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Research Paper

Role of Bleomycin Sclerotherapy as a Non-Surgical Treatment Modality for Cystic Hygroma: An Institutional Study

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ABSTRACT

Background: *Cystic hygroma is a congenital lymphatic malformation that frequently presents during infancy and early childhood. Surgical excision, though effective, is often challenging due to proximity to vital structures and the risk of recurrence or complications. Bleomycin sclerotherapy has emerged as a minimally invasive alternative, yet outcome variability persists across lesion types and locations.*

Aim of the study: *To evaluate the efficacy and safety of intralesional bleomycin as a non-surgical treatment modality for macrocystic and mixed cystic hygromas in a pediatric population.*

Methods: *This prospective observational study was conducted at the Department of Pediatric Surgery, Bangladesh Institute of Child Health and Dhaka Shishu Hospital from January 2012 to June 2013. Sixty children with clinically and ultrasonographically confirmed cystic hygroma underwent bleomycin sclerotherapy (0.2–0.6 mg/kg/session) under ultrasonographic guidance. Patients were followed clinically and radiologically for treatment response and complications. Outcomes were categorized as excellent (≥91% reduction), good (51–90%), fair (25–50%), or poor (<25%). Associations between lesion characteristics and treatment response were analyzed using Chi-square/Fisher's exact tests.*

Result: *The mean age was 28.8 ± 29.6 months, with macrocystic lesions comprising 80% of cases. Overall, 46.67% achieved excellent regression and 33.33% achieved good regression, yielding an 80% excellent–good combined response. Mean number of sessions was 1.8 ± 0.7, and mean time to regression was 8.4 ± 3.2 weeks. Macrocystic lesions showed significantly better outcomes compared to mixed lesions ($p = 0.01$). Neck lesions demonstrated a higher excellent response rate than non-cervical lesions ($p = 0.03$). Complications were minor and transient, including skin redness (16.67%), pain (13.33%), fever (6.67%), and temporary lesion enlargement (10%); no major adverse events occurred.*

Conclusion: *Bleomycin sclerotherapy is an effective and safe non-surgical treatment option for pediatric cystic hygroma, particularly for macrocystic and cervical lesions. The high rate of excellent–good responses, low complication profile, and minimal invasiveness support its use as a first-line therapeutic modality.*

Keywords: *Cystic hygroma; Lymphatic malformation; Bleomycin sclerotherapy; Pediatric; Minimally invasive therapy; Ultrasonography-guided intervention.*

I. INTRODUCTION

Cystic hygroma, or macrocystic lymphatic malformation, is a benign congenital lesion resulting from aberrant lymphatic channel development and typically manifests as a soft, compressible, transilluminant lymph-filled mass, most frequently located in the head and neck region [1]. According to the Fetal Medicine Foundation, cystic hygroma occurs in approximately 1 in 800 pregnancies, corresponding to an estimated prevalence of about 0.125% globally [2]. In India, lymphangiomas have been reported to account for approximately 6.4% of all pediatric neck masses [3]. Cystic hygroma results from abnormal fetal lymphatic development, where embryonic

