

Treatment Response of Intralesional Pentavalent Antimonials in Cutaneous Leishmaniasis in Children

Manzoor Ali Khan¹, Ishtiaque Ahmed², Amna Mushtaque³, Faiza Behram⁴, Sarosh Mumtaz⁵, Maham Baig⁶

- 1 Assistant Professor, Department of Pediatric medicine, AJK Medical College, Muzaffarabad Pakistan
Wrote first draft of manuscript
- 2 Senior Registrar, Department of Pediatric medicine, AJK Medical College, Muzaffarabad Pakistan
Contribution data collection and manuscript writing
- 3 Consultant Pediatrician, Department of Pediatrics, Abbas Institute of Medical Sciences, Muzaffarabad Pakistan
Review the literature and finalized the draft
- 4 Consultant Dermatologist, Department of Dermatology, Abbas Institute of Medical Sciences, Muzaffarabad Pakistan
Contribution in data collection and analysis
- 5 Consultant Dermatologist, Department of Dermatology, Abbas Institute of Medical Sciences, Muzaffarabad Pakistan
Contribution data collection and manuscript writing
- 6 Consultant Pediatrician, Department of Pediatrics, Abbas Institute of Medical Sciences, Muzaffarabad Pakistan
Data analysis and format the draft

CORRESPONDING AUTHOR

Dr. Manzoor Ali Khan
Assistant Professor, Department of Pediatric
Medicine, AJK Medical College, Muzaffarabad
Pakistan
Email: drmanzooral46@gmail.com

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ABSTRACT

Background: Cutaneous leishmaniasis is a parasitic infection transmitted by the bites of infected sand flies, which can lead to skin ulcers and other clinical manifestations. The disease is prevalent in many parts of the world, particularly in developing countries, and affects children disproportionately. Pentavalent antimonials are one of the main treatments for cutaneous leishmaniasis. However, intralesional pentavalent antimonials can be an effective treatment for cutaneous leishmaniasis, in terms of effectiveness and safety. **Objective:** To determine the effectiveness of intralesional pentavalent antimonials in cutaneous leishmaniasis in children at a tertiary care Hospital. **Study Design:** descriptive cross-sectional study. **Settings:** Pediatric department of AJK Medical College, Muzaffarabad Pakistan. **Duration:** A period of one year from January 2021 to December 2021. **Methods:** All the children aged 2 to 14 years old diagnosed with cutaneous leishmaniasis undergoing Intralesional administration of pentavalent antimonials (sodium stibogluconate or meglumine antimoniate) for the treatment of cutaneous leishmaniasis were included. Pentavalent antimonials are administered intralesionally once a week for up to 4-6 weeks. 0.5 to 1ml injection was given directly into the lesion using a sterile syringe and needle. Participants are followed up at specific intervals to assess the treatment response. The treatment response is evaluated by comparing the baseline lesion size and characteristics with those at the follow-up assessments. Complete healing is defined as complete resolution of the lesion, partial healing is defined as a reduction in the lesion size by at least 50%, and no healing is defined as no reduction in the lesion size. All the information was collected via study proforma and SPSS version 26 was used for the purpose of analysis. **Results:** A total of 64 cases were studied, their mean age was 6.71 ± 3.87 years, males were 62.5% and females were 37.5%. Out of all 53.10% cases were successfully treated, in 12.50% cases treatment response not found, while 34.40% cases lost the follow-up. Treatment response was statistically insignificant according to age ($p=0.097$), while it was statistically significant according to gender ($p=0.001$). **Conclusion:** Intralesional pentavalent antimonials have been observed to be an effective treatment for cutaneous leishmaniasis in children.

Keywords: Intralesional, Pentavalent antimonials, Cutaneous leishmaniasis.

INTRODUCTION

Cutaneous leishmaniasis is a parasitic infection caused by protozoa of the *Leishmania* species,¹ that affects the skin. It is prevalent in many parts of the world, including Africa, Asia, the Middle East, Mediterranean region and South America.^{2,3} Children are particularly vulnerable to cutaneous leishmaniasis due to their

weaker immune systems and increased exposure to sandflies, the vector responsible for transmitting the disease.⁴ The clinical presentation of cutaneous leishmaniasis in children can vary, ranging from painless, non-ulcerative skin lesions to more severe, ulcerative lesions that can cause scarring and disfigurement. Early diagnosis and treatment are crucial to prevent the spread of the disease and minimize long-term complications. In

addition, the broad selection of medications that have been described for CL suggests that there is not yet a therapy that is considered to be perfect.⁵

Pentavalent antimonial, also known as sodium stibogluconate or meglumine antimoniate, are medications that are frequently utilized in the treatment of cutaneous and mucocutaneous leishmaniasis. Unfortunately, therapy with these pharmaceuticals can be quite costly, and it comes with the risk of major side effects, such as heart toxicity and an increase in the levels of liver enzymes.^{6,7} Moreover, there is a chance that the treatment will not work, or that it will only have a low success rate.^{6,8}

