ORIGINAL ARTICLE

EFFICACY OF INTRALESIONAL BLEOMYCIN INJECTION SCLEROTHERAPY IN MACROCYSTIC LYMPHANGIOMA IN PAEDIATRIC PATIENTS

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Background This study is aimed to assess the efficacy of intralesional Bleomycin sclerotherapy in macrocystic lymphangioma in children **Methods:** This prospective observational study included 40 children diagnosed with macrocystic lymphangioma and treated with intralesional injection of Bleomycin from March 2016 to Dec 2018. We excluded all the patients above 12 years of age, lesions with size less than 2 cm, and post-surgical recurrent lesions. The response to the treatment was monitored clinically by assessing length, breadth and area of the lesion and ultrasonographically. Mean follow-up period was 2 years. Study variables were analysed by simple descriptive statistics. Mean and standard deviation were calculated for numerical variables (age). Frequency and percentage were calculated for gender, site, size and type of cystic lymphangioma and total number of treatment sessions. **Results:** The mean age of patients was 3.51±2.98 years. Out of 40 patients, there were 26 (65%) male and 14 (35%) females with female to male ratio of 1:1.8. The commonest site and type of cystic lymphangioma was neck and macrocystic, i.e., 77.5% and 85% respectively. The pre and post procedure size of lesion was 9.71±3.95cm and 3.11±1.02 cm, respectively. Outcome was excellent in 20% patients, good in 72.5% and poor in 7.5% patients. **Conclusion:** Intralesional Bleomycin sclerotherapy is effective in the treatment of macrocystic lymphangioma and is found to be harmless as there was no grave complication observed in this study.

Keywords: Lymphangioma; Intralesional; Bleomycin

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INTRODUCTION

Lymphangiomas, characterized by multiple communicating lymphatic channels and cystic spaces, are benign slow growing hamartomatous tumour of lymphatic vessels.[1] This tumour mostly involves children, but incidence has been described in adults. It appears at birth in about 65% of the cases and, the age of 2 years in 80–90% of cases.[2,3]

The frequency of lymphangioma is believed to be 1.5–2.8 per 1000, and it has no predilection for either gender or any ethnic group.[4,5] Swelling and cosmetic deformity are the commonest symptoms. Vital structures of neck can be compressed by huge swelling and this can be the reason of dysphagia, respiratory obstruction and nerve compression symptoms.[6] It may involve any part of body. The areas commonly affected are the head and neck region, axilla and mediastinum.[7] Microcystic, macrocystic and mixed are the three different types of cystic lymphangiomas on ultrasonography.[8]

Surgical excision remains the backbone of the traditional treatment, nevertheless owing to its propensity to involve deeper structures like muscles and nerves, complete excision is not always possible.[9] The widespread surgical treatment may sometimes lead to deformity, injury to contiguous vital structures, difficulty in accomplishing comprehensive removal, horrible scar and re-appearance which could be as high as 20%.[10,11] To escape the injury linked with operative removal, intra lesional injection of a sclerosing agent has long been utilized.[12]

Numerous nonsurgical remedies have been recommended, comprising cryotherapy, diathermy, fibrin glue, radiotherapy, and percutaneous injection sclerotherapy.[13,14] Intralesional sclerotherapy has turned out to be a technique of management for lymphangiomas in paediatric population. Several sclerosing agents have been utilized in the management of infantile lymphangiomas.[15] Previously, 50% dextrose, boiling water, absolute alcohol, or hypertonic saline has been utilized. The results were not very promising. With the introduction of agents like acetic acid, Bleomycin, Doxycycline, OK-432, various centres are using these as principal

therapies with acceptable outcomes.[16] Sclerosing agents cause injury to the endothelial cell lining of the cystic lymphangiomas, resulting in inflammation, fibrosis and involution. Other modalities of treatment, for example radiation therapy and incision and drainage have shown poor outcomes.[17] The purpose of this study was to assess the efficacy of intralesional bleomycin injection therapy in cystic lymphangioma in paediatric population.

MATERIAL AND METHODS

This observational study was conducted in the Department of Paediatric Surgery, Children Hospital & Institute of Child Health, Multan from March 2016 to Dec 2018 after approval from hospital ethical committee which included 40 patients with age less than 12 years who presented with swelling diagnosed as macrocystic lymphangioma based on clinical assessment and ultrasound imaging and contained straw-coloured serous fluid on aspiration. We excluded all the patients above 12 years of age, lesions with size less than 2 cm and post-surgical recurrent lesions. Informed consents were taken from parents. The patients underwent aspiration of the cystic lesions with 18G needle under oral / IV sedation and under local anaesthesia in the operative room and 0.3 IU per Kg body weight of diluted Bleomycin was injected. Patients were observed for any complications for 24 hours after the procedure. Response of intralesional injection of bleomycin was recorded after four weeks by clinical examination and with ultrasound measurements. This procedure was repeated after four weeks if the cystic component persisted and measured greater than 1 cm^3 volume.