lymphatic tissue fails to connect with the venous system. This sequestration of lymphatic tissue prevents proper drainage, causing accumulation of lymph fluid and the formation of characteristic multiloculated cystic lesions [4]. Genetic abnormalities play a significant role in cystic hygroma. Many cases are linked to chromosomal syndromes, including Turner syndrome, Noonan syndrome, and various trisomies. Additionally, somatic (non-inherited) mutations, particularly in the PIK3CA gene, have been implicated in driving lymphatic malformations [5,6]. While genetics are important, environmental factors can also contribute to cystic hygroma. Maternal viral infections and exposure to certain substances during pregnancy have been associated with an increased risk of lymphatic malformations [7]. In the fetus, jugular lymphatic obstruction is a critical cause of cystic hygroma. Impaired drainage of neck lymphatic vessels leads to fluid accumulation and can progress to hydrops fetalis, characterized by widespread fetal edema [8]. Cystic hygroma can have significant clinical consequences, largely determined by its size, location, and progression. Large cervical lesions may compress the airway, causing stridor, respiratory distress, or life-threatening obstruction. In severe cases, urgent airway management, including surgical intervention or tracheostomy, may be required to ensure adequate ventilation [9]. Feeding difficulties may occur when a cystic hygroma compresses the esophagus. Dysphagia is relatively common with larger lesions, potentially compromising nutrition and growth in affected infants and children [10]. Cosmetic disfigurement is a notable consequence of cystic hygroma. Lesions in visible regions, such as the neck or face, can cause swelling, asymmetry, and skin changes, potentially leading to psychosocial stress for the child and family [11]. Cystic hygromas are prone to internal complications. Spontaneous hemorrhage can make cysts tense, yielding hemorrhagic fluid on aspiration. Secondary infection, often post-respiratory infection, can cause warmth, tenderness, erythema, fever, and may progress to abscess requiring antibiotics or drainage. Large or deep lesions risk nerve and vascular compromise, with adjacent cranial nerves or vessels potentially compressed or damaged during progression or surgery [9]. Large cystic hygromas carry systemic risks, with reported mortality of 2–6%, often from secondary complications like pneumonia, chronic airway compromise, or bronchiectasis. Prenatally detected lesions may be associated with hydrops fetalis and chromosomal abnormalities, markedly worsening prognosis [12]. The aim of this study was to evaluate the efficacy and safety of intralesional bleomycin sclerotherapy as a non-surgical treatment modality for cystic hygroma, by examining response rates, complications, and recurrence in an institutional patient study.

II. METHODOLOGY & MATERIALS

This prospective observational study was conducted at the Department of Pediatric Surgery, Bangladesh Institute of Child Health (BICH) and Dhaka Shishu (Children) Hospital between January 2012 and June 2013. The study protocol was approved by the institutional Thesis & Ethical Review Committee, and written informed consent was obtained from the parents or guardians of all participants. The study adhered to the principles outlined in the Declaration of Helsinki.

Inclusion & Exclusion criteria

A total of 60 children diagnosed with cystic hygroma were enrolled consecutively. Diagnosis was confirmed clinically and with ultrasonography. Inclusion criteria were: (1) age ≤12 years, (2) macrocystic or mixed cystic hygroma suitable for percutaneous aspiration and sclerotherapy, and (3) no prior definitive surgical or sclerotherapy intervention. Exclusion criteria included infection at the lesion site, extensive microcystic lesions not amenable to aspiration, previous neck surgery, or hypersensitivity to bleomycin.

Pre-Procedural Assessment

All patients underwent detailed clinical evaluation and ultrasonography using a high-frequency linear probe (7.5–12 MHz) to determine lesion size, cystic architecture, number of locules, and proximity to vital structures. Lesions were categorized as macrocystic or mixed. Baseline laboratory investigations included complete blood count, renal function tests, and coagulation profile. Parents or guardians were counseled regarding the nature of the disease, treatment modalities, potential complications, and expected outcomes, and written informed consent was obtained for study participation and intralesional therapy.

Sclerotherapy Procedure

Patients were admitted for each injection session. Oral Cephradine was administered as prophylaxis at a dose of 50–100 mg/kg/day in four divided doses, beginning on the morning of the procedure and continued for three days. Procedures were performed under aseptic conditions in the operation theatre. Under ultrasonographic guidance, cystic fluid was aspirated completely using a 22–24 G needle, and the aspirate's volume, color, and characteristics were recorded. In lesions with multiple non-communicating locules, each cavity was aspirated individually.

Bleomycin hydrochloride was prepared in sterile normal saline at a concentration of 1 mg/mL. Following aspiration, the sclerosant was injected through the same needle, at a dose of 0.2–0.6 mg/kg body weight, adjusted

according to lesion size, site, and structural complexity. Gentle manual compression was applied post-injection to facilitate uniform distribution. All patients were observed as inpatients for at least 24 hours to monitor for early adverse effects, including fever, localized swelling, pain, or respiratory distress.

Follow-Up Protocol

Patients were evaluated on the day following the injection, at one week, four weeks after each session, and eight weeks after the final injection. Early follow-up visits focused on detecting acute complications, while later follow-up assessed therapeutic response. Clinical examination and ultrasonography were used to evaluate lesion size. Any measurable reduction in cyst size was considered a positive response. Additional sclerotherapy sessions were performed at four-week intervals if residual or recurrent cysts were present. The total number of sessions required per patient ranged from one to four.