The use of lower overall dosages of antimony (and hence less harmful effects) and a more flexible schedule without the requirement of daily medication administration are two potential advantages of intralesional infiltration.⁵ Both of these advantages could be beneficial. In addition, antimony therapy is a non-equipment-intensive treatment technique, which means that it may be quickly put into practice without the need for an upfront financial expenditure.⁵ Intralesional-pentavalent antimonials (IL-SbV) are suggested for simple cutaneous leishmaniasis.⁹ Pain, arthralgia, myalgia, cardiotoxicity, and nephropathy are some of the adverse effects that might occur when intramuscular injection is performed. Milder side effects can also occur.^{9,10} Yet, to the best of our knowledge, the percentage of success that may be expected from employing this strategy has never been collated at local level. However, the current study has been done to evaluate the effectiveness of intralesional pentavalent antimonials in cutaneous leishmaniasis in children at a tertiary care Hospital.

METHODS

This descriptive cross-sectional study was done at pediatric department of AJK Medical College Muzaffarabad during a period of one year from January 2021 to December 2021.

Study was done after taking ethical approval for ERC committee. All the children aged 2 to 14 years old diagnosed with cutaneous leishmaniasis undergoing Intralesional administration of pentavalent antimonials (sodium stibogluconate or meglumine antimoniate) for the treatment of cutaneous leishmaniasis were included.

All the children with concomitant systemic illness or other skin infections that may affect the response to the treatment, leishmaniasis lesions in critical areas such as eyes, mouth, and nose, children who have received previous treatment with antimonials for cutaneous leishmaniasis within the past 6 months and children with history of used systemic or topical corticosteroids or any

other immunomodulatory agents within the past 4 weeks were excluded.

Informed consent is obtained from parents or legal guardians of the participants. Pentavalent antimonials are administered intralesionally once a week for up to 4-6 weeks. 0.5 to 1ml injection was given directly into the lesion using a sterile syringe and needle. Participants are followed up at specific intervals to assess the treatment response. The assessments may include measurement of the lesion size, clinical examination, and laboratory tests. The follow-up assessments may be done at 2, 4, and 8 weeks after the start of treatment. The treatment response is evaluated by comparing the baseline lesion size and characteristics with those at the follow-up assessments. The response is categorized as complete healing, partial healing, or no healing. Complete healing is defined as complete resolution of the lesion, partial healing is defined as a reduction in the lesion size by at least 50%, and no healing is defined as no reduction in the lesion size. All the information was collected via study proforma and SPSS version 26 was used for the purpose of analysis.

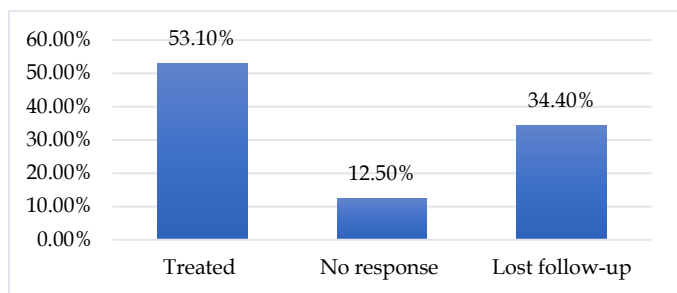
RESULTS

A total of 64 cases were studied, their mean age was 6.71 ± 3.87 years, males were 62.5% and females were 37.5%. size of lesion, sites of lesion and dosage of injection presented in table 1.

Table 1: Demographic and clinical characteristics of patients (n= 64)

Variables		Statistics	
Mean age		6.71±3.87 years	
Gender	Male	40	62.5%
	Female	24	37.5%
Size of lesion	less than 1.5cm	22	34.4%
	1.5 to 2.5cm	26	40.6%
	greater than 2.5cm	16	25.0%
Duration of disease	Less than 2 months	24	37.5
	Two to six months	34	53.1
	Greater than six months	6	9.4
Dose of injection	0.5ml	28	43.8
	1ml	22	34.4
	>1ml	14	21.9

Out of all 53.10% cases were successfully treated, in 12.50% cases treatment response not found, while 34.40% cases lost the follow-up. (Figure 1)

Figure 1: Treatment response among patients (n= 64)

Treatment response was statistically insignificant according to age ($p=0.097$), while it was statistically significant according to gender ($p= 0.001$) as shown in table 2.

