

# Compare the Outcomes of Sclerotherapy with Bleomycin Versus 15% Hypertonic Saline in Children with Cystic Hygroma

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## ABSTRACT

**Objective:** The goal of this research is to evaluate the efficacy of bleomycin sclerotherapy against hypertonic saline (at 15%) in treating cystic hygroma in children.

**Study Design:** Comparative study

**Place and Duration:** Children Hospital, Pakistan Institute of Medical Sciences PIMS Islamabad. July 2021-Feb 2022.

**Methods:** There were 52 children of both genders with cystic hygroma were included in this study. Included children had age 2 months to 12 years. After taking informed written consent from the parents of children detailed demographics age, sex, weight and place of living were recorded. Patients were equally categorized in two groups. 26 patients in group I received sclerotherapy with bleomycin and in group II 26 children received 15% hypertonic saline. Post-treat outcomes among both groups were assessed and compared. SPSS 22.0 was used to analyze all data.

**Results:** Among 52 children, there were 32 (61.5%) males and 20 (38.5%) females. Mean weight of the children was 14.7±5.37 kg and mean age was 6.9±9.54 years. Majority of the cases 34 (65.4%) were from rural areas and 18 (34.6%) were had urban residency. Most common site of lymphangioma was neck and axilla. In group I 18 (69.2%) children received four sessions of bleomycin. We found higher number of effectiveness in patients of group I 25 (96.2%) as compared to group II in 22 (84.6%) cases with p value <0.009. Frequency of wound infection and recurrence rate was also higher in group II.

**Conclusion:** We concluded in this study that the use of sclerotherapy with bleomycin was an effective and useful in the treatment cystic hygroma children in terms of higher number of excellent results as compared to 15% hypertonic saline. Except this recurrence rate and complications were also not seen in sclerotherapy with bleomycin group.

**Keywords:** Bleomycin, Sclerotherapy, Cystic Hygroma, Recurrence, Wound Infection, 15% Hypertonic Saline

## INTRODUCTION

Multiloculated lymphatic system malformations like cystic hygroma (CH) are extremely rare, affecting just 1 in 6,000 to 12,000. In around 50% to 65% of instances, cystic hygroma (a congenital lymphatic malformation) is evident at birth, and in the remaining 80% to 90%, it becomes apparent by the age of 2 years [1]. A majority of cystic hygromas (75%) are found in the neck, 20% are found in the axilla, and 5% are found elsewhere (e.g., the mediastinum, retroperitoneum, pelvis, or groin) near major veins or lymphatic ducts [2]. Compression of essential tissues, breathing obstruction, dysphagia, and signs of nerve compression can all result from a major lesion in the neck [3]. Lymphangiomas are often treated with surgical removal; however, this can be challenging due to the tumor's tendency to spread and infiltrate neighbouring tissues. As a result, it is not unusual for surgeons to make mistakes during surgical care, leading to partial excision or nerve damage [2]. Non-invasive therapies for cystic hygroma include aspiration, drainage operations, radiation, cryotherapy, diathermy, laser therapy, chemotherapy, and intralesional sclerotherapy. Examples of sclerosants include sodium morrhuate, dextrose, hypertonic saline, tetracycline, doxycycline, acetic acid, ethanol, boiling water, alcoholic solution of zein (ethibloc), fibrin sealant, triamcinolone, OK-432, and bleomycin [4].

Since 1977 [5], cystic hygromas have been treated with bleomycin as a sclerosing agent. 88% of instances, according to studies, have a positive outcome. The injection site discoloured, the cystic hygroma grew rapidly in size, the patient had fever, vomiting, cellulitis, interstitial pneumonia, and pulmonary fibrosis [6]. Doxycycline, however, is a tetracycline derivative, is a broad-spectrum antibiotic that is both commonly used and affordable. For the treatment of cystic hygroma, doxycycline has been used successfully by a number of writers [7-9].

