oral and Maxillofacial Surgery department

of Sharif Medical and Dental College, Lahore. Prior permission to conduct the study was sought from the Institutional Ethical Review Committee (IRB No. SMDC/SMRC/166-21 dated 20th Feb 2021). VM were diagnosed on the basis of clinical findings such as soft, fluctuant blue/purple lesion present anywhere in the oro-facial area which showed blanching on diascopy. When in doubt, the diagnosis was confirmed using Doppler ultrasonography. A sample size of 16 was calculated using Scalex SP calculator at a 95% confidence interval (5% precision value) and taking the expected prevalence of venous malformation as 1.00%.<sup>2</sup>

**Inclusion Criteria:** All patients presenting with VM of the head and neck region at superficial location, easily accessible for injection, irrespective of their age and gender were included in study.

**Exclusion Criteria:** Patients not willing to take part in the study, presenting with arterial (high-flow) or lymphatic malformations, having a known bleeding disorder, previously treated at some other center for their VM or having a known allergy to the sclerosing agent were excluded from the study.

After enrolment, demographic data and clinical features of the lesion like chief complaint, site, size and color were noted on a specially designed proforma which was used as a data collection tool for the study. The size of the lesion was measured using a flexible ruler in 02 dimensions, antero-posteriorly and medio-laterally/bucco-lingually or supero-inferiorly as the case may be and the mean of the two readings was used to determine the overall size. Patients, in which diagnosis was uncertain, were referred to the radiology department for Doppler ultrasonography to confirm the diagnosis. The protocol used to treat VM was as follows; depending upon the size of the malformation 0.5-2ml (at a ratio of 0.5ml for each cm of lesion size) of 3% STS (Setrol 60mg/2ml Samarth Life Science Pharma, India) was injected after mixing it with equal amount of 2% Lignocaine.<sup>11</sup> This was done to improve patient discomfort upon injection and to increase the volume of the drug to in order to make it more manageable to inject. All injections were given percutaneously or permucosally using a 27-gauge fine needle after confirming negative aspiration. The solution was given until blanching was observed and a compression dressing was placed at the injection site for a period of 02 hours post operatively. The 3% STS injections cause post operative burning and pain therefore in order to improve patient comfort all the patients were prescribed Tab Ibuprofen 400mg three

times daily for 03 days (4-10mg/kg body weight for pediatric patients) or Tab Acetaminophen 500mg three times daily (10-15mg/kg body weight for pediatric patients) in case of allergy or contraindication to use of NSAID. All patients were given three similar injections at an interval of 02 weeks and were followed up for the next three months for recurrence. At each subsequent visit outcome was assessed and lesion characteristics were noted by an independent consultant following the Achauer's scale.<sup>12</sup> According to this scale, response was graded as poor when there was 0-25% reduction in size, fair with 26-50% reduction in size, good with 51-75% reduction in size, excellent with 76-90% reduction in size and complete when reduction was between 91 and 100%. Overall STS was considered effective when there was at least 50% reduction in size and when the outcome was fair or poor after three injections, it was labelled as ineffective. Any post operative complications other than recurrence or no response were also noted and were treated accordingly.

Data was analyzed using Statistical Package for Social Sciences software version 23. Frequency, percentages mean and standard deviation were calculated for various study variables. Sample t-test was applied to determine statistical significance and  $p < 0.05$  was considered significant.

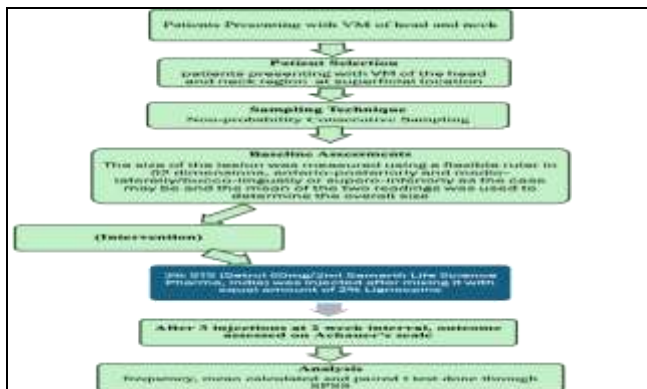


Figure: Study Methodology

**RESULTS**

A total of 25 patients were enrolled in the study. Out of these 25, 3 patients did not present for follow up hence they were excluded and the total sample size was 22. In these cases, 7(31.8%) were male and 15(68.1%) were female with an overall male to female ratio of 1:2.1. Age in the study ranged from 4 years to 52 years with a mean of 17+11.93 years. When site was analyzed, tongue 7(31.8%) and buccal mucosa 7(31.8%) were the most common sites with an equal distribution. This was followed by upper lip 3(13.6%), lower lip 2(9.1%),

forehead 1(4.5%), nose 1(4.5%) and neck 1(4.5%). When the reason for seeking treatment was analyzed, esthetic concern was the most common reason 9(40.9%) followed by difficulty eating 6(27.3%), frequent trauma 4(18.2%), swelling 2(9.1%) and bleeding 1(4.5%).