No further attempts were made if there was a poor response to four treatment sessions. The response to the treatment was monitored clinically by assessing length, breadth and area of the lesion and ultrasonography. The response was graded as excellent when complete disappearance, good (>50%reduction) and poor (<50% reduction). Mean follow-up period was 2 years.

The data was entered into SPSS version 20, computer program and analysed accordingly. Study variables were analysed by simple descriptive statistics. Mean and standard deviation were calculated for numerical variables (age). Frequency and percentage were calculated for gender, site, size and type of cystic lymphangioma and total number of treatment sessions.

RESULTS

Characteristics of cystic lympahngioma are shown in table-1. The mean age of patients was 3.51±2.98 years. There were 26 (65%) male and 14 (35%) females with female to male ratio of 1:1.8. The commonest site and type of cystic lymphangioma was in the neck, i.e., 77.5% and macrocystic, i.e., 85% respectively. The pre and post procedure size of lesion was 9.71±3.95 cm and 3.11±1.02 cm, respectively. Outcome is shown in figure-1.

Table-1: Characteristics of cystic lymphangioma

Parameters		No. of patients (%)
Site	Face	1 (2.5)
	Neck	31 (77.5)
	Axilla	6 (15)
	Chest wall	2 (5)
	Abdomen	0 (0)
	Back	0 (0)
	Limb	0 (0)
	Others (mediastinum)	0 (0)
Type of cystic lymphangioma	Macrocystic	34 (85)
	Microcystic	0 (0)
	Mixed	6 (15)
Pre procedure Size (cm) (mean±SD)		9.71±3.95
No of treatments	1	8 (20)
	2	15 (37.5)
	3	14 (35)
	>3	3 (7.5)
Post procedure size (cm) (mean±SD)		3.11±1.02
Complications of procedure	Fever	1 (2.5)
	Local tenderness	3 (7.5)
	Injection site infection	0 (0)
	Skin changes	2 (5)
	Increase in swelling size	0 (0)
	Excessive scarring	0 (0)
Post procedure swelling	Present	3 (7.5)
	Absent	37 (92.5)

Figure-1: Pie chart of Outcome

DISCUSSION

This clinical trial conducted on efficacy of intralesional Bleomycin injection therapy in cystic lymphangioma included 40 patients. In our study, the mean age of patients was 3.51±2.98 years. In a study by Ainippully AM *et al*, the median age was 18 months.[18] In a study by Erikçi V *et al*, with the exception of five new-born patients, the average age was 3.8 years (2 months-9 years).[19] In a study by Bhatnagar A *et al*, age ranged from 3 months to 52 years (median 14 years).[20] There were 26 (65%) male and 14 (35%) females, with female to male ratio of 1:1.8 in our study. The male preponderance was seen in a study by Ainippully AM *et al,* i.e., 58.8%.[18] In another study by Pan P, there were 75% male and 25% female with a F:M ratio of 1:3.[21] In a study by Bhatnagar A *et al*, 66.67% patients were <17 years (male: female = 11:7) while 33.34% patients were older than 17 years (male: female = 4:5).[20]

In this study, the commonest site of cystic lymphangioma was neck, i.e., 77.5% followed by axilla (15%), chest wall (5%) and face (2.5%). Similarly, in a study by Ainippully AM *et al*, the commonest site was neck, i.e., 73.5% followed by axilla (8.82%), chest wall (8.82%), limb (5.88%) and face (2.94%).[18] In another study by Pan P, the neck region was the most common site, i.e., 72.3% patients, followed by axilla (19.5%), face (5.6%), and chest wall (2.78%).[21] In a study by Erikçi V *et al*, most of the lesions were located in the cervical region, i.e., 47.05% followed by thoracic wall (23.52%), shoulder (11.76%), gluteus (5.88%), lumbar region (5.88%) and abdominal wall (5.88%).[19] In a study by Kumar V *et al*, the neck region was the most common site with 62.86% patients, followed by face with 20%, 8.57% in chest wall, 5.71% in axilla, and 2.86% in buttock and thigh.[22] In a study by Bhatnagar A *et al*, the neck region was most common site found in 55.6% patients followed by axilla and chest in 25.9% patients, face in 3.70% patients, and lumbar region in 3.70% patients.[20]

