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EFFICACY OF INTRALESIONAL BLEOMYCIN SCLEROTHERAPY INJECTION IN CHILDREN WITH CYSTIC HYGROMA

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Abstract

Objective: *This study aimed to evaluate the efficacy of intralesional bleomycin sclerotherapy as a treatment for cystic hygroma in children, focusing on its ability to achieve complete resolution of the condition while assessing associated side effects.*

Methodology: *A quasi-experimental study was conducted at the Department of Pediatric Surgery, Lady Reading Hospital, Peshawar from [06-July-2024 to 06-January-2025]. Ninety-seven children aged 1 to 8 years with clinically diagnosed cystic hygroma in the cervico-facial region were enrolled using consecutive non-probability sampling. Exclusion criteria included arteriovenous malformations and thoracic or abdominal lymphangiomas. After obtaining informed consent, each participant received intralesional bleomycin sclerotherapy under sedation with oral chloral hydrate (25 mg/kg). Bleomycin (0.5 mg/kg), diluted in 10–15 cc of distilled water, was injected into the cyst following fluid aspiration, with the procedure overseen by an experienced consultant. Efficacy, defined as complete cyst disappearance after three weeks, was assessed clinically.*

Results: *Of the 97 participants (mean age 4.80 ± 2.183 years), Sixty (61.9%) were male and 37 (38.1%) female. Complete resolution occurred in 82 children (84.5%), while 15 (15.5%) showed no such outcome. Side effects were minimal, with 87 (89.7%) experiencing none, 6 (6.2%) reporting skin discoloration, and 4 (4.1%) developing residual fibrotic nodules. Statistical analysis revealed no significant influence of age, gender, BMI or socioeconomic factors on efficacy.*

Conclusion: *Intralesional bleomycin sclerotherapy proved highly effective and safe, achieving an 84.5% complete resolution rate with few complications, supporting its use as a primary treatment for pediatric cystic hygroma. These findings advocate for its broader application in clinical practice.*

INTRODUCTION

Cystic hygroma is a non-cancerous congenital condition which primarily manifests in newborns.[1]The prevalence rate varies from 1 in 6,000 to 1 in 16,000 newborns in the United States.[2] Cystic hygroma can occur in different places throughout the body; however, it is predominantly found in the neck, with 70–80% of cases occurring especially in left posterior cervical triangle.[3]Lymphangiomas are typically categorized into three distinct categories: capillary, cavernous, and cystic lymphangiomas. The

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classification can also be approached more conveniently by considering the size of the contained cysts, categorizing them as microcystic, macrocystic, as well as mixed lymphangiomas. Microcystic lymphangioma is characterized by cysts that measure less than 2 cm, in contrast to macrocystic lymphangioma, where the cysts exceed 2 cm in size. [4, 5]

Cystic hygromas are non-cancerous cysts resulting from abnormalities in the lymphatic system. The precise embryonic origin remains uncertain; however, it is thought that these conditions arise from defects in development or cystic abnormalities of dilated lymphatic vessels.It has been established that these originate from the parts of embryonic lymphatic tissue, which retains the capacity for proliferation. These have been identified as being linked to specific conditions, including hydrops fetalis, chromosome aneuploidies, as well as intrauterine death.[6, 7]

In a trial involving 70 patients, intralesional bleomycin resulted in complete clinical remission for 47% of participants, while 35.8% experienced a reduction above 50%, and 17.1% had a reduction of less than 50%.[8] However, sclerotherapy presents several adverse effects such as localized swelling at the lesion site, potential scarring, pulmonary fibrosis, risk of hemorrhage, as well as the possibility of infection.[9] Furthermore, sclerotherapy may prove ineffective in treating cysts that are not attainable for injections. Therefore, we suggest a more efficient strategy that integrates sirolimus with the previously discussed modalities. [10, 11] According to a study, the efficacy of intralesional bleomycin sclerotherapy injection in children with cystic hygroma was recorded 90%. [12]

Intralesional bleomycin sclerotherapy injection has emerged as a valuable treatment option for children with cystic hygroma. Its minimally invasive nature, outpatient setting make it an suitable choice for healthcare providers. However there is no such data available on its efficacy in our local level. The goal of this study is to find out the efficacy of intralesional bleomycin sclerotherapy injection in children with cystic hygroma. The results of this research work will be beneficial for medical professionals to understand the role of intralesional bleomycin sclerotherapy, offering hope to children and their families facing this congenital condition. Moreover, careful patient selection, monitoring, and consideration of potential complications will be crucial aspects of ensuring successful outcomes in the management of cystic hygroma with this innovative approach.