Table 2: Treatment response according to age, gender and dosage of injection (n=64)

Variables		Treatment response			Total	P-value
		Treated completed	No response	Lost follow-up		
Age groups	1-5 years	16	6	6	28	0.097
		25.0%	9.4%	9.4%	43.8%	
	6-10 years	12	2	12	26	
		18.8%	3.1%	18.8%	40.6%	
	11-15 years	6	0	2	8	
	9.4%	0.0%	3.1%	12.5%		
	>15 years	0	0	2	2	
		0.0%	0.0%	3.1%	3.1%	
Gender	Male	26	8	6	40	0.001
		40.6%	12.5%	9.4%	62.5%	
	Female	8	0	16	24	
		12.5%	0.0%	25.0%	37.5%	

DISCUSSION

Cutaneous leishmaniasis is a parasitic disease caused by the protozoan *Leishmania*, which is transmitted to humans by sandflies. The disease is endemic in several regions of the world, including the Middle East, Central and South America, and parts of Asia and Africa. Cutaneous leishmaniasis in children is a particularly challenging condition, as traditional systemic treatments, such as antimonials and amphotericin B, can be toxic and cause severe adverse effects. In recent years, intralesional pentavalent antimonials have emerged as a promising treatment option for cutaneous leishmaniasis in children. This study has been done to evaluate the effectiveness of intralesional pentavalent antimonials in cutaneous leishmaniasis in children, a total of 64 cases were studied, their mean age was 6.73 ± 3.72 years, males were 61.5% and females were 38.5%.

Consistently Hussein NR *et al*¹¹ reported that the average age of the subjects was 8.6 ± 2 years and males were in majority 56.9%, while females were 43.1%. In the

comparison of this study Hussein NR *et al*¹² reported that the mean age of the children was 3.64 ± 2.4 years, while they found male 48.3% and females 51.7%. On the other hand, Hussein NR *et al*¹³ reported that the mean age of the patients was 13.6 ± 2.7 months, while 50% were males and 50% were females. The above difference in mean age and gender distribution may be because of difference in sample size of the studies and study selection criteria.

In this study Out of all 53.10% cases were successfully treated, in 12.50% cases treatment response not found, while 34.40% cases lost the follow-up. Treatment response was statistically insignificant according to age ($p=0.097$), while it was statistically significant according to gender ($p= 0.001$). In the comparison of this study Rojas Cabrera E *et al*¹⁴ reported that the intralesional medication was administered in a cycle of five applications on alternate days and out of 152 participants who were enrolled in the study, after six months of therapy revealed the 77% healing rate as well as a 5% therapeutic failure rate. In another study by KAWEN AA *et al*¹⁵ reported that, in Trimethoprim plus sodium stibogluconate antimony group showed higher success rate in six weeks 31(67.39%). Several other studies have investigated the good efficacy and safety of intralesional pentavalent antimonials for cutaneous leishmaniasis in children.^{16,17}

A study conducted in Iran found that ILPA was highly effective in treating CL in children, with a cure rate of 92.7% after 6 weeks of treatment. The study also found that the treatment was well-tolerated and had minimal side effects.¹⁸ Another study conducted in Pakistan found that ILPA had a cure rate of 94.4% in children with CL, with no serious adverse effects reported.¹⁹ On the other hand in a study found that there was a complete healing in 58.3% of the lesions that were treated in group 1, while there was a cure rate of 93.3% in group II and 92.3% in group II, correspondingly.²⁰

The use of intralesional pentavalent antimonials offers several advantages over systemic treatments. First, the treatment can be administered on an outpatient basis, which reduces the need for hospitalization and the associated costs. Second, the risk of systemic toxicity is minimized, as the drug is delivered directly to the site of infection. Finally, intralesional treatment may reduce the risk of relapse, as the high local concentration of the drug may prevent the development of resistant strains of the parasite. However, there are also some potential drawbacks to intralesional treatment. One major limitation is the need for multiple injections, which can be painful and may require local anesthesia. Additionally, the effectiveness of the treatment may depend on the location and size of the lesions, as well as the species of *Leishmania* causing the infection. Some studies have also reported treatment failure or relapse after intralesional treatment, although this appears to be relatively rare.

There were several limitations like sample size, which can limit the generalizability of the findings and the ability to draw definitive conclusions about the effectiveness and safety of the treatment. Additionally, a small sample size may increase the risk of bias and limit the statistical power of the study. Some patients may be lost to follow-up during the course of the study, which can further limit the reliability of the results. Loss to follow-up may occur due to a variety of reasons, such as the patient moving or discontinuing treatment, and can introduce bias into the study findings. However further large-scale studies are recommended on such subject.

CONCLUSION

Intralesional pentavalent antimonials have been observed to be an effective treatment for cutaneous leishmaniasis in children. However, it is important to note that treatment outcomes may vary depending on the species of *Leishmania* causing the infection, and the location and severity of the lesions. Additionally, close monitoring is necessary to detect any potential adverse effects or treatment failure. Overall, intralesional pentavalent antimonials offer a promising treatment option for cutaneous leishmaniasis in children, but further research is needed to optimize treatment protocols and improve outcomes.

LIMITATIONS

Limited sample size and loss to follow-up by some patients, which can affect the reliability and generalizability of study findings.

SUGGESTIONS / RECOMMENDATIONS

It is suggested that the, further large-scale studies are needed to draw more definitive conclusions about the safety and effectiveness of ILPA

CONFLICT OF INTEREST / DISCLOSURE

None.

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