The mean size of the lesion at the start of the treatment was 2.64+0.93cm. Mean size after 3 injections was 1.02+0.85cm while the mean size was found to be 1.19+0.97cm at 03 months follow up. When pre-op and post-op mean values were compared, the results were found to be statistically significant ( $p$ -value  $< 0.05$ ).

On the basis of Achauer's scale, complete response was observed in 6(27.3%), excellent in 1(4.5%), good in 7(31.8%), fair in 4(18.2%) and poor in 4(18.2%). Overall treatment was found to be effective in 14(63.6%) of the cases and ineffective in 8(36.4%) cases.

When treatment related complications were assessed, 11(50%) patients did not report any untoward side effect. Post op pain was reported in 2(9.1%) cases, recurrence and no response was seen in 2(9.1%) cases respectively. (Table-I)

**DISCUSSION**

VM of the head and neck area, although not very common, yet a significant entity for oral and maxillofacial surgeon and plastic surgeons as they can have a deep impact on the psychosocial well-being of the afflicted individual.<sup>13,14</sup> In addition to esthetic problems posed by these lesions, disturbance in eating/speaking, pain and swelling can also impel the patients to seek treatment.<sup>15-17</sup> Among various treatment modalities proposed in the literature for the management of these lesions, intralesional sclerotherapy remains a viable minimal invasive option which has been shown to have reasonable efficacy for these lesions as surgical excision of these lesions tend to produce a cosmetic deformity which may be even more than the lesion itself.<sup>18</sup>

In our study we used 3% Sodium Tetradecyl Sulphate as sclerosant as it was readily available and is considered relatively safe for use in these cases with minimum reported side effects and morbidity.<sup>19</sup> Other agents that have been used by clinicians are ethanol, bleomycin, hypertonic saline, OK 32 etc., each having its own merits and demerits. Most of the lesions were superficially located and hence we were able to inject directly in these lesions. For lesions which are located deeper in the tissues, it is recommended that sclerosing agent should be given under guidance in order to

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**Table-I: Showing Pre-treatment and Post-treatment Findings of the Venous Malformations of the Head and Neck. (N=22)**

Sr no.	Age /sex	Site	Major complaint with the lesion	Size (pretreatment) in cm	Size (posttreatment) in cm after 3rd injection	Size at 3 months follow up	Outcome	Efficacy	Complications
1	7/m	Upper Lip	Esthetics	1.5	0.1	0.15	complete	Yes	Post op pain
2	16/f	Buccal mucosa	Difficulty in chewing	2.0	1.5	1.8	poor	No	No response
3	20/f	Lower Lip	Esthetics	3.2	2.0	2.2	fair	No	Mucosal sloughing
4	21/f	Buccal mucosa	Bleeding on trauma	2.4	0.5	0.7	good	Yes	Nil
5	6/f	Tongue	Pain and difficulty speaking	1.5	0	0	complete	Yes	Mild superficial ulceration
6	41/m	Tongue	Bleeding on trauma	4.0	3.5	3.8	No change	No	No response
7	5/f	Lower Lip	Esthetics	2.5	1.8	1.5	fair	No	Nil
8	24/m	Buccal mucosa	Troublesome swelling	1.5	0.5	0.5	good	Yes	Mild pain after first injection
9	52/f	Buccal mucosa	Chronic injury and pain	1.0	0.1	0.1	complete	Yes	Nil
10	17/f	Tongue	Increase in size causing concern	4.5	1.5	1.7	good	Yes	Nil
11	4/m	Upper Lip	Esthetics	3.5	1.0	1.2	good	Yes	Nil
12	5/f	Tongue	Difficulty eating and speaking	2.0	0.2	0.2	complete	Yes	Nil
13	4/m	Forehead	Esthetics	3.0	1.0	2.5	poor	No	Recurrence
14	5/f	Nasal tip	Esthetics and occasional bleeding	1.5	0.1	0.1	complete	Yes	Superficial ulceration of the skin
15	21/m	Tongue	Difficulty in eating	3.0	1.0	1.0	good	Yes	Mild ooze after first injection
16	16/f	Buccal mucosa	Frequent trauma	4.0	1.0	1.2	good	Yes	Nil
17	11/f	Neck	Esthetics	2.5	1.6	1.8	fair	No	Nil
18	18/f	Buccal mucosa	Difficulty in eating	3.5	0.5	0.7	Excellent	Yes	Nil
19	16/m	Buccal mucosa	Occasional bleeding	3.0	0.2	0.2	Complete	Yes	Nil
20	24/f	Tongue	Difficulty in speaking	2.5	1.0	1.0	Good	Yes	Nil
21	22/f	Upper lip	Esthetics	3.0	1.5	2.0	Fair	No	Recurrence
22	19/m	Tongue	Eating difficulty	2.5	2.0	2.0	Poor	No	Ulcer formation

