OPEN ACCESS

Global Academic Journal of Medical Sciences

Available online at www.gajrc.com
DOI: 10.36348/gajms.2023.v05i01.002

ISSN: 2706-9036 (P)
ISSN: 2707-2533 (O)

Original Research Article

Oral Sildenafil in the Treatment of Cystic Hygroma in Infant

Ullah, M. S[1], Ferdous, K. M. N[2*], Hasan, M. N[3]

[1]Md. Saif Ullah, Associate Professor, Department of Burn & Reconstructive Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh
[2]Kazi Md Noor-ul Ferdous, Associate Professor, Department of Pediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh
[3]Mohammad Nazmul Hasan, Assistant Register, Department of Pediatric Surgery, Cumilla Medical College & Hospital, Cumilla, Bangladesh

***Corresponding Author**
Kazi Md Noor-ul Ferdous
Kazi Md Noor-ul Ferdous, Associate Professor, Department of Pediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh

Article History
Received: 29.11.2022
Accepted: 03.01.2023
Published: 06.01.2023

Abstract: ***Introduction:*** Cystic hygroma is a type of cyst that occurs when lymphatic fluid collects in the lymph nodes which occurs in infants and can cause significant swelling in the neck or other parts of the body. Sildenafil is a possible medication that can be used to treat erectile dysfunction in infant. ***Aim of the study:*** The aim of this study was to assess the effectiveness of oral sildenafil in the treatment of cystic hygroma in infant. ***Methods:*** This retrospective study was conducted from January 2020 to June 2022 in The Division of Pediatric Surgery, Bangladesh Shishu Hospital & Institute and three other private clinics at Dhaka. Total 55 patients (aged between 2 months to 1 year) with cystic hygroma were included in the study. ***Result:*** In the present study, the median (Range) age of 55 patients was 6.2 (2-12) months. The median (Range) weight of 55 patients was 6.5 (4-12) kg. In this study, majority (60%) of the patients were male. More than half (52.73%) patients had the lesion on neck. The median (Range) pretreatment size of lesion was 13.30 (9.88-16.93) cm^2. The median pretreatment size of lesion was 13.30 cm^2 and median post treatment size of lesion was 0.00 cm^2. There was highly significant difference ($p < 0.001$) between pre-treatment and post-treatment size. In this study, excellent response was found in 69.09% patients, good response was found in 21.82% patients. In the current study, 3 patients (5.45%) had cough, 4 patients (7.27%) had fever, 2 patients (3.64%) had rhinorrhoea and 3 patients (5.45%) had vomiting. In the current study, 12 (21.82%) patients had adverse effects. Cost of sildenafil per tablet was 34 cents (100 cents =1 $). ***Conclusion:*** Oral sildenafil resulted excellent size regression and low adverse effects for the treatment of cystic hygroma. It was also very cost effective and convenient to administer.

Keywords: Sildenafil, Cystic Hygroma, and Infant.

I. INTRODUCTION

Cystic hygroma (CH) which is also called lymphatic abnormality affects around 1 in 6000 live births [1]. Compared to other forms of lymphangiomas, cystic hygromas are more common and might consist of one or more macrocystic lesions that hardly communicate with healthy lymphatic channels [2]. It mostly impacts the head and neck (75%) and the axilla is impacted in around 20% of instances, whereas the mediastinum, groin, and retroperitoneum are less frequent locations [3]. Usually manifests as an expanding, painless mass that can be seen, which causes deformity and may or may not put pressure on nearby structures [3]. Cystic hygromas is also associated with signs of localized infection, inflammation, and bleeding [4]. It is uncommon for lymphatic abnormalities to be cured with therapy [5, 6]. Because lymphatic

