Original Article

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MRI Evaluation of Response to Percutaneous Sclerotherapy in Slow Flow Vascular Malformations

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Abstract

Background: Percutaneous sclerotherapy is an effective treatment for slow flow vascular malformations. **Objectives:** To evaluate the role of MR imaging in response evaluation after completion of image guided sclerotherapy in patients with slow flow vascular malformation, and to evaluate subsequent symptomatic relief. **Subjects and Methods:** A cohort observational study of 35 patients was done in our department. After appropriate measures the MRI and Sclerotherapy treatment was done, under ultrasound and fluoroscopy guidance. After 4 sessions or after complete thrombosis of lesion as seen on ultrasound, MRI was done after 30 days of last session**. Statistical Analysis:** Data was coded and recorded in MS Excel spreadsheet program. SPSS version 21 has been used for data analysis Mean diameter of lesion in two planes was calculated and reduction in size of lesion was evaluated and classified. Assessment of patient's symptom relief was done according to Likert scale. **Results & Conclusion:** In our study we found that there was no change in size of lesion in 20% cases, minor improvement in 40% cases and major improvement in 40% cases based on reduction in size as evaluated on MRI. The mean Percentage Reduction of Size was 34.23 %. Symptomatic improvement in 8.6% patients was same as before, 48.6% patients had fairly good improvement, 37.1% patients had good improvement and 5.7% patients had very good improvement.

Keywords: Slow flow vascular malformations, sclerotherapy**.**

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Introduction

Slow-flow vascular malformations are congenital anomalies that usually appear at birth. They are irregular, variably dilated, dysmorphic channels having thin basement membrane and flattened endothelium in contrast to hypercellularity seen in vascular tumours. They can be diffuse, localized, superficial or deep.[1] Simple slow flow vascular malformations can be of 3 types- venous, lymphatic and capillary.[2,3] According to International society for study of vascular anomalies (ISSVA 2018), vascular anomalies are classified into two main groups: proliferative vascular tumours and non-proliferative vascular malformations.[5,6] Diagnosis of slow flow vascular malformation is typically based on history, clinical presentation, evaluation with doppler ultrasound and confirmation by MR imaging. Percutaneous sclerotherapy is the best treatment because it is a simple, safe and effective method. [2] Many kinds of sclerosants can be used in treating vascular malformations. Although each sclerosant has a different mechanism of action with different rates of success and complications, they all result in a thrombus composed of erythrocytes and fibrin which organizes with subsequent contraction and recanalization leading to regression of the lesion.[3] Commonly used sclerosants are 3% sodium tetradecyl sulfate, sodium morrhuate, 3% polidocanol, bleomycin, absolute ethanol, doxycycline and hypertonic saline 23.4% solution.[1,3-5] Our objectives in this study is to evaluate the role of MR imaging in response evaluation after completion of image guided sclerotherapy and to evaluate subsequent symptomatic relief.

Subjects and Methods

Selection of participants-
35 patients with slow flow vascular malformations were selected
Sample size-
Saima Ahmad has performed study to evaluate the efficacy of percutaneous sclerotherapy in terms of improvement (>50% decrease in size) on MR imaging.[6] The efficacy

found in this article is 90%. Therefore, assuming (p)=90% with 10% margin of error, the minimum required sample size at 5% level of significance is 35 patients.

Formula used

$$n = \frac{Z^2_{\alpha/2}\, pq}{d^2}$$

$$= \frac{1.96*1.96*0.90*0.10}{(0.10*0.10)}$$

$$= 34.57$$

where p is the observed efficacy of percutaneous sclerotherapy

q = 1 - p

d is the margin of error

$Z_{\alpha/2}$ is the ordinate of standard normal distribution at α% level of significance

Inclusion Criteria

All patients with slow flow vascular malformations as diagnosed on MRI, ultrasound and clinical assessment.

Exclusion Criteria

The following patients shall not be considered for the study:

- Patients with high flow vascular malformations and vascular tumours.
- Patients with previous treatment with sclerosant.
- Patients with superficial and deep vein thrombosis.
- Pregnant patients.
- Patients with hypercoagulable state.
- Patients in whom MRI is contraindicated

Methodology

A cohort observational study was carried out in the department of radiodiagnosis, VMMC and Safdarjung hospital, New Delhi for period of 18 months. A total of 35 patients were included in our study who met inclusion criteria. After informed written consent, history, local examination and ultrasound examination, MRI was done using discovery MR750W 3-T MR machine with standard head and surface coils. 3mm sections were taken fat saturated T2 weighted/STIR images in axial and coronal/sagittal planes. T1 weighted FSE images in axial and coronal/sagittal planes in pre and post contrast phase. Mean diameter of the lesion in two planes were recorded. Lesions were divided based on size. Sclerotherapy treatment was done. After 4 sessions or after complete thrombosis of lesion as seen on ultrasound, MRI was done after 30 days of last session. Follow up of patient was taken for symptomatic relief and side effects of treatment