Intralesional sclerotherapy for lymphangiomas in children has gained popularity in recent years as a viable therapeutic option [10]. In this method, a sclerosing substance is used to irritate the lymphangioma's endothelium lining, causing it to enlarge, involute, and eventually scar over [11]. Prior methods, such as using hot

water, 50% dextrose water, hypertonic saline, or 100% alcohol, did not yield promising results [12]. The use of sclerosing agents such as Bleomycin, acetic acid, OK-432, and Doxycycline as first-line treatment is becoming commonplace at many facilities. [13,14] This kind of therapy is preferable to surgical excision since it may be used on lesions that have already engulfed essential tissues [15]. To evaluate the efficacy and safety of sclerotherapy against 15% hypertonic saline in the treatment of cystic hygroma in children, the current study was carried out.

## MATERIAL AND METHODS

This comparative study was conducted at Children Hospital, Pakistan Institute of Medical Sciences PIMS Islamabad and comprised of 52 children. After taking informed written consent from the parents of children detailed demographics age, sex, weight and place of living were recorded. Patients who had previously received sclerotherapy, older than 15 years, or who had a recurrence were not included in this research.

All of the patients were split up into two different groups, which were: Group I comprised of 26 patients who were treated with sclerotherapy intra-lesionally using bleomycin at a dosage of 0.3 mg/kg of body weight and a number of sessions ranging from one to four for each individual patient. Following each session, the patients were kept in the hospital for a period of 24 hours. Patients might receive a maximum of four sessions every single month. Group II, comprised of 26 patients who were given 15% hypertonic saline. Maximum three sessions of 15% hypertonic solution among each individual was given. Complications following the procedure were documented. Examined were the outcomes in terms of excellent (complete resolution), good (>50% resolution), and bad (less than 50% resolution). The rate of recurrence was examined at the last follow-up. After sclerotherapy, follow-up was performed three and six months later. In order to evaluate how well the procedure went, pre- and post-operative ultrasonography were performed. The data were analyzed using SPSS 22.0. In order to analyze the differences in results between the two groups, a Chi-square test and a student t test were conducted.

**RESULTS**

Among 52 children, there were 32 (61.5%) males and 20 (38.5%) females. Mean weight of the children was 14.7±5.37 kg and mean age was 6.9±9.54 years. Majority of the cases 34 (65.4%) were from rural areas and 18 (34.6%) were had urban residency.(table 1)

Table-1: Included patients with detailed demographics

Variables	Frequency	Percentage
Mean age (years)	6.9±9.54	
Mean Weight (kg)	14.7±5.37	
Gender		
Male	32	61.5
Female	20	38.5
Residency		
Urban	18	34.6
Rural	34	65.4

Most common site of lymphangioma was neck 30 (57.7%) followed by axilla 12 (23.1%), face 6 (11.5%) and trunk 4 (7.7%).(figure 1)

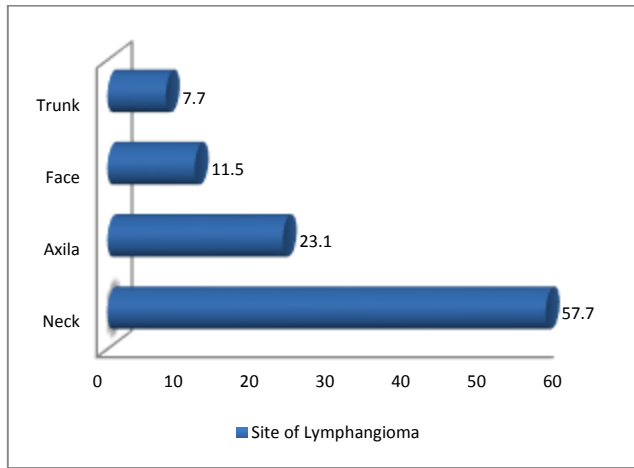


Figure-1: Different sites of lymphangioma among all cases

In group I 18 (69.2%) children received four sessions of bleomycin, 6 (23.1%) cases received three sessions and two sessions were given to 2 (7.7%) cases.(figure 2)