Outcome Measures

The primary outcome was the degree of lesion regression following bleomycin therapy, categorized as excellent (≥91% reduction), good (51–90% reduction), fair (25–50% reduction), or poor (<25% reduction). Secondary outcomes included the number of sclerotherapy sessions required, the time to achieve significant regression, and the incidence of procedure-related complications. Adverse events, including pain, tenderness, erythema, fever, vomiting, and temporary enlargement of the lesion, were systematically documented.

Statistical Analysis

Data were analyzed using SPSS version 16.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Associations between lesion characteristics and treatment outcomes were assessed using Chi-square or Fisher's exact tests, with $p < 0.05$ considered statistically significant.

III. RESULT

A total of 60 patients with cystic hygroma were included in the present study. The mean age was 28.8 ± 29.6 months, with the majority of patients (50%) aged 13–30 months and 43.33% aged 0–12 months. Males accounted for 56.67% of cases, whereas females comprised 43.33%. The neck was the most common lesion site (70%), followed by the axilla (13.33%), trunk (6.67%), forearm (5%), and cheek (5%). The mean lesion size was 6.8 ± 2.7 cm, with 80% of lesions classified as macrocystic and 20% as mixed type (Table 1). Following intralesional bleomycin sclerotherapy, 46.67% of patients achieved excellent regression (≥91% reduction), while 33.33% showed good regression (51–90%). Fair (25–50%) and poor (<25%) responses were observed in 13.33% and 6.67% of cases, respectively. The mean number of treatment sessions required was 1.8 ± 0.7, and the mean time to regression was 8.4 ± 3.2 weeks (Table 2). A significant difference was observed between cyst types ($p = 0.01$). Macrocystic lesions responded markedly better, with 54.17% achieving excellent outcomes, whereas only 16.67% of mixed lesions achieved similar results. Importantly, half of the mixed cystic lesions (50.00%) fell into the fair/poor category. Lesion location was also significantly associated with treatment outcome ($p = 0.03$), with neck lesions demonstrating the highest rate of excellent improvement (57.14%) (Table 3). Table 4 summarizes the adverse effects, which were mostly mild and transient. Skin redness (16.67%) and tenderness or pain (13.33%) were the most commonly reported. Temporary lesion enlargement (10.00%) was also observed. Less frequent complications included fever (6.67%) and vomiting (3.33%).

Table 1: Baseline demographic and clinical characteristics of the study population (n = 60)

Variable	Frequency (n)	Percentage (%)
Age (months)		
0–12	26	43.33
13–30	30	50.00
>30	4	6.67
Mean ± SD	28.8 ± 29.6	
Gender		
Male	34	56.67
Female	26	43.33
Lesion Location		
Neck	42	70.00
Axilla	8	13.33
Trunk	4	6.67
Forearm	3	5.00
Cheek	3	5.00
Lesion Size (cm)		
Mean ± SD	6.8 ± 2.7	

Cyst Type		
Macrocystic	48	80.00
Mixed	12	20.00

Table 2: Treatment outcomes following treatment among the study population

Outcome Category	Frequency (n)	Percentage (%)
Excellent (≥91% reduction)	28	46.67
Good (51–90%)	20	33.33
Fair (25–50%)	8	13.33
Poor (<25%)	4	6.67
Number of Sessions		
Mean ± SD	1.8 ± 0.7	
Time to Regression (weeks)		
Mean ± SD	8.4 ± 3.2	

Table 3: Association between lesion characteristics and treatment outcome

Variable	Excellent n (%)	Good n (%)	Fair/Poor n (%)	p-value*
Cyst Type				
Macrocystic	26 (54.17)	16 (33.33)	6 (12.50)	0.01
Mixed	2 (16.67)	4 (33.33)	6 (50.00)	
Location				
Neck	24 (57.14)	14 (33.33)	4 (9.52)	0.03
Axilla	2 (25.00)	4 (50.00)	2 (25.00)	
Trunk	2 (50.00)	2 (50.00)	0 (0.00)	
Forearm	0 (0.00)	2 (66.67)	1 (33.33)	
Cheek	0 (0.00)	0 (0.00)	3 (100.00)	