malformations can become entangled inside muscles or organs and because inadequate excision of lymphatic malformations can induce recurrence, surgery is not always an option [7, 8]. Due to the lymphangioma's propensity to infiltrate nearby tissues, partial resection or unintentional nerve damage may occur. It nevertheless has a complication rate of up to 12-33% and a recurrence rate of 15-53%, even in the most skilled hands [9]. For treating microcystic and mixed lesions, sclerosants such ethanol, doxycycline, bleomycin, and OK-432 are less effective. Although large cystic lesions may at first respond nicely to sclerotherapy, patients frequently require recurrent sessions throughout their lifespan [5, 10]. The best approach for treating lymphatic abnormalities may be oral medicines. Recent studies have shown that the selective phosphodiesterase-5 inhibitor sildenafil citrate is useful in curing lymphatic abnormalities [11]. Sildenafil prevents the degradation of cyclic guanosine monophosphate by specifically inhibiting phosphodiesterase-5 [12]. Phosphodiesterase-5 inhibition results in vasodilation by reducing the contractility of vascular smooth muscle. The medication appears to be safe and effective when taken off-label in infant with pulmonary hypertension; it has been authorized for the treatment of pulmonary hypertension in adults [13]. It is thought that primitive lymphatic sacs, which emerge from mesenchyma or embryologic endothelial networks, are the source of lymphatic abnormalities. Cystic dilatation might result from the contraction of thicker muscle linings, which could also raise intramural pressure [14]. The relaxation of smooth muscle followed by cystic decompression is one theory explaining the therapeutic effect. As an alternative, sildenafil may restore lymphatic endothelial dysfunction or relaxation may cause secondary lymphatic spaces to open [15]. When taken alone or in conjunction with other therapies, sildenafil, according to Swetman *et al*., [11] 's research, provides an optimistic, favorable treatment for lymphatic malformations. Though, there are no sufficient studies about the effectiveness of oral sildenafil in the treatment of cystic hygroma in infant. Therefore, the current study was conducted to assess the effectiveness of oral sildenafil in the treatment of cystic hygroma in infant.

II. OBJECTIVES

To assess the effectiveness of oral sildenafil in the treatment of cystic hygroma in infant.

III. METHODOLOGY & MATERIALS

This retrospective study was conducted from January 2020 to June 2022 in The Division of Pediatric Surgery, Bangladesh Shishu Hospital & Institute and three other private clinics at Dhaka. Total 55 patients with cystic hygroma were included in the study. Patients aged between 2 months to 1 year had clinical and radiologic evidence of cystic hygroma were included. Patients having history of preterm born, immediate life-threatening lesion such as having intra-thoracic or intra-abdominal lesion, infected lesion, hypersensitivity or contraindication to sildenafil, history of priapism or any other disorder that might predispose to priapism, and patients/ their guardians who were not willing to participate in the study were excluded from this study. In each included case information about the patient was recorded and we colleted frim hospital records. Which included detailed history, thoroughly examination findings and diagnosis (confirmed by clinical examination and relevant investigations). The lesion was measured along long axis and perpendicular to the long axis in centimeters. USG of the lesion was also done to measure the pre-treatment and post-treatment volume. CBC, BT, CT, SGPT and S. creatinine, C XR and Echo-cardiogram were done in suspected cases of mediastinal extension or to evaluate condition of heart in patient having murmur. Patients were given tablet sildenafil (Vigorex 25 mg) oraly as 1mg/ kg/ dose thrice daily for 20 weeks. The adverse effects of sildenafil were also noted.

Patients were advised to come after one week. Second and subsequent procedure was performed at 4 weeks interval in necessary cases. In each follow up visit size of the swelling were measured by measuring tape. If any complication developed, then they advised to report earlier. Any sign of complication was also recorded and treated accordingly. If the lession regress more than 90%, considered excellent, good response - if size regress 50 to 90%, and poor regression in size less than 50% or no change.

Data were collected in a pre-designed, semi-structured questionnaire, after taking consent from guardians in the consent form. The statistical analysis was conducted using SPSS (statistical package for social science) version 25 statistical software. Pearson's Chi-square test was used to compare categorical variables. A P-value of <0.05 was considered significant.

IV. RESULT

Table I shows the demographic characteristics of the study people. In the present study, the median (Range) age of 55 patients was 6.2 (2-12) months. The median (Range) weight of 55 patients was 6.5 (4-12) kg. In this study, majority (60%) of the patients were male (Figure 1). Figure 2 demonstrates the location of the cystic hygroma.

More than half (52.73%) patients had the lesion on neck. Table II demonstrates the pre-treatment and post treatment size of cystic hygroma. The median (Range) pretreatment size of lesion was 13.30 (9.88-16.93) cm^2. The median pretreatment size of lesion was 13.30 cm^2 and median post treatment size of lesion was 0.00 cm^2. There was highly significant difference ($p < 0.001$) between pre-treatment and post-treatment size. In this study, excellent response was found in 69.09% patients, good response was found in 21.82% patients (Figure 3). Table III shows the adverse effects of the study patients. In the current study, 3 patients (5.45%) had cough, 4 patients (7.27%) had fever, 2 patients (3.64%) had rhinorrhoea and 3 patients (5.45%) had vomiting. In the current study, 12 (21.82%) patients had adverse effects. Cost of sildenafil per tablet was 34 cents (100 cents =1 US dollar).

