Original research article

Comparative Assessment of Fusidic Acid and Mupirocin in Patients Suffered from Impetigo

Mrigendra Kumar,

Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India.

Received: 03-08-2020 / Revised: 08-10-2020 / Accepted: 27-10-2020

Abstract

The data generated from the present study concludes that the Mupirocin Ointment had shown more efficacy as compared to Fusidic acid cream in the selected patients. The usage of topical treatment for impetigo, mainly with Mupirocin and Fusidic acid is still prevalent today. It has the advantage of minimizing antibiotic resistance, although recent study done in Greece demonstrated increased resistance to these products among certain staphylococcal clone. Topical anti bacterial are used to accelerate clinical cure, prevent recurrences in affected individuals, and to minimize the spread of infection. They are considered more appropriate as they target only infected area and thus avoid the side effects of the oral treatment and the associated drug interactions. Indiscriminate and universal use of topical medications including antibiotics has led to widespread resistance (molecular, group, and class) to the same. Hence based on above conditions present study was planned for Comparative Assessment of Fusidic Acid and Mupirocin in Patients Suffered from Impetigo. **Methodology:**The present study was planned in Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India,from nov 2019 to April 2020. In the present study 50 patients diagnosed with the impetigo were enrolled. The patients were divided into two groups as 2% fusidic acid cream with topical 2% mupirocin ointment. The diagnosis of impetigo was confirmed clinically. Scoring system of the lesions was done with reference to parameters like erythema, edema, vesiculation, pustulation and crusting.

Keywords: Fusidic Acid, Mupirocin, Impetigo, treatment, etc.

Introduction

Impetigo is the most common bacterial infection in children. This acute, highly contagious infection of the superficial layers of the epidermis is primarily caused by Streptococcus pyogenes or Staphylococcus aureus. Secondary skin infections of existing skin lesions (eg, cuts, abrasions, insect bites, chickenpox) can also occur. [1] Methicillin-resistant S aureus (MRSA) [2] and gentamicin-resistant S aureus strains have also been reported to cause impetigo. [3] Impetigo is classified as either nonbullous (impetigo contagiosa) (about 70% of cases [4]) or bullous.

**Correspondence*

Dr. Mrigendra Kumar

Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India.

E-mail: drmkumar23@gmail.com

Children with nonbullous impetigo commonly have multiple coalescing lesions on their face (perioral, perinasal) and extremities or in areas with a break in the natural skin defense barrier. The initial lesions are small vesicles or pustules (< 2 cm) that rupture and become a honey-colored crust with a moist erythematous base. Pharyngitis is absent, but mild regional lymphadenopathy is commonly present. Nonbullous impetigo is usually a self-limited process that resolves within 2 weeks.

Bullous impetigo is considered to be less contagious than the nonbullous form. [5] It tends to affect the face, extremities, axillae, trunk, and perianal region of neonates, but older children and adults can also be infected. [4] The initial lesions are fragile thin-roofed, flaccid, and transparent bullae (< 3 cm) with a clear, yellow fluid that turns cloudy and dark yellow. Once the bullae rupture, they leave behind a rim of scale around an erythematous moist base but no crust, followed by a brown-lacquered or scalded-skin

appearance, with a collarette of scale or a peripheral tubelike rim.

Bullous impetigo also differs from nonbullous impetigo in that bullous impetigo may involve the buccal mucous membranes, and regional adenopathy rarely occurs. However, extensive lesions in infants may be associated with systemic symptoms such as fever, malaise, generalized weakness, and diarrhea. Rarely, infants may present with signs of pneumonia, septic arthritis, or osteomyelitis.

Treatment of impetigo typically involves local wound care in conjunction with either a topical antibiotic or a combination of systemic and topical agents. In general, the antibiotic selection has coverage against both S aureus and S pyogenes. In areas with a high prevalence of community-acquired MRSA with susceptible isolates, children older than 8 years may take clindamycin or doxycycline in cases. Trimethoprim-sulfamethoxazole can be used in situations in which group A streptococci are unlikely.

Impetigo is an acute, highly contagious gram-positive bacterial infection of the superficial layers of the epidermis. Skin lesions such as cuts, abrasions, and chickenpox can also become secondarily infected (impetiginized) with the same pathogens that produce classic impetigo. Impetigo occurs most commonly in children, especially those who live in hot, humid climates. The name is believed to be derived from the Latin impetere (to assail).