METHODOLOGY:

This investigation adopted a quasi-experimental approach and was conducted within the Department of Pediatric Surgery at Lady Reading Hospital in Peshawar, spanning from [06-July-2024 to 06-January-2025]. The study population consisted of 97 children, a sample size determined using the WHO sample size calculator, based on an anticipated efficacy rate of 90%[12] for intralesional bleomycin sclerotherapy, a 95% confidence level, and a 6% margin of error. Participants were selected through a consecutive non-probability sampling method, ensuring a practical yet representative cohort for analysis.

The research commenced after receiving ethical clearance from the hospital. Children aged between 1 and 8 years, irrespective of gender, who presented with cystic hygroma characterized by a soft, fluctuating, freely mobile mass with a bluish tint in the cervico-facial region, confirmed through clinical evaluation were included in the study. Those with arteriovenous malformations or lymphangiomas located in the thoracic or abdominal regions were excluded to maintain focus on the specific condition under investigation.

Prior to enrollment, informed consent was obtained from the parents or guardians of each participant after thoroughly explaining the study's purpose, procedures, potential risks, and benefits, while assuring them of the confidentiality of their child's information and the absence of personal risk tied to participation. Demographic details, including age, gender, body mass index (BMI), socioeconomic background, parental education and employment status, and residential location, were meticulously documented for each child. The intervention involved administering intralesional bleomycin sclerotherapy, wherein each child was sedated using oral chloral hydrate at a dose of 25 mg/kg. Subsequently, an 18-gauge needle was inserted into the lesion to aspirate cystic fluid, followed by the injection of bleomycin at a dosage of 0.5 mg/kg,

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diluted in 10–15 cc of distilled water, with the needle rotated in three-quarters of a circle to ensure even distribution within the cyst. This procedure was performed under the careful supervision of a consultant with at least five years of post-fellowship experience, ensuring precision and safety throughout. Patient details and treatment outcomes were recorded using a specially designed proforma tailored to capture all relevant data.

To evaluate the efficacy of the treatment, defined as the complete resolution of the cystic hygroma three weeks post-intervention based on clinical assessment, follow-up examinations were conducted. The collected data were analyzed using SPSS version 23. Numerical variables such as age, weight, height, and BMI were summarized with means and standard deviations or medians and interquartile ranges, depending on their distribution. Categorical variables, including gender, efficacy (complete disappearance), side effects (such as skin discoloration or residual fibrotic nodules), and demographic factors like socioeconomic status and place of residence, were expressed as frequencies and percentages. To explore potential effect modifiers age, gender, side effects, and socioeconomic variables—data were stratified, and statistical significance was assessed using either the Chi-square test or Fisher's exact test, depending on sample size constraints, with a 5% significance level. The results were then organized and presented through tables and graphs to facilitate clear interpretation of the findings.

RESULTS:

In our study examining the efficacy of intralesional bleomycin sclerotherapy injections in children with cystic hygroma, we included a total of 97 participants. The average age of these children was 4.80 years, with a standard deviation of ±2.183 years, reflecting a fairly broad age distribution. Their body mass index averaged 15.3341 kg/m², with a standard deviation of ±0.74723 kg/m², suggesting a relatively uniform physical profile across the group.