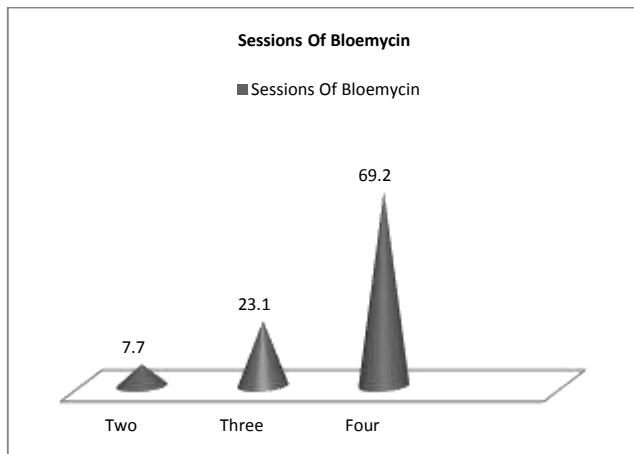


Figure-2: Frequency of bleomycin sessions in group I

In group II 15 (57.7%) patients received three sessions of 15% hypertonic solution, 8 (30.8%) received two sessions and 3 (11.5%) received one session of 15% hypertonic solution.(figure 2)

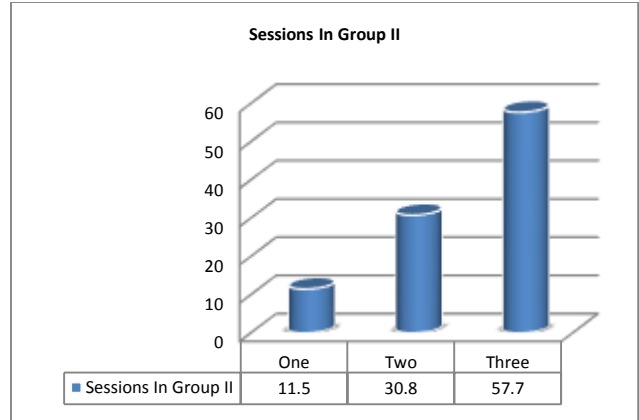


Figure-2: Sessions of 15% hypertonic solution in group II

We found higher number of effectiveness in patients of group I 25 (96.2%) as compared to group II in 22 (84.6%) cases with p value <0.009.(table 2)

Table-2: Post-treatment outcomes among both groups

Variables	Group I	Group II
Effectiveness		
Yes	25 (96.2%)	22 (84.6%)
No	1 (3.8%)	4 (15.4%)
Distribution of Outcomes		
Excellent	17 (65.4%)	13 (50%)
Good	5 (19.2%)	4 (15.4%)
Fair	3 (11.5%)	5 (19.2%)
Poor	1 (3.8%)	4 (15.4%)

Frequency of wound infection 3 (11.5%) and recurrence rate 2 (7.7%) was in group II but there was no any recurrence found in group I and wound infection found only in 1 (3.8%) children.(table 3)

Table-3: Post-treatment comparison of wound infection and recurrence rate

Variables	Group I	Group II
Wound Infection		
Yes	1 (3.8%)	3 (11.5%)
No	25 (36.2%)	23 (88.5%)
Recurrence Rate		
Yes	0	2 (7.7%)
No	26 (100%)	24 (92.3%)

**DISCUSSION**

According to their clinical behaviour and cellular dynamics, vascular abnormalities can be divided into two categories: vascular tumours and vascular malformations. Vascular tumours are distinguished from vascular malformations by the presence of endothelial hyperplasia, whereas vascular malformations develop as a result of vascular dysmorphogenesis and display normal endothelium turnover. In our research, we found a total of eight vascular tumours and nine vascular abnormalities, specifically cystic hygromas (hemangiomas). Sclerotherapy and surgical excision are the treatment options for these lesions, respectively. [16]

A lymphangioma is a benign tumour that forms as a result of a developmental defect in the lymphatic system. The development of a multilocular cystic mass that varies in size is one of the hallmarks of this condition. It is believed that lymphangiomas are caused by a combination of the following factors: failure of the lymphatic system to link to the venous system; abnormal budding of lymphatic tissue; and lymphatic rests that have been sequestered but still have their embryonic development potential. [17]