In our study, lymphangiomas were of macrocystic variety, i.e., 85% followed by mixed type, i.e., 15%. Cystic lymphangiomas of microcystic type were not included in this study. However, in a study by Ainippully AM *et al*, the commonest type was macrocystic cystic lymphangioma, i.e., 88.2% followed by microcystic type, i.e., 11.8% and no mixed type was observed in their study.[18] In a study by Erikçi V *et al*, most of the lesions were macrocystic type (76.47%), followed by mixed type (23.52%); there were no microcystic lesions in this series.[19] In our study, the pre and post procedure size of lesion was 9.71±3.95cm and 3.11±1.02cm, respectively. In a study by Ainippully AM *et al*, the mean size of the swelling was 6 cm X 5cm (±3X2).[18] In a study by Bhatnagar A *et al,* initial and final volume of lesions were 156±50.01 and 24.67±20.06 ml, respectively.[20]

In our study, 37.5% patients required treatments twice while 35% patients required three sessions of treatment. In our study, 20% patients responded to single treatment however, more than three treatments were required to 7.5% patients. In a study by Ainippully AM *et al*, 5.88% patients required three sittings of procedure, 35.5% required two and 58.8% patients required single sitting of procedure.[18] In another study by Pan P, 8.3% patients required single dose, 30.5% patients required two doses, 38.8% patients required three doses, 11% patients required four doses, and 11% patients required six doses of intralesional bleomycin.[21] In a study by Kumar V *et al*, 20% required single dose, 57.14% required two doses, 5.71% required three doses, 11.42% required four doses, and 5.71% required five doses of intralesional bleomycin.[22] In a study by Bhatnagar A *et al*, 59.25% patients received 3 or <3 sessions while rest 40.74% needed 4–6 sessions of sclerotherapy for desired response. Interestingly, 14.81% patients only required single session for complete resolution of symptoms.[20]

In our study, post procedure fever was noticed in 2.5% patients, local tenderness in 7.5% and skin changes in 5%. Injection site infection, increase in the swelling size and excessive scarring were not observed in our study. In another study by Pan P, 33.3% patients developed fever, 33.3% had a transient increase in size of swelling, 22.2% developed mild tenderness and fever, and 11.1% patients showed skin discoloration at injection site.[21] In a study by Kumar V *et al*, 30% patients had transient increase in size of swelling, 20% developed local infection, 10% developed intraluminal bleed, and 10% showed skin discoloration.[22] In a study by Bhatnagar A *et al*, 40.74% patients developed side effects, i.e., fever in 14.81%; local infection in 7.40%; transient increase in size in 3.70%; intracystic bleed in 3.70%; and local skin discoloration in 7.40% patients.[20]

Cystic lymphangioma was completely resolved in 92.5% patients however, residual lesion was observed in 7.5% patients. In a study by Ainippully AM *et al*, lesion was completely resolved in 67.6% patients however, in 32.4% patients, it was present after treatment with bleomyin injection.[18] In our study, the outcome was excellent in 20%, good in 72.5% and poor in 7.5% patients. In a study by Ainippully AM *et al*, the post procedure result was excellent in 68% patients, good in 26% and poor in 9% patients.[18] In another study by Pan P, 50%

patients showed complete resolution, and 50% showed good response.[21] In a study by Erikçi V *et al*, good response was seen in 50% of the lesions, complete resolution in 35.7%, and poor response in 14.3% patients.[19] In a study by Kumar V *et al*, 25% patients showed excellent response, 71.42% showed good response, and 3.57% patients showed poor response.[22] In a study by Bhatnagar A *et al*, the response was excellent in 81.48% patients while 18.51% patients showed good response and none of the patient had poor response.[20]

This study had certain limitations. It was a single centre study and requires a larger sample size.

CONCLUSION

It is concluded that Intralesional injection of Bleomycin is safe and effective in the treatment of cystic lymphangiomas especially in the neck region and in macrocystic variety as the lesion regressed in size to an acceptable level, and is found to be a harmless modality of treatment in the management of macrocystic lymphangiomas, as there was no grave complication observed in this study.

AUTHORS' CONTRIBUTION

This study was conducted under the supervision of MH and SA, who helped to conduct the study, selection of patients, interpretation of results in collaboration with the co-author, Kashmala, the anaesthesiologist.

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