MRI Categorization

Grade 1-Well-defined ≤5 cm diameter
Grade 2A-Well-defined >5 cm diameter
Grade 2B-Ill-defined ≤5 cm diameter
Grade 3-Ill-defined >5cm diameter [6]

Procedure

Foam was prepared by Tessari's method in which we took 2 ml sclerosant (2% sodium tetradecyl sulfate) with 2ml mixture of contrast and normal saline in 10 ml luer lock syringe. 4 to 6 ml air was taken in other 10 ml luer lock syringe and was connected via 3 way stop cock to other syringe. Foaming was done by to and fro movements of both syringes. Percutaneous sclerotherapy was performed under ultrasound (GE) and fluoroscopic guidance (Philips Allura Xper FD20/20) under local anaesthesia and aseptic precautions as an OPD procedure.

- A 21-24G scalp vein needle was put into vascular channels of malformation percutaneously under ultrasound guidance until a free blood return is observed.
- Phlebography was done using low osmolar, water soluble nonionic iodinated contrast material to confirm needle position within vascular malformation and assess venous drainage.
- Tourniquet, cuff or direct pressure was applied over draining vein.
- Freshly prepared sclerosant foam was injected into venous malformation under fluoroscopic guidance. When sclerosant entered the vascular malformation, it replaced the previously injected contrast material, pushing it into draining vein which appeared as negative contrast on digital subtraction angiography.
- Post procedure patients were put on short course of broad spectrum antibiotics, analgesics and anti-inflammatory drugs.
- Repeat session was done after 4-6 weeks interval depending upon resolution of lesion as decided clinically and by ultrasound.

Patient was evaluated after 30 days of last session of sclerotherapy. In post treatment MRI, size of each lesion was measured in 2 planes. Evaluation was based on mean diameter of the lesion in two planes.

Small lesion ≤5cm in maximum diameter (Grade 1 or 2B)
Large lesion > 5cm in maximum diameter (Grade 2A or 3)
Categorization on MRI follow up:

1. Worse (Lesion is larger in follow up scan)
2. No change
3. Minor improvement (<50% decrease in size)
4. Marked improvement (≥50% decrease in size)
5. Cured (Lesion no longer visible on MRI)

Any side effect of treatment like nausea, vomiting, infection, skin discoloration over injected site, ulceration, peripheral nerve injury and veno-thromboembolism was recorded.

Statistics

Descriptive statistics were analyzed with SPSS version 21.0 software. Continuous variables were presented as mean ± SD. Categorical variables were expressed as frequencies and percentages. The chi-square test/Fisher test of association was used to determine if there is a relationship between two variables. P<0.05 was considered statistically significant.

Ethics

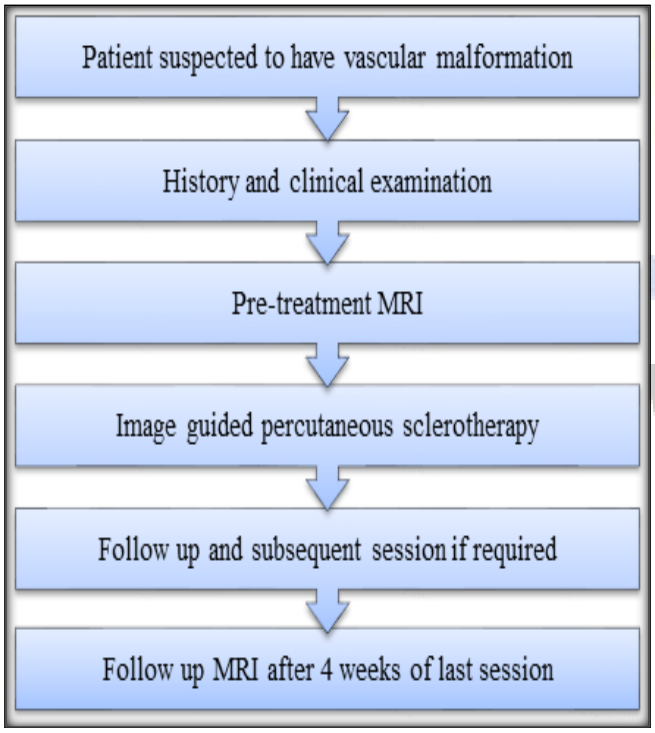
Ethical clearance was duly obtained from the Institutional

Ethical Committee and informed consent of all the participants was taken.