Demographically, our sample had a slight male predominance, with 60 children (61.9%) being male and 37 (38.1%) female. Parental education showed that 53 parents (54.6%) were educated, while 44 (45.4%) had no formal education. Employment status indicated that 45 parents (46.4%) were employed, compared to 52 (53.6%) who were unemployed. Residence patterns revealed that 42 children (43.3%) came from rural areas, while 55 (56.7%) resided in urban environments. Socioeconomic status varied across the cohort, with 22 children (22.7%) from low-income families, 55 (56.7%) from middle-income households, and 20 (20.6%) from high-income background (Table 1).

In terms of treatment efficacy, we found that complete disappearance of the cystic hygroma occurred in 82 children (84.5%), while 15 (15.5%) did not experience this outcome, underscoring a robust success rate (Table 2). As for side effects, 87 children (89.7%) experienced no adverse effects. However, 6 children (6.2%) developed discoloration of the skin, and 4 (4.1%) had residual fibrotic nodules (Figure 1). When exploring the relationship between efficacy and side effects, among the 82 children with complete disappearance, 3 (3.7%) had skin discoloration, 1 (1.2%) showed residual fibrotic nodules, and 78 (95.1%) reported no side effects. In contrast, among the 15 children without complete disappearance, 3 (20.0%) experienced skin discoloration, 3 (20.0%) had fibrotic nodules, and 9 (60.0%) showed no side effects (P = 0.0001) (Table 3). However we could not find any notable association of efficacy with demographic effect modifiers. These findings highlight the treatment's high efficacy and relatively low incidence of complications in our study population.

Table 1 Demographics

Demographics		N	%
Gender	Male	60	61.9%
	Female	37	38.1%
Education status of parents	Educated	53	54.6%
	Uneducated	44	45.4%

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Employment status of parents	Employed	45	46.4%
	Unemployed	52	53.6%
Residence area	Rural	42	43.3%
	Urban	55	56.7%
Socioeconomic status	Low	22	22.7%
	Middle	55	56.7%
	High	20	20.6%

Figure 1 Side effects

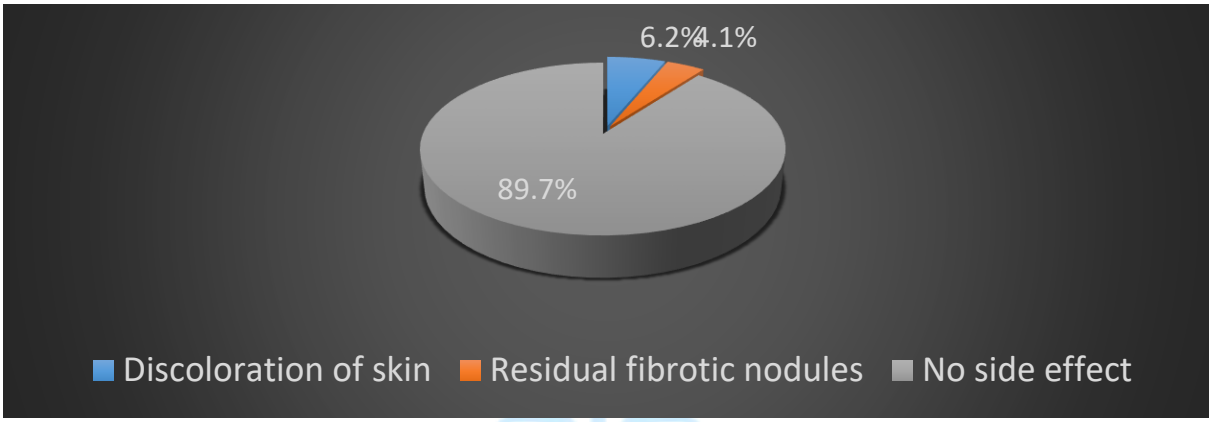

Table 2 Efficacy

Efficacy (Complete disappearance)	Frequency	Percent
Yes	82	84.5
No	15	15.5
Total	97	100.0

Table 3 Stratification of efficacy with side effects

		Side effects			Total	P value
		Discoloration of skin	Residual fibrotic nodules	No side effect		
Efficacy (Complete disappearance)	Yes	3	1	78	82	0.0001
		3.7%	1.2%	95.1%	100.0%	
	No	3	3	9	15	
		20.0%	20.0%	60.0%	100.0%	
Total		6	4	87	97	
		6.2%	4.1%	89.7%	100.0%	