Impetigo occurs in 2 forms: bullous and nonbullous, as shown in the photographs below. Nonbullous impetigo is the more common form, constituting approximately 70% of impetigo cases. [4] It tends to affect skin on the face or extremities that has been disrupted by bites, cuts, abrasions, other trauma, or diseases such as varicella. [1]

Nonbullous impetigo, also known as impetigo contagiosa, is the most common skin infection in children, accounting for approximately 10% of all cutaneous problems in pediatric clinics. It is more contagious than the bullous type. [5] Common impetigo is the term applied when the infection occurs in preexisting wounds. Impetigo as a secondary infection of preexisting skin disease or traumatized skin has also been referred to as impetiginous dermatitis. Nonbullous impetigo is caused by Staphylococcus aureus, group A beta hemolytic streptococci (GABHS, also known as Streptococcus pyogenes), or a combination of both. Most infections begin as a streptococcal infection, but staphylococci replace the streptococci over time.

Methicillin-resistant S aureus (MRSA), which can be hospital or community acquired, is an increasingly common cause of impetigo [2] ; this pathogen is observed more often with the nonbullous form of impetigo than the bullous form. Over the last decade, an increasing number of community-acquired MRSA and gentamicin-resistant S aureus strains have been reported as a cause of impetigo. [3]

Bullous impetigo may affect intact skin and is caused almost exclusively by S aureus. Bullous impetigo is a toxin-mediated erythroderma in which the epidermal layer of the skin sloughs, resulting in large areas of skin loss. Ecthyma is a deeper, ulcerated infection, often occurring with lymphadenitis that may be a complication of impetigo.

Impetigo seldom progresses to systemic infection, although poststreptococcal glomerulonephritis is a rare complication with GABHS infection only. Certain serotypes of GABHS (eg, types 49, 55, 57, 59) are associated with impetigo and acute glomerulonephritis. Impetigo can also present as folliculitis, which is considered to be impetigo of the hair follicles caused by S aureus. Chronic recalcitrant impetigo/folliculitis can result in sycosis barbae (similar to lupoid sycosis) with scarring and a presentation similar to that of discoid lupus. Tinea may also cause this presentation.

Diagnosis of impetigo is usually based solely on the history and clinical appearance. Treatment typically involves local wound care, along with antibiotic therapy, either topical or systemic plus topical. Intact skin is usually resistant to colonization or infection by S aureus or GABHS. These bacteria can be introduced from the environment and only transiently colonize the cutaneous surface. Experimental studies have shown that inoculation of multiple strains of GABHS on to the surface of subjects did not produce cutaneous disease unless skin disruption had occurred.

The teichoic acid adhesions for GABHS and S aureus require the epithelial cell receptor component, fibronectin, for colonization. These fibronectin receptors are unavailable on intact skin; however, skin disruption may reveal fibronectin receptors and allow for colonization or invasion in these disrupted surfaces. Factors that can modify the usual skin flora and facilitate transient colonization by GABHS and S aureus include high temperature or humidity,

preexisting cutaneous disease, young age, or recent antibiotic treatment.

Treatment of impetigo typically involves local wound care along with antibiotic therapy. Antibiotic therapy for impetigo may be with a topical agent alone or a combination of systemic and topical agents. Gentle cleansing, removal of the honey-colored crusts of nonbullous impetigo using antibacterial soap and a washcloth, and frequent application of wet dressings to areas affected by lesions are recommended. Good hygiene with antibacterial washes, such as chlorhexidine or sodium hypochlorite baths, may prevent the transmission of impetigo and prevent recurrences, but the efficacy of this has not been proven.

For antibiotic therapy, the chosen agent must provide coverage against both Staphylococcus aureus and Streptococcus pyogenes. The prevalence of methicillin-resistant S aureus (MRSA) and macrolide-resistant Streptococcus has changed empiric treatment options for impetigo. MRSA was responsible for 78% of all community staphylococcal-related skin and soft tissue skin infections in a multicenter US study. [6]

Community-acquired MRSA (CA-MRSA) infection most commonly manifests as folliculitis or abscess because it possesses the Panton-Valentine leukocidin gene rather than the exfoliative toxin gene. CA-MRSA is thus less likely to cause exfoliative infections such as impetigo and more likely to cause suppurative infections such as abscesses. Therefore, beta-lactam drugs remain an appropriate initial empiric choice for systemic antibiotics for the treatment of impetigo. However, the continued increased presence of CA-MRSA may limit the utility of these agents. In this situation, trimethoprim/sulfamethoxazole, clindamycin, or doxycycline in children older than 8 years can be used if the isolate is susceptible. [7-8]