Results

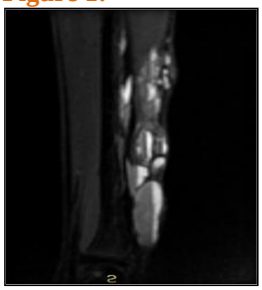
In our study, 62.9% of the patients were male and 37.1% were female. In 94.3% of the patients, sodium tetradecyl sulfate was used and 5.7% of the patients, polidocanol was used as sclerosant. The mean Percentage Reduction of Size was 34.23 %.

Symptomatic improvement in 8.6% patients was same as before, 48.6% patients had fairly good improvement, 37.1% patients had good improvement and 5.7% patients had very good improvement. Most common complication was pain (74.3%) followed by oedema (40%). Other complications were hyperpigmentation, scarring and mouth ulcers. In our study, 40% of the patients showed significant reduction in size of the lesion based on MR imaging. 42.8% of patient showed good symptomatic relief after completion of sclerotherapy treatment.

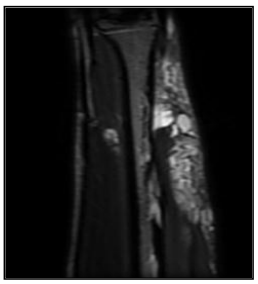


Study flow chart

Figure 1:



A



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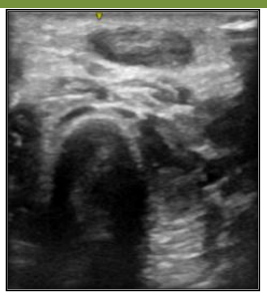

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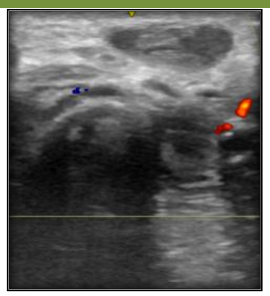

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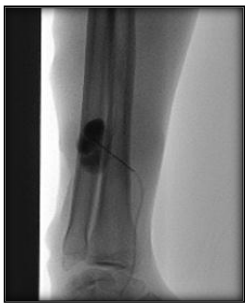

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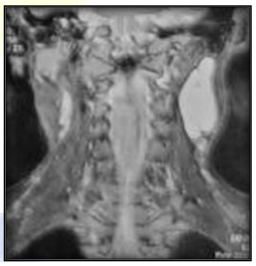
Figure 2:



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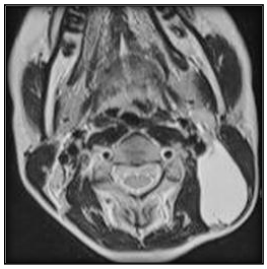

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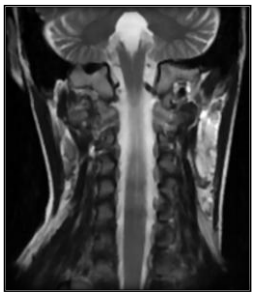

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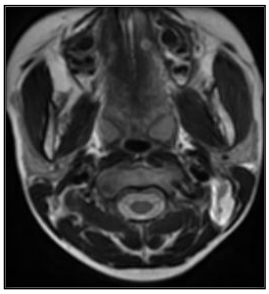

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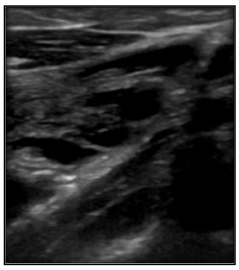

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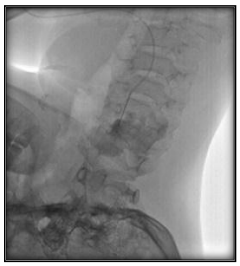