maximize effect and to minimize any chance of complication.<sup>20</sup>

One to six sessions of intralesional injections of 3% STS have been reported in the literature for management of these lesions.<sup>21</sup> In our predetermined

protocol, we used 03 injections spaced over a period of two weeks unless lesion regressed completely or the patient refused further treatment. In our case series, majority were given injections according to the above-mentioned protocol without any significant issue.



In our study there was a female predominance (M:F=1:2.1). Similar results have been reported by Alakailly *et al.*<sup>22</sup> However, the results reported by Karimi *et al.*<sup>23</sup> and Inbaraj *et al.*<sup>24</sup> have shown a slight male predominance. The mean age in our study group was 17+11.9 years which is almost in concordance with what has been reported by Alakailly *et al.*<sup>22</sup> and Karimi *et al.*<sup>23</sup> This shows that patients who seek treatment are mostly adolescents and young adults. This also highlights the importance of these lesions as young females are comprise the most vulnerable group in terms of psychosocial issues.

Esthetics was the most prominent reason for which our patients seek treatment followed by difficulty eating and trauma. Swelling, bleeding and pain were the significant reasons reported by Inbaraj *et al.*<sup>24</sup> However, cosmetic disfigurement as major reason for seeking treatment has also been reported in the case series by Alakailly *et al.*<sup>22</sup> In our study buccal mucosa and tongue were the most common sites of presentation with an equal distribution of 31.8%. Karimi *et al.*<sup>23</sup> in their study also reported that buccal mucosa and the tongue were the most common sites of presentation. Buccal mucosa and the tongue are two important anatomical sites which are regularly involved in eating, speaking and chewing and can impose a significant functional issue for the patient and hence can be a potential reason for the patients to present for treatment.

Mean size of the lesion at the time of presentation in our study was 2.64+0.93cm. Overall around 50% reduction in size was observed with a mean size of 1.19+0.97cm at the end of the 3 month follow up period. Mean size of the lesion reported by Alakailly *et al.* was 3.2 cm and that reported by Inbaraj *et al.* was 3.8 cm.<sup>22,24</sup> This shows that lesion size in our series was almost similar to what has been reported in other studies.

We used Achauer's scale to objectively grade the outcome and according to this scale complete response was observed in 27.3% cases while good to excellent response was seen in 36.3% cases. In the remaining 36.4% cases, the results were not optimal and the treatment was declared unsuccessful. Whenever there was at least 50% or more reduction in size from the start, the treatment was labelled effective and according to this grading overall effectiveness in our study was 63.6% which meant that in 63.6% cases a reduction of at least 50% was observed in the size of the lesion. Karimi *et al.*<sup>23</sup> in their study have pointed out a 67.3% efficacy using a similar protocol for follow up. Inbaraj *et al.*<sup>24</sup> in

their study report a 50% efficacy with 3% STS injections in VMs of the tongue. A similar finding has also been reported by Alakailly *et al.*<sup>21</sup> where they report good to complete response in around 60% of their cases when using 3% intra lesional STS.

Pain and swelling are the most commonly reported side effect of STS therapy in literature.<sup>25</sup> In our case series it was observed infrequently. A possible explanation could be that we advised NSAIDs for pain and edema control from the start and this could be a reason that pain and swelling was observed in around 10% cases only.

#### LIMITATION OF STUDY

Although the results of the study have been in favor of using 3% STS as intralesional sclerosant for VM of the head and neck region yet a small sample size and a relatively smaller follow up period of 03 months precludes us to draw definitive conclusions that can be generalized to a bigger population hence the authors recommend conducting large scale multi-center studies with longer follow ups so that conclusive results can be obtained on the subject matter.

#### CONCLUSION

The results of the study show that 3% STS was effective in reducing the size of the lesion to approximately 50% to the original size. Overall efficacy was found to be 63.6% with minimum morbidity and side effects. Therefore, it is recommended that 3% STS should be considered as first line cost effective and minimally invasive therapy for the management of VM of the head and neck region.

**Conflict of Interest:** None.

#### Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MRBK: & KQ: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AR: & MMK: Data acquisition, data analysis, approval of the final version to be published.

SZ: & IA: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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