Table-I: Demographic characteristics of the study people (n=55)

Characteristics	Median (Range)
Age (Months)	6.2 (2-12)
Weight (kg)	6.5 (4-12)

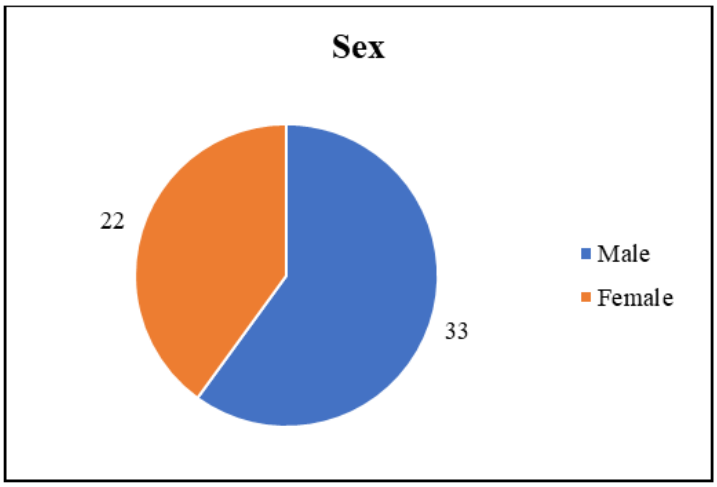

Figure 1: Sex distribution of the study people (n=55)

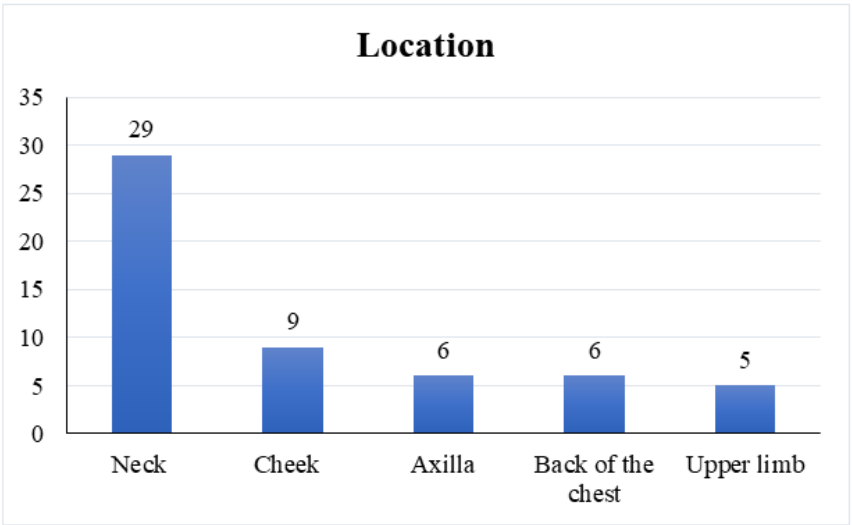

Figure 2: Location of the cystic hygroma (n=55)

Table-II: Pre-treatment and post treatment size (n=55)

	Pre-treatment size (in cm^2)	Post-treatment size (in cm^2)	P value
Median (Range)	13.30 (9.88-16.93)	0.00 (0.00-1.89)	<0.001

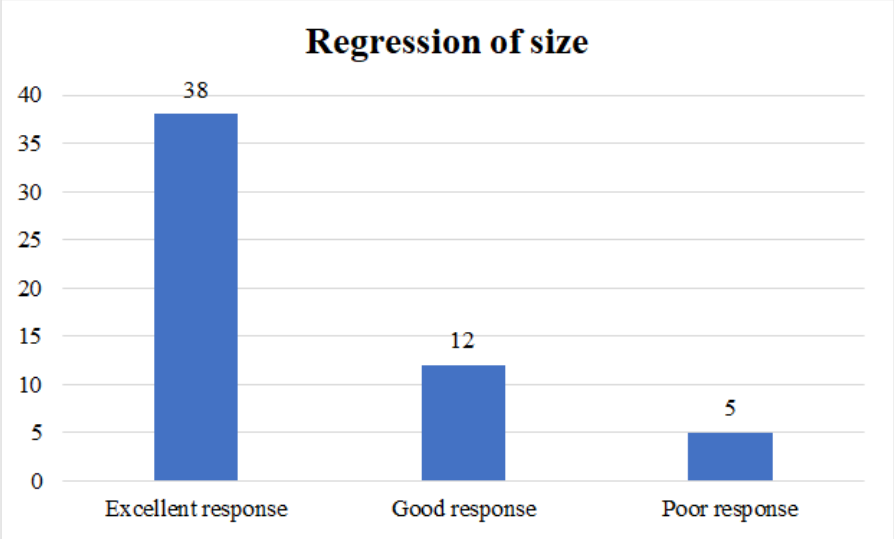

Figure 3: Regression size (n=55)