DISCUSSION:

In our study the average age hovered around 4.80 years with a variability of ±2.183 years. This age range aligns closely with findings from other investigations, such as that by Hashmi et al., where the mean age was reported as 3.51 years with a standard deviation of ±2.98 years, suggesting that cystic hygroma predominantly affects children in their early years, often becoming apparent before the age of five[13]. Similarly, Niramis et al. documented a

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broader age span from one month to 14 years among 70 patients, yet the majority were still within the preschool age group, reinforcing the notion that this condition manifests early in life[8].

Demographically, our study revealed a male predominance, with 60 children (61.9%) being male compared to 37 (38.1%) female, yielding a male-to-female ratio of approximately 1.6:1. This finding echoes Hashmi et al.'s observation of 26 males (65%) versus 14 females (35%), translating to a ratio of 1.8:1.[13] Niramis et al. also reported a similar skew, with 42 males (60%) and 28 females (40%) among their 70 participants.[8] However, Saha et al.'s smaller cohort showed a near-even split with four males and three females, though the sample size limits generalizability.[14] Pan's study of 36 children indicated a stronger male bias, with 27 males (75%) and nine females (25%), suggesting potential variability across populations.[15]

Turning to efficacy, our research demonstrated a robust response, with complete disappearance of the cystic hygroma in 82 children (84.5%), while 15 (15.5%) showed no such resolution. This high success rate surpasses several comparative studies. For instance, Hashmi et al. graded outcomes as excellent in 20% (complete disappearance), good in 72.5% (>50% reduction), and poor in 7.5% (<50% reduction), indicating a lower rate of total resolution compared to ours.[13] Niramis et al. reported an excellent response in 33 cases (47.1%), good in 25 (35.8%), and poor in 12 (17.1%), again showing a less frequent complete resolution than our findings.[8] Saha et al. achieved complete resolution in six of seven cases (86%), a figure remarkably close to ours, though their small sample cautions against overgeneralization.[14] Pan noted complete resolution in 16 of 36 cases (44.4%), with 17 (47.2%) showing good response and three (8.3%) poor, falling short of our efficacy rate.[15] Nabi et al.'s bleomycin group saw an excellent response in 18 of 30 (60%), with 10 (33.3%) good and two (6.7%) poor, suggesting doxycycline outperformed bleomycin in their context, yet still lagging behind our 84.5% complete resolution.[16].

Side effects in our study were minimal, with 87 children (89.7%) experiencing no adverse effects, six (6.2%) noting skin discoloration, and four (4.1%) developing residual fibrotic nodules. Hashmi et al. reported fever in one child (2.5%), local tenderness in three (7.5%), and skin changes in two (5%), with 92.5% complication-free, aligning closely with our findings.[13] Niramis et al., however, observed side effects in 30 cases (42.9%), including fever, swelling, redness, and pain, a much higher incidence than ours, possibly due to larger or more invasive lesions.[8] Saha et al. noted mild fever, swelling, redness, and pain in three of seven cases (43%), again higher than our rate.[14] Pan reported complications in nine of 36 patients (25%), including fever, transient swelling, tenderness, and skin discoloration, exceeding our adverse event frequency.[15] Nabi et al.'s bleomycin group experienced adverse effects in 19 of 30 (63.3%), far outstripping our 10.3% total, highlighting doxycycline's milder profile in their comparison.[16] Our lower side effect profile could reflect a more conservative dosing strategy.

Reflecting on our findings, the high efficacy and low complication rate position intralesional bleomycin as a compelling alternative to surgery, particularly for macrocystic hygromas where complete excision risks vital structures.

CONCLUSION:

Our study demonstrates that intralesional bleomycin sclerotherapy is highly effective, achieving complete resolution in 84.5% of children with cystic hygroma, with minimal side effects, affirming its role as a safe and potent alternative to surgery.

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