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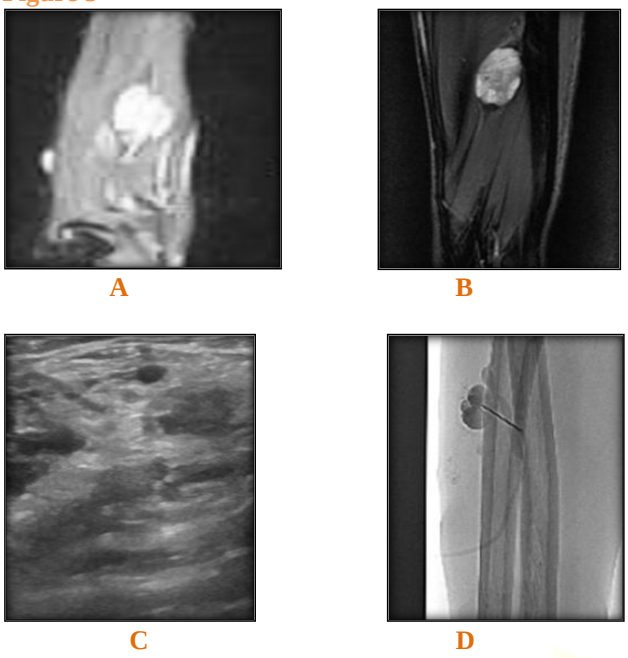
Figure 3



Legends

Figure 1: 15-year-old male with swelling in distal part of right forearm since birth and is increasing. Pain for two years. On examination there was ill-defined swelling. No skin discolouration/visible pulsation or bruit.

a) Pre-sclerotherapy MRI(STIR), b) Post-sclerotherapy MRI(STIR), c) and d) Ultrasound and Doppler showed thrombosed channels, e) Sclerosant injected under fluoroscopy guidance

Figure 2: 22-year female with swelling on left side of neck for 2 years with on and off pain. On examination there was ill-defined swelling. No skin discolouration/visible pulsation or bruit.

a) & b) Pre-sclerotherapy MRI coronal and axial respectively(STIR), c) Post-sclerotherapy MRI (coronal STIR), d) Post sclerotherapy MRI (Axial T2), e) Ultrasound showed patent anechoic channels, f) Sclerosant injected under fluoroscopy guidance

Figure 3: 15-year-old female with swelling and pain in right forearm for 9 years. On examination there was ill-defined swelling. No skin discolouration/visible pulsation or bruit.

a) Pre-sclerotherapy MRI(STIR), b) Post sclerotherapy MRI(STIR), c) Ultrasound showed thrombosed channels, d) Sclerosant injected under fluoroscopy guidance.

Discussion

In our study, one or more sclerosant injections proved effective in decreasing the volume of VMs and LMs. The effect of the treatment was best represented by the percentage of size reduction as there was considerable variability in size of lesions at baseline. The mean size reduction was 34.23%. There were no major complications. Significant improvements were obtained as 40% patients showed more than 50% reduction in size as seen on MRI. There was symptomatic improvement in pain, discomfort, cosmesis and swelling. There was overall improvement in the patient-perceived changes in health and treatment satisfaction.

Lesion volume is generally used to assess the efficacy of treatments for vascular malformations. In most studies, a reduction of at least 50% defined a good to excellent result and we used the same threshold.[6-15] In most of the studies done previously, results were mainly based on clinical assessment.[10-20]

Prospective study was done by Tuoretmaa et al. in 41 patients with venous malformation in head and neck area or extremities using two sclerosants- polidocanol and ethanol. It was observed using MRI evaluation that 17% patient showed decrease in size more than 50%. However in our study, 40% patients showed this result.[9] They concluded that 46 % patients benefited from the treatment but in our study more than 90% patients benefited.[9]

Haq et al. evaluated reduction of lesion on MRI in 14 patients of venous malformation using bleomycin foam as sclerosant. In their study, a mean of 66% reduction was observed however in our study mean reduction of 34.23% was observed.[21] In their study more than 60% reduction was observed in 57% cases but in our study only 14.28% showed more than 60% reduction in size. In their study, one patient had 3% increase in size of lesion; however in our study no patient had increase in size of lesion.[21]

Spence et al. in their study of 37 patients with facial venous malformations used bleomycin for sclerotherapy. They evaluated the lesion using MR imaging and found that 65.6% patients showed objective improvement. Of all the lesions, 34.3% showed a marked decrease in size (>50%).[8] In our study 40% patients showed marked decrease in size and 80% showed objective improvement. In their study, no vascular malformation got worse and none of them showed a complete cure after the treatment similar to our study.[8]]

Saima Ahmad found in her study that there was complete obliteration of lesion in 37% with sclerotherapy alone in a sample size of 35 patients with malformation in head and neck and extremities. Sclerosants used in this study were sodium tetradecyl sulphate and bleomycin.[6] In our study no lesion showed complete obliteration.

