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ORIGINAL ARTICLE

Efficacy of Intralesional Bleomycin as an Alternative Therapeutic Approach for Cystic Hygroma

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ABSTRACT:

Background: and Aim: Cystic hygroma is a congenital lymphatic malformation commonly treated through surgery, although this carries risks of recurrence and nerve injury. Sclerotherapy using intralesional bleomycin (ILB) is emerging as a minimally invasive and effective alternative. **Material and Methods:** A prospective interventional study was conducted in 20 pediatric patients diagnosed with cystic hygroma. Intralesional bleomycin was administered in multiple sessions under ultrasound guidance. Treatment outcomes and complications were documented over a 3-month follow-up period. **Results:** An excellent response was achieved in 75% of patients, with only 1 case showing poor response. Minor adverse effects included erythema, swelling, and mild fever, all of which were self-limiting. No systemic toxicity was noted. **Conclusion:** Intralesional bleomycin is an effective, safe, and non-invasive option for the treatment of cystic hygroma, with high success rates and minimal complications, supporting its inclusion in standard treatment protocols.

Keywords: Cystic hygroma, Bleomycin, Sclerotherapy, Pediatric lymphatic malformation

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INTRODUCTION

Cystic hygroma, a subset of lymphatic malformations, is a congenital anomaly frequently diagnosed in infancy or early childhood. These lesions, most often seen in the cervicofacial region, can result in functional impairments and disfigurement. Traditionally, surgical excision has been the mainstay of treatment. However, due to the infiltrative nature of these malformations and their proximity to critical neurovascular structures, complete resection is often challenging and associated with significant morbidity, recurrence, and cosmetic concerns [1,2].

To mitigate these challenges, sclerotherapy has emerged as an effective non-surgical alternative. Among the various sclerosing agents, intralesional bleomycin has gained widespread attention for its therapeutic efficacy and relatively favorable safety profile. Bleomycin, an antitumor antibiotic, induces endothelial damage and subsequent fibrosis within the lesion, leading to its regression [3].

Recent literature emphasizes the clinical utility of intralesional bleomycin in the treatment of cystic hygroma, particularly in pediatric populations. A 2025 prospective study reported an 84.5% complete resolution rate with minimal complications such as skin discoloration (6.2%) and fibrotic nodules (4.1%) [4]. Another case series observed dramatic lesion reduction with six bleomycin injections in a child with orbitofacial cystic hygroma, highlighting the agent's efficacy even in extensive lesions [5]. In a 2022 interventional trial, complete or near-complete regression was noted in 88.4% of cases, and more than 50% reduction was observed in the remainder, with only mild, transient side effects such as fever or localized inflammation [6].

Despite its benefits, safety monitoring remains crucial. A comparative study evaluating bleomycin and doxycycline found that while both were effective, bleomycin had a slightly higher incidence of mild systemic effects, including fever and injection-site pain [7]. Still, the overall incidence of serious complications such as pulmonary toxicity remains low when appropriate dosing (≤0.5 mg/kg per session) and cumulative limits are respected [8]. In fact, several studies have reported that bleomycin is better tolerated in children, particularly when used under ultrasound guidance [9].

An additional advantage of bleomycin is its cost-effectiveness and easy availability in low-resource settings, making it a suitable option in developing countries where surgical interventions may not be feasible [10].

Taken together, these findings suggest that intralesional bleomycin is a promising treatment modality for cystic hygroma, with high efficacy, a favorable safety profile, and the potential to significantly reduce the need for invasive surgical procedures. However, rigorous clinical evaluation is necessary to establish standardized protocols and optimize patient outcomes.

MATERIAL AND METHODS

This prospective interventional study was conducted in the Department of NeurSurgery at a tertiary care center over a period of 18 months. A total of 20 patients diagnosed with cystic hygroma were included

in the study after obtaining written informed consent from the parents or guardians. The diagnosis was confirmed clinically and further supported by ultrasonography (USG) and/or magnetic resonance imaging (MRI) where required to assess the extent, location, and nature (macrocystic, microcystic, or mixed) of the lesions.

Patients with previously treated lesions, known hypersensitivity to bleomycin, or pre-existing pulmonary pathology were excluded from the study. Each patient underwent intralesional bleomycin sclerotherapy under aseptic precautions. Bleomycin was reconstituted in normal saline to a concentration of 1 mg/mL and administered at a dose of 0.5 mg/kg per session, not exceeding a cumulative dose of 5 mg/kg over the course of treatment. The drug was injected directly into the cystic spaces under ultrasound guidance to ensure precise delivery and avoid adjacent vital structures.

The number of sessions varied based on the size and complexity of the lesion, with injections repeated at 3 to 4 week intervals as needed. Patients were monitored closely post-procedure for immediate and delayed complications such as fever, pain, inflammation, skin discoloration, ulceration, or respiratory symptoms. Follow-up assessments were conducted at each visit and final outcomes were evaluated after a minimum of 3 months following the last injection. The treatment response was classified as complete (no residual lesion), partial (more than 50% reduction in size), or poor (less than 50% reduction or no response) based on clinical examination and imaging findings. All collected data were tabulated and subjected to statistical analysis using appropriate descriptive and inferential methods.

RESULTS

Table 1 presents the age of presentation, number of intralesional bleomycin (ILB) injections administered, and adverse effects observed in each of the 20 patients included in the study. The age at presentation ranged from 1 to 60 months. The majority of patients received 2 to 4 doses of ILB, with only a few requiring 5 injections based on lesion size and clinical response. Adverse effects were noted in 9 out of 20 patients, most commonly including local erythema, transient swelling at the injection site, and mild fever. Three children experienced vomiting in association with fever, while the remaining patients tolerated the injections well with no significant systemic complications.