Table-III: Adverse effects (n=55)

		n	%
Adverse effects	Absent	43	78.18
	Present	12	21.82
Type of adverse effects	Cough	3	5.45
	Fever	4	7.27
	Rhinorrhoea	2	3.64
	Vomiting	3	5.45

V. DISCUSSION

The current study was conducted to assess the effectiveness of oral sildenafil in the treatment of cystic hygroma in infant. In the present study, the median age of patients was 6.2 months. More than 60% of cystic hygroma have onset at birth and up to 90% becomes overt by age of two years [16]. Majority of the study patients (60%) were male in the current study. Similar findings were made in the Saha *et al*., [17] research, when it was shown that cystic hygromas were more common in men. In the present investigation, the neck accounted for more than half of the lesions; others were discovered in the axilla, cheek, back of the chest, and upper limb. Similar to our study, Rawat *et al*., [18] similarly discovered that 57.9% of lesions occurred in the neck area. Six months of follow-up were given to every patient. The median pretreatment size of lesion was 13.30 cm^2 and median post treatment size of lesion was 0.00 cm^2. There was highly significant difference ($p < 0.001$) between pre-treatment and post-treatment size. All patients saw considerable size decline at this time. 69.09% of patients showed excellent response, while 21.82% of patients showed good response. Few research has been done on the use of oral sildenafil in infants to treat cystic hygromas. In the study of Hasan MN [19], the median pretreatment size of lesion was 14.70 cm^2 and median post treatment size of lesion was 0.00 cm^2. The difference between pre-treatment and post-treatment size was statistically significant, as the $p < 0.001$. After studying three people, Swetman [11] discovered that the lymphatic anomalies greatly improved. In the study by Danial *et al*., [20] that comprised seven patients, six of the seven patients shown therapeutic response. The lymphatic vasculature's relaxation may have made it feasible for lymphatic gaps to widen, lessening the size of the lymphatic malformation and explaining the therapeutic effect. In the current trial, oral sildenafil had little negative effects. Among the trial participants, side symptoms such as fever, vomiting, rhinorrhea, and cough were discovered. Patients were treated symptomatically. These individuals had no negative effects while taking sildenafil. Oral sildenafil medication, according to Swetman [11], had no severe adverse effects. Denial *et al*., [20] found that using oral sildenafil had relatively mild adverse effects, such as nausea, fever, coughing, and vomiting. Quddusi *et al*., [21] found no specific side effects during the course of the treatment. Throughout the investigation, no subject had a lesion reoccur. Hasan MN [19] found that 39.3% had adverse effect after treatment, which is similar to our study. The expense of healthcare is a major worry in a country like Bangladesh. When compared to surgical or other treatment methods, the cost of sildenafil per tablet (25 mg) for oral usage was

shown to be extremely cost-effective at 34 cents (100 cents = $1). Rare congenital vascular anomalies called lymphatic malformations can damage vital organ function, cause recurring infections, and cause deformities [22]. As a result, prompt and efficient therapy is necessary. The use of sildenafil in infants has increased substantially in the past 10 years [23]. According to our research, sildenafil is the most effective and efficient drug for treating cystic hygroma. Still, further research is necessary.

Limitations of the study

In our study, there was small sample size and absence of control for comparison. Study population was selected from only Dhaka city, so may not represent wider population. The study was conducted at a short period of time.

VI. CONCLUSION AND RECOMMENDATIONS

In treating cystic hygroma, oral sildenafil produced excellent size reduction and low side effects. Additionally, it was easy to use and quite affordable. In light of the study's findings, it is advised that sildenafil be included as another efficient medication to the list of therapy options for infant with cystic hygroma. It is advised to conduct a randomized controlled trial with a significant sample size and long-term follow up to demonstrate the safety profile of oral sildenafil.

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