In our study 52 children with age 2 months to 12 years were presented in this study. Among 52 children, there were 32 (61.5%)

males and 20 (38.5%) females. Mean weight of the children was  $14.7 \pm 5.37$  kg and mean age was  $6.9 \pm 9.54$  years. Results of our study was comparable to the studies conducted in past.[18,19] Most common site of lymphangioma was neck 30 (57.7%) followed by axilla 12 (23.1%), face 6 (11.5%) and trunk 4 (7.7%). It is important to distinguish hemangiomas from vascular malformations, which are not real neoplasms but rather are localised anomalies of vascular morphogenesis caused by failure in embryogenesis and vasculogenesis. Hemangiomas are generated by endothelial cell hyperplasia. Since the cellular growth of a tumour is what the Greek suffix "oma" refers to, using the term "hemangioma" to refer to a malformation is technically incorrect. Hemangiomas are the most common benign soft-tissue tumour of infancy and childhood, occurring in 12% of all infants. They are found in greater frequency in girls, whites, premature infants, and twins, and they are typically born to mothers of higher maternal age. Hemangiomas can be found in greater frequency in premature infants. They are classified as infantile hemangiomas and congenital hemangiomas, and the head and neck area is where they manifest themselves the most commonly at a rate of sixty percent, followed by the trunk at a rate of twenty-five percent and the extremities at a rate of fifteen percent.[20]

Conrad Pienaar and colleagues successfully treated hemangiomas with an injection of bleomycin at a normal dose of 0.3–0.6 mg/kg each injection. Bleomycin is a cell cycle drug that disrupts the S-phase of the cell cycle by cutting the DNA chain during the mitotic phase of the cell cycle. Accordingly, it is hypothesised that the actions of bleomycin on hemangiomas disrupt the growth of vascular endothelial cells. After being treated with bleomycin for a number of times, the change in colour that often signals the beginning of involution is a transition from a brilliant red to a purple or grey tint. We acquired positive results by using bleomycin as a sclerosing agent in order to control the angiogenesis of the hemangiomas. Corticosteroids (either intralesional or systemic corticosteroids), interferon-alpha, laser therapy, cryotherapy, and surgical excision are some of the well-established therapies that are available.[21,22]

Bleomycin has a dual mode of action; first, it has a cytotoxic impact, and second, it causes sclerosis. It is a DNA synthesis inhibitor, and its exact mechanism of action in cystic hygroma is not known; nevertheless, it is hypothesised that it may induce a non-specific inflammatory process that culminates in the fibrosis of the cysts. This is because it inhibits the formation of new DNA. Intralesional It has been reported that the bleomycin microsphere in oil emulsion has a favourable reaction because it is kept for a long length of time. Treatment with a high dose of bleomycin is linked to an increased risk of developing pulmonary fibrosis. The maximum dose of bleomycin that should ever be administered in a single treatment session is 30 mg/m<sup>2</sup>. There was no instance of pulmonary fibrosis in any of the patients who participated in any of the published trials that utilised low dosages of bleomycin.[23]

Hypertonic solutions are those in which the solute concentration is higher than that of the cell and the volume of the solution is lower. In addition to problems, we need to be familiar with solutions in order to grasp its meaning. The dissolving solute and the dissolving solvent are both components of a solution. Lemonade, intravenous saline solution, glucose solutions for feeding cultured cells, and so forth are all examples of solutions. A cell is surrounded by solutions and protected by a membrane that is only partially permeable. Osmosis is the process by which water travels into or out of a cell depending on the nature of the solution. During osmosis, liquid travels from a region of low solute concentration to a region of high solute concentration.[24]

In our study, group I (sclerotherapy with bleomycin) 18 (69.2%) children received four sessions of bleomycin, 6 (23.1%) cases received three sessions and two sessions were given to 2 (7.7%) cases. We found higher number of effectiveness in patients of group I 25 (96.2%) as compared to group II in 22 (84.6%) cases with p value <0.009. Previous studies presented same results.[25] Frequency of wound infection 3 (11.5%) and recurrence rate 2

(7.7%) was in group II but there was no any recurrence found in group I and wound infection found only in 1 (3.8%) children. Previous research has shown that surgical excision has a higher recurrence and wound infection incidence than sclerotherapy [26,27]. The amount of post-operative care required for hypertonic solution is substantially more than for sclerotherapy, as we noticed.

## CONCLUSION

We concluded in this study that the use of sclerotherapy with bleomycin was an effective and useful in the treatment cystic hygroma children in terms of higher number of excellent results as compared to 15% hypertonic saline. Except this recurrence rate and complications were also not seen in sclerotherapy with bleomycin group.

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