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Original Research Article

An Analysis Comparing Topical 1% Ozenoxacin Cream and 2% Mupirocin Cream For Management of Impetigo in Paediatric Patients

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Conflict of interest: Nil

Abstract:

Background: The Food and Drug Administration has approved ozenoxacin, a new topical antibiotic with strong bactericidal action against gram-positive bacteria, for the proper therapeutic management of impetigo, an exceedingly infectious bacterial skin illness.

Objectives: The aim of this study was to compare the safety, bacteriological effectiveness, and clinical results of 1% ozenoxacin cream and 2% mupirocin cream in paediatric impetigo patients. The patients were treated topically twice daily for seven days.

Material and Methods: Thirty-three impetigo sufferers who visited a Medical College Hospital in southern India for dermatological outpatient care participated in this single-centre, open-label, random allocation trial. Two groups of subjects were randomly assigned; group A was given topical ozenoxacin and group B was given mupirocin. Microbiological culture and the skin infection assessment scale were used to evaluate the clinical and bacteriological effectiveness. Tolerability and safety were also assessed.

Results: Ozenoxacin's clinical efficacy was demonstrated to be superior than mupirocin's, as demonstrated by the quicker attainment of favourable treatment outcomes following 4-day duration. (8 of 16 versus 2 of 17; p = 0.0381). Ozenoxacin also revealed higher clinical (14 of 16 compared to 13 of 17) as well as microbiological (15 of 16 against 14 of 17) effectiveness when compared with mupirocin, following 7 days of treatment. Only one patient on topical mupirocin experienced a minor side effect, indicating that both medications were well tolerated.

Conclusion: When used topically, ozenoxacin as well as mupirocin have each demonstrated great tolerance and success in treating impetigo in paediatric children between the ages of 2 and 10. According to the study, ozenoxacin's quick onset of action was a significant advantage.

Keywords: Impetigo; Mupirocin; Ozenoxacin; Paediatric patients.

Introduction

Impetigo is a highly infectious illness of the superficial epidermis that can affect people of any age, although it often affects children between the ages of two and five. Impetigo is the third most common skin illness overall and the most common bacterial skin infection in children.[1] Topical antibiotic therapy combined with local wound care is the standard treatment for impetigo. The preferred course of treatment for patients with simple localised impetigo is topical antibiotic therapy. The antibiotic of choice for topical treatment needs to be effective against Streptococcus pyogenes as well as Staphylococcus aureus. Isolated illnesses are eradicated and their community spread is curbed by topical treatment. It is now well acknowledged that topical mupirocin, a well-researched antibacterial drug that has been shown to be efficacious and may be comparable to oral antibiotics, can cure impetigo.[2] In April 2002, the Food and Drug Administration (FDA) approved mupirocin for use in impetigo. Recently, the FDA approved the use of ozenoxacin, a powerful topical antibiotic, to treat impetigo in patients two months of age and beyond in December 2017.[3] The topical antibiotics mupirocin, retapamulin, & fusidic acid are most frequently used in impetigo patients. However, there is always a need for topical formulations with improved action due to concerns about antibiotic resistance and other adverse effects.

Aim & Objectives: This research compares the safety, bacteriological efficacy, and clinical efficacy of ozenoxacin with mupirocin in the management of paediatric impetigo.

Material and Methods:

Study design: In a single-centre, open-label, random allocation trial, the clinical as well as bacteriological effectiveness of topical administration of ozenoxacin cream 1% (w/w) & mupirocin cream 2% (w/w) were evaluated in 33 participants with impetigo susceptible to topical antibiotic treatment. This study was conducted at a Medical College Hospital in southern India in the outpatient department of the dermatology, venereology, and leprosy department. The Institutional Ethics Committee authorised the study, and as all of the subjects were younger than 12 years age, the subjects' legal guardians were contacted and asked for written informed permission after being fully briefed about the study protocol in their native tongue.

When it came to eligibility for the study, a participant's age ranged from two months to twelve years, as long as they had a medical diagnosis of impetigo and a minimum overall score of three on the Skin Infection Rating Scale (SIRS). This score encompassed a minimum exudates and/or pus score of one out of a possible three. The original measured affected area was between 2 and 100 cm^2, or less than 2 percent of the total surface area of the body.

Individuals with indications of the illness spreading throughout the body or those with other forms of pyodermas were not included. The study excluded participants with other systemic illnesses, diabetes, and immunosuppressed patients. Prior to enrolment, participants' histories of allergic reactions to topical formulations were collected; those who had a positive history of these reactions were not included in the study. Likewise, those who reported having had systemic or topical antibiotic medication concurrently within the previous four weeks were not allowed to participate.

Following their completion of all inclusion and exclusion requirements, the individuals were assigned at random to treatment groups. Randomly selected participants were assigned to treatment groups A (ozenoxacin therapy) and B (mupirocin therapy), with a total of 16 and 17 individuals, respectively.