Retrospective study was done by Nevensy et al. in 26 patients with slow flow vascular malformations.[15] patients had venous malformation and 11 had lymphatic malformation. Bleomycin was used as sclerosant. On MRI in case of venous malformations decrease in size of >70% was seen in 27% cases (out of 11) and in lymphatic malformations, decrease in size of >70% was seen in 80% cases(out of 10).[15] In our study we observed decrease of size >70% only in 2.8% cases. So it is also concluded that bleomycin is superior to sodium tetradecyl sulfate in treatment of slow flow vascular malformations as seen in studies by Haq et al, Raichura et al, Helal et al, Nevensy et al.[15, 21-23]

It should be noted that volume reduction of lesion on MRI does not always correlate with symptomatic improvement. Of note, nine (26%) of the thirty-five patients in whom the volume reduction by MRI was less than 50% reported

symptomatic relief of six points (>50% relief) or more on the numerical score.

Patients tend to perceive subtle changes rather than drastic improvements in their overall condition. Thus, only 42.8% of our patients reported a good improvement (>50% symptomatic relief) in overall satisfaction. In contrast, in a study by Li et al. where the physicians evaluated the improvement, they found an overall good response for 93% of vascular malformations after sclerotherapy treatment with sodium morrhuate.[24] Also in a study done by Stimpson et al. in which sodium tetradecyl sulfate was used as sclerosant that 83% patients showed good response based on evaluation by clinician.[25] This discrepancy underlines the importance of collecting outcomes as reported by patients. Most of our patients had expectations that exceeded what could be realistically achieved. The lifelong nature of venous and lymphatic malformations should be explained to the patients at the time of the diagnosis and feasible improvements should be described so that patients can adjust their expectations to reality. Spence et al. in their study using bleomycin found out that 90.6% of the patients showed subjective improvement on basis of patient's perception of response and 93.8% showed improvement as evaluated by treating clinician.[8] In our study 91.4% cases showed subjective improvement as evaluated on Likert scale from the patients.

In our study no significant correlation was seen between number of sessions, amount of sclerosant given and symptomatic relief. In previous studies no such correlation was tried to establish. We also observed that as the lesion size increases, number of sessions required was also increased.

None of our 35 patients experienced major complications and twenty-seven (77%) had minor complications that resolved completely. Khandpur and Sharma conducted a study in 2010 using sodium tetradecyl sulfate as sclerosant in which nearly all the patient experienced transient pain and scarring was seen in 30.7% cases.[10] In our study 74.3% patients experienced pain and 8.6% had scarring as complication.

Sodium tetradecyl sulfate is a synthetic long-chain fatty acid that has seen extensive industrial use as a synthetic surfactant as soap. In previous studies, it has been associated with success rates of 43–84% for the treatment of venous malformations.[26] In our study success rate was 40%. The principal side effect of this drug is a tendency to cause hyperpigmentation.[27] In our study hyperpigmentation was seen in 4(11.4%) cases. No serious complications were seen in our study which is comparable with most of the studies in which sodium tetradecyl sulphate was used. Most of the studies showed no serious complications. [6,25]

Sodium tetradecyl sulfate is commonly used as it is widely available, has long shelf life of 36 months, easy to administer and has comparatively low cost as compared to other agents. The efficacy of sodium tetradecyl sulfate also compares well with that of other commonly used sclerosing agents. Ethanol has long been recognized as the strongest sclerosing agent, with a remission rate upto 95% and is widely used.28 It is avoided because of concerns about potential nerve damage or thromboembolism. Major complications include pulmonary hypertension, pulmonary embolism, rhabdomyolysis, anaphylaxis, consumptive coagulopathy, cardiovascular collapse and death.[29] Sodium tetradecyl sulfate has safety profile which is well documented. So it is preferred over ethanol as an the initial option for sclerotherapy.[25] Foam sclerotherapy with sodium tetradecyl sulfate is beneficial as maximum sclerosant action can be obtained at lesser concentration and quantity as foam increases the surface area for action which increases contact with endothelial surfaces over a period of up to several weeks.[25,27]

In practice, sodium tetradecyl sulfate sclerotherapy as the first choice in our study was at the discretion of the interventional radiologist. In our study no patient had complete obliteration of the lesion.

Conclusion

Vascular malformation management and treatment requires a multidisciplinary approach that involves specialists in radiology, interventional radiology, surgery and primary physician care. We found that image guided percutaneous sclerotherapy is an effective, safe and inexpensive method for treating slow-flow venous malformations. Sodium tetradecyl sulfate and polidocanol are effective sclerosing agents. In this study significant symptomatic relief was observed with this treatment. Considering the side effects and results of this treatment it is safe to say that sclerotherapy should be first line treatment for various vascular malformations before proceeding to surgery. MRI although expensive yet it is best modality to compare the result of sclerotherapy treatment. However clinical comparison based on patient's and clinician's subjective analysis cannot be undermined.

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