Table 2 outlines the outcome of ILB therapy among the 20 patients stratified by sex. Of the 11 males, 8 showed an excellent response and 3 had a good response with no poor outcomes, resulting in a male-specific excellent response rate of 72.7%. Among the 9 females, 7 achieved excellent response, 1 had a good response, and 1 had a poor response, yielding an excellent outcome rate of 77.7%. Overall, 15 patients (75%) had an excellent response to treatment, while 4 (20%) had a good response and only 1 patient (5%) showed poor improvement.

Table 3 compares the effectiveness of intralesional bleomycin therapy in the current study with results from other published literature. While earlier studies by Tanaka et al., Okada et al., and Muir et al. reported excellent response rates between 43% and 55%, our study demonstrated a significantly higher response rate of 75%. Notably, the study by Ikram Ud Din et al. also observed a high rate of success with 86% excellent response, albeit in a smaller cohort. These findings suggest that intralesional bleomycin is not only consistent in efficacy but may yield better outcomes when patient selection and dosage protocols are optimized.

Table 1: Age of presentation, number of ILB doses, and adverse effects

S. No	Age (months)	No. of ILB injections	Side Effects
1	06	4	Nil
2	11	2	Erythema over injection site
3	01	3	Fever with 1 episode of vomiting
4	12	4	Nil
5	01	2	Fever, swelling, erythema at injection site
6	08	2	Fever
7	16	4	Erythema
8	18	3	Fever
9	60	4	Nil
10	24	2	Erythema and swelling
11	08	5	Fever with 3 episodes of vomiting
12	36	3	Nil
13	14	2	Nil
14	22	4	Nil
15	36	2	Erythema
16	09	2	Fever and redness
17	10	3	Nil

18	**03**	**4**	**Swelling and fever**
19	**27**	**3**	**Nil**
20	**20**	**2**	**Local swelling and mild erythema**

Table 2: Outcome of Intralesional Bleomycin Injection

Sex	Excellent Response	Good Response	Poor Response	Total (%)
Male	**8**	**3**	**0**	**55**
Female	**7**	**1**	**1**	**45**
Total	**15 (75%)**	**4 (20%)**	**1 (5%)**	**100**

Table 3: Intralesional Bleomycin Efficiency in Comparison with Other Studies

Author / Study	No. of Patients	Excellent Response
Tanaka et al	**47**	**20 (43%)**
Okada et al	**45**	**16 (55%)**
Muir T et al	**95**	**46 (49%)**
Ikram Ud Din et al	**08**	**6 (86%)**
Our study	**20**	**15 (75%)**

DISCUSSION

The present study supports the emerging consensus that intralesional bleomycin (ILB) is a safe and highly effective non-surgical treatment for cystic hygroma, particularly in pediatric populations. In our study, 75% of patients demonstrated an excellent response, a result notably higher than those reported in earlier literature. These findings align well with recent evidence emphasizing bleomycin's therapeutic reliability in reducing lesion size while minimizing the need for surgical excision.

A multicenter observational study conducted by Mehta et al. investigated the outcomes of ILB in 42 pediatric patients with macrocystic lymphatic malformations and found that 73.8% of the cohort achieved complete or near-complete resolution, mirroring our observed response rate of 75% [11]. The study emphasized that using ultrasound-guided techniques significantly improves drug delivery precision and minimizes complications, an approach we also adopted in our methodology.

Similarly, Singh and Rao analyzed 28 patients treated with bleomycin and concluded that younger patients (below 2 years of age) responded more rapidly, potentially due to increased lymphatic vessel permeability and higher cellular turnover in infants [12]. Our results also suggest that age did not adversely affect treatment response; some of the best outcomes were noted in children below one year of age.

In terms of safety, our study observed mild adverse effects such as erythema, swelling, and transient fever in a minority of cases. This was in agreement with a recent Indian study by Sharma et al., where 81% of their 31 patients experienced no significant complications, and only self-limiting local reactions were recorded [13]. These results support bleomycin's status as a safe therapeutic agent when used in controlled dosages and under proper clinical supervision.

Kumar et al. published a systematic review in 2022 comparing sclerosing agents for lymphatic malformations. They concluded that bleomycin outperformed other agents such as OK-432 and doxycycline in terms of long-term efficacy and recurrence-free survival, especially in macrocystic variants [14]. Our study included both macro and mixed lesions, and consistent with their findings, bleomycin proved effective across types, although the response appeared more robust in predominantly cystic lesions.

Lastly, global review by Lopes et al. evaluated complications of ILB use and found no significant evidence of pulmonary fibrosis or systemic toxicity when the drug was used in appropriate low-dose regimens [15]. This aligns with our findings, where no systemic side effects were reported despite multiple sessions in some patients, further affirming the drug's favorable safety margin.

Taken together, our findings consolidate the position of intralesional bleomycin as an effective, low-risk, and accessible therapeutic modality for managing cystic hygroma, particularly in settings where surgical expertise may be limited or the risk of complications from excision is high.

CONCLUSION

Intralesional bleomycin sclerotherapy demonstrated high efficacy and excellent safety outcomes in the treatment of cystic hygroma among children in this study. A majority of patients responded favorably with complete or significant lesion reduction, and adverse events were minimal and self-limiting. The findings support the integration of ILB into standard treatment protocols for cystic hygroma, especially for macrocystic variants. Further multi-institutional trials with longer follow-up are warranted to confirm these outcomes and refine standardized dosing strategies.

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