In the course of our investigation, we employed the brands Zimba® Cream from Sun Pharmaceuticals Industries Ltd. in Mumbai, India for ozenoxacin and T-bact® Cream from GlaxoSmithKline Pharmaceuticals Ltd. in Mumbai, India for mupirocin. After applying soap and water to remove any sick crusts and debris, the participants' carers were instructed to apply a thin layer of the prescribed cream twice a day for a period of seven days.

During their visits, the individuals' baseline features and pertinent medical history were documented on a case proforma. The participants' clinical evaluations were carried out at the beginning of therapy (visit 1), four days later (visit 2), and seven days later (visit 3). The bacteriological evaluations were carried out by swab culturing from the afflicted location both before to the start of the therapy and following the conclusion of seven days of treatment. Additionally, clinical images of the participants that were recruited were acquired.

Assessments: A blinded observer, a specialist from the department who was not participating in this investigation, evaluated the clinical and bacteriologic effectiveness. A complete elimination of the treated lesions was a key indicator of the treatment's clinical success. The lack of blisters, exudate and/or pus, crusting, itching and/or discomfort (with a SIRS score of 0), as well as limited erythema and/or inflammation (with a SIRS score of $\leq$1), were all considered in measuring this. More antibiotic medication was considered unnecessary for the afflicted region if these conditions were satisfied. Reductions of greater than 10% in the total Systemic Inflammatory Response Syndrome (SIRS) score from the baseline were considered improvements. The criteria for specific SIRS values that indicate a cure are not met by this definition. On the other hand, a failure occurred when the patient's health deteriorated or there was no clinical improvement.

A cure was determined by measuring the elimination of the pathogen causing the persistent lesions at the end of therapy or, in the event that no lesion persisted, by looking for the lack of culture material. This definition was used in the evaluation of bacteriological efficacy. The pathogen that was first detected after therapy was determined to be the cause of the failure.

Individuals who did not exhibit a response to the recommended therapeutic intervention at the end of the trial period, or who had adverse reactions, were switched to appropriate systemic antibiotics. A physical examination, vital signs, and unfavourable events were taken into account while evaluating safety.

With $P < 0.05$ signifying statistical significance, the data were examined using a 2-group $\chi 2$ test.

Observation and results:

A total of thirty-three impetigo participants were included in the research. The respondents' ages varied between 2 to 10 years old. The study population's mean age was 5.48 years, with a 2.17 standard deviation.

The male to female ratio was 1.36:1, indicating a higher proportion of males. Patients' socioeconomic level was evaluated using a modified version of the Kuppuswamy scale. Most of the participants were from the upper and lower middle classes. Prior to the presentation, the illness had been present for an average of 2.85 days. Most of the participants (82%) had non-bullous impetigo at the time of presentation.

In terms of baseline characteristics, the two therapy groups were similar [Table 1].

Table 1: Demographic Profile

Variable	Category	Ozenoxacin-treated [group A] n=16	Mupirocin-treated [group B] n=17	Total (N=33)	p-value
Age (in years)	Mean	5.6	5.4		0.9861
	Range	2 -10	2 - 10		
Gender	Male	10	09	19	0.7279
	Female	06	08	14	
Socioeconomic status	Upper class	01	01	02	1.0001
	Upper-middle class	02	03	05	
	Lower middle class	06	07	13	
	Upper-lower class	07	06	13	
	Lower class	0	0	0	
Duration of disease before presentation	Mean	2.8	2.9		1.0001
	Range	1 - 5	1 - 5		
Clinical presentation	Bullous impetigo	03	03	6	1.0001
	Non-bullous impetigo	13	14	27	
Symptoms	Only pain	04	05	09	1.0001
	Only itching	02	01	03	
	Both	10	11	21	
Severity	Mild	05	06	11	1.0001
	Moderate	10	10	20	
	Severe	01	01	02	

Table 2 displays the bacteriological and clinical results of treatment for the two groups.

Both antibiotics worked just as well overall. Following a seven-day course of treatment, 87.5% of participants experienced a clinical cure from ozenoxacin, whereas 76.5% of subjects receiving mupirocin experienced the same outcome. On the fourth day of medication, a clinical evaluation showed that 12% of individuals treated with mupirocin demonstrated full cure, whereas 50% of those treated with ozenoxacin did. With a p-value of 0.0381, this difference was statistically significant.

One patient in group B did not get a clinical evaluation as their therapy was discontinued owing to an adverse response.

Table 2: Clinical and bacteriological outcomes of topical treatment

Variables	Categories	Ozenoxacin-treated [group A] (n=16)	Mupirocin-treated [group B] (n=17)	Total (n=33)	p-value
Clinical assessment on day 4	Cure	08	02	10	**0.0381***
	Improvement	08	14	22	
	Failure	0	0	0	
	Not done	0	01	01	
Clinical assessment on day 7	Cure	14	13	27	1.0001
	Improvement	02	03	05	
	Failure	0	0	0	
	Not done	0	01	01	
Isolates in culture	Staphylococcus aureus alone	10	09	19	1.0001
	β-haemolytic streptococci alone	03	04	07	
	Staphylococcus aureus + β-haemolytic streptococci	02	03	05	
	No isolate	01	01	02	
Bacteriological efficacy	Cure	15	14	29	1.0001
	Failure	0	01	01	
	Not evaluated	01	02	03	

***p-value: Significant**

In both groups, the outcomes of the bacteriological profiling were comparable. The two most common pathogens identified from our research population were Streptococcus pyogenes and Staphylococcus aureus. Two subjects—one in each group—lacked isolates, and one participant in group B experienced an adverse response, thus the bacterial effectiveness of the treatment was not assessed in that person.