Table 4: Complications following treatment among study population

Complication	Frequency (n)	Percentage (%)
Skin redness	10	16.67
Tenderness / pain	8	13.33
Fever	4	6.67
Vomiting	2	3.33
Temporary increase in lesion size	6	10.00
Major complication	0	0.00

IV. DISCUSSION

Cystic hygroma continues to pose a therapeutic challenge in pediatric surgical practice due to its unpredictable clinical behavior, tendency for progressive enlargement, and close proximity to vital neurovascular structures [13-14]. Over the past decade, the therapeutic paradigm has gradually shifted from extensive surgical excision toward minimally invasive image-guided sclerotherapy, driven by the need to reduce morbidity and preserve functional and cosmetic outcomes [15-16]. Within this evolving landscape, bleomycin has emerged as one of the most widely adopted sclerosants, yet variations in response across cystic subtypes and anatomical regions continue to warrant clinical investigation [17]. The present study adds to the growing body of evidence supporting bleomycin as a first-line option, particularly for macrocystic lesions in pediatric populations. In our study, the majority of patients were infants and young children, consistent with the known early-life presentation of cystic hygromas. The neck was the predominant site (70%), aligning with prior epidemiological observations reporting cervical involvement in 75–80% of cases [18]. In our present study, intralesional bleomycin sclerotherapy demonstrated a strong therapeutic effect, with 80% of patients achieving excellent or good regression after a mean of 1.8 ± 0.7 treatment sessions. The mean regression time of 8.4 ± 3.2 weeks underscores the rapid and meaningful clinical improvement achievable with this minimally invasive modality, particularly in macrocystic lesions. These outcomes reinforce bleomycin's role as a preferred first-line intervention, especially in pediatric patients where surgical excision is often associated with higher morbidity and a greater risk of neurovascular injury. A notable finding in our study was the significant association between cyst type and therapeutic response. Macrocystic lesions showed markedly superior outcomes, with 54.17% achieving an excellent response compared with only 16.67% among mixed lesions ($p = 0.01$). This pattern aligns closely with previously published evidence [19]. Rozman et al. reported excellent or good outcomes in 63% of cases, while Niramis et al. observed favorable responses in 83% of treated lesions [20]. Similarly, Baskin et al. documented response rates approaching 95%, collectively suggesting robust sclerosant efficacy of bleomycin across varied clinical settings [21]. Orford et al. further substantiated these findings, demonstrating excellent and good responses in 44% and 44% of patients, respectively, with only 12% showing minimal benefit. Their report highlights that bleomycin provides outcomes comparable to surgical excision while avoiding operative complications, scarring, and the inherent risks of open dissection [22]. Lesion location also influenced treatment outcomes. Cervical lesions

responded significantly better (57.14% excellent) than lesions at less common sites such as the cheek or forearm (0% excellent), neck-region lymphatic malformations often respond more favourably to bleomycin, likely because of the rich lymphatic network in the cervical area. In contrast, lesions with less effective drainage or less favourable anatomical access tend to exhibit poorer outcomes [17]. The safety profile observed in the present study was favorable, with only minor, transient complications including skin redness (16.67%), pain (13.33%), fever (6.67%), and temporary lesion enlargement (10%). No major complications were observed. These results are consistent with previously published pediatric series indicating that intralesional bleomycin at low doses is safe, with minimal systemic toxicity [1].

Limitations of the study: This study was limited by its single-center design, short follow-up duration, and reliance on ultrasonography-based assessment, which may introduce operator variability. The absence of a comparison group receiving alternative sclerosing agents or surgical management restricts direct therapeutic benchmarking. Additionally, lesion heterogeneity and procedural technique differences may have influenced treatment responses, limiting broader generalizability.

V. CONCLUSION AND RECOMMENDATIONS

Bleomycin sclerotherapy demonstrated high efficacy and safety as a minimally invasive treatment for cystic hygroma in children. In this study, most patients achieved excellent or good regression with a low mean number of sessions and minimal transient complications. Macrocystic lesions, in particular, showed significantly better therapeutic response, underscoring the suitability of bleomycin for this subtype. The absence of major adverse events further supports its favorable safety profile. Overall, bleomycin represents a reliable, well-tolerated first-line alternative to surgery in appropriately selected patients.

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