One patient who used mupirocin experienced an adverse reaction, complaining of slight burning, itching, and erythema at the application site. The patient was switched from topical treatment to systemic amoxicillin/clavulanate and instructed to cease taking it.

Discussion:

Impetigo is a highly common skin infection caused by superficial bacteria, accounting for about 140 million occurrences globally. [4] Topical antibiotic treatment is frequently started in cases of confined impetigo in order to slow the infection's progression and hasten its clinical cure.

The innovative medication ozenoxacin inhibits DNA synthesis by blocking DNA gyrase A and topoisomerase IV. The quinolone antibiotic exhibits bactericidal properties against gram-positive bacteria, such as strains of Staphylococcus aureus and Staphylococcus epidermidis that are resistant to ofloxacin, MRSA (methicillin-resistant Staphylococcus aureus), MRSE (methicillin-resistant Staphylococcus aureus), Streptococcus pyogenes, and MSSA (methicillin-sensitive Staphylococcus aureus).[5] A cream formulation has been created to treat bacterial infections of the skin, such as impetigo.

In our investigation, we discovered that ozenoxacin and mupirocin both work well to relieve impetigo symptoms and signs. They also provide efficient bacteriologic cures. Zenoxacin, however, produced a faster reaction time than mupirocin, which helped the participants receive a cure sooner. The results of Santhosh P et al. indicate that, in animal models, ozenoxacin shows a faster rate of microbiological clearance than mupirocin. It's crucial to remember that no comparative human trials have been carried out as of yet. [6]

The fact that ozenoxacin is a special substance that sets it apart from all other antibiotics is an additional advantage. Because there is no chance of cross-resistance leading to the development of resistance to other antibiotics, its usage may be considered safe. Zeoxacin 1% cream costs around INR 22 to INR 28 per gramme in the Indian market, whereas mupirocin 2% cream costs roughly INR 13 to INR 19 per gramme. However, taking into account ozenoxacin's shorter time to cure, the overall cost of therapy would be the same as mupirocin. However, mupirocin is available in both ointment and cream forms, offering additional alternatives to treating physicians, whereas only cream formulation is accessible for ozenoxacin. While local side effects including burning, itching, and reddening have frequently been observed with mupirocin usage in trials, no substantial adverse effects have been recorded with the use of ozenoxacin thus far.[7,8] Both molecules in our investigation were well tolerated, with the exception of one instance when mupirocin 2% cream caused skin irritation.

Concern is growing about the growing incidence of antibiotic resistance in the dermatological area. The chance of developing antimicrobial resistance is positively correlated with the length of time that antibiotics are used. In the scientific literature, Staphylococcus aureus's acquisition of mupirocin resistance through plasmid-mediated pathways has been well-documented. Numerous published studies have produced data demonstrating a favourable link between the growing clinical usage of mupirocin and the establishment of resistance. The incidence of mupirocin resistance is greater in methicillin-resistant Staphylococcus aureus (MRSA) strains as opposed to methicillin-susceptible Staphylococcus aureus (MSSA) strains. Multiple studies have been undertaken to examine the prevalence of Staphylococcus aureus resistance to mupirocin, indicating varied incidence rates that span from 6.8% to 24%. [10,9]

In this investigation, we have got Staphylococcus aureus as the most prevalent bacterial isolate, similar to previous studies completed recently.[11] The Staphylococcus aureus resistance pattern should be taken into account when selecting a medication for impetigo. Ozenoxacin has a lower risk of generating the formation of spontaneous resistance mutations across both quinolone-susceptible and quinolone-resistant bacterial strains. Moreover, it has been effective against isolates of methicillin-resistant Staphylococcus aureus (MRSA). [12] The limitation of our study was the enrolment of a limited study population; additionally we had not undertaken sensitivity testing of our bacterial isolates. Additionally, there was no evaluation of the products' systemic absorption. Nevertheless, topical drugs are especially engineered to have little absorption, thereby reducing the possibility of systemic complications. [13]

Conclusion

In the past four years, ozenoxacin is the first novel topical antibiotic to be licenced for the management of impetigo.

According to the results of the current study, ozenoxacin 1% cream has stronger antibacterial

qualities and achieves clinical efficacy more quickly than mupirocin 2% cream.

However, in order to preserve this special medicinal ingredient's inherent value, care and moderation must be used when utilising it. Ozenoxacin may have a wider therapeutic function in the management of localised impetigo if there is a significant increase in mupirocin resistance, even if mupirocin is still the primary treatment choice for impetigo and is available in a more affordable form.

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