Topical mupirocin or retapamulin is adequate treatment for single lesions of nonbullous impetigo or small areas of involvement. Systemic antibiotics are indicated for nonbullous impetigo with extensive involvement, in athletic teams, childcare clusters, multiple family members, or for bullous impetigo. In patients with bullous impetigo who present to the emergency department with large areas of involvement resulting in denuded skin from ruptured bullae, management also includes intravenous fluid resuscitation. Fluid is given at a volume and rate similar to standard volume replacement for burns. Inpatient care is required for patients with impetigo who have widespread disease or for infants at risk of sepsis and/or dehydration due to skin loss. If inpatient care is warranted in the child with untreated impetigo, contact isolation is recommended. [9]

Mupirocin ointment (Bactroban) has been used for both the lesions and to clear chronic nasal carriers. Although it is expensive, it has been shown to be superior to topical polymyxin B and neomycin and to be equally effective as oral cephalexin. Both mupirocin and oral cephalexin are superior to bacitracin. It is applied to the affected area 2 times daily. A 5-day course is usually standard, although few large studies have been performed to verify this as the most effective approach. Unfortunately, S aureus and MRSA resistance to mupirocin has emerged at estimated rates ranging from 5-10%. [10]

Topical sodium fusidate (fusidic acid), currently not available in the United States, has been recognized as first-line therapy in Europe and other parts of the world. High resistance rates have been reported with the use of fusidic acid, however, ranging from 32.5-50%. A Swedish study of 38 patients with impetigo showed resistance of S aureus to fusidic acid in 75% of bullous cases and 32% of nonbullous ones. The authors recommended restricted use of fusidic acid in order to limit the rising levels of resistance. [11]

Topical antibacterials are used to accelerate clinical cure, prevent recurrences in affected individuals, and to minimize the spread of infection. They are considered more appropriate as they target only infected area and thus avoid the side effects of the oral treatment and the associated drug interactions. Indiscriminate and universal use of topical medications including antibiotics has led to widespread resistance (molecular, group, and class) to the same. Hence based on above conditions present study was planned for Comparative Assessment of Fusidic Acid and Mupirocin in Patients Suffered from Impetigo.

Methodology:

The present study was planned in Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India, from November 2019 to April 2020.In the present study 50 patients diagnosed with the impetigo were enrolled. The patients were divided into two groups as 2% fusidic acid cream with topical 2% mupirocin ointment. The diagnosis of impetigo was confirmed clinically. Scoring system of the lesions was done with reference to

parameters like erythema, edema, vesiculation, pustulation and crusting.

Results & Discussion:

Dermatologists are faced with an ever-changing spectrum of bacterial infection in cutaneous diseases. Studies have stated that uncomplicated bacterial skin infections may account for up to 17–25% of clinical visits in India. [12-14] This high incidence of bacterial infections is due to various precipitating factors such as low socioeconomic status, poor hygiene, malnutrition, overcrowding, and certain immunodeficiency syndromes.

Complications of impetigo are rare, but they can occur and occasionally be serious. Without treatment people typically get better within three weeks. Complications may include cellulitis, guttate psoriasis, Scarlet fever or post streptococcal glomerulonephritis. Rheumatic fever and Septicaemia are very rare. Globally Impetigo affected about 140 million people (2% of the population) in 2010. [15] It is most common in young children but can occur at any age. Aim of treatment include relieving discomfort and improving cosmetic appearance of lesions, preventing further spread within patient and to others, and preventing recurrence. Treatments should be effective, inexpensive, and have limited side effects. Topical antibiotics have the advantage of being applied only where needed, which minimizes systemic side effects. Topical antibiotic therapy is considered the treatment of choice for individuals with uncomplicated localized impetigo. Topical therapy eradicates isolated disease and limits the individual-to-individual spread. The topical agent is applied after removal of the infected crusts and debris with soap and water. Disadvantages of topical treatment are that it cannot eradicate organisms from the respiratory tract and that applying topical medications to extensive lesions is difficult.

Impetigo is a highly contagious infection, direct contact being the main mode of transmission. Patients with impetigo can easily inoculate themselves and spread the infection to people in close contact after excoriating an infected area. This fact may lead to a rapid dissemination of infection, mostly in grade schools, kindergartens, nurseries and day care centers. It is known today that children usually become infected through contact with other children; however, fomites are another important source of infection. Adults may develop impetigo from contact with children or by fomites as seen when sharing grooming devices, in barber shops, in beauty parlors etc. [16]

Table 1: Basic Details

Groups	**Group A**	**Group B**
Administration of	**2% Fusidic acid cream**	**2% Mupirocin ointment**
Sex: Male Females	 17 8	 15 10
Age: 1 – 10 years 11 – 20 years 21 – 30 years	 16 7 2	 17 5 3
Type of Lesions: Non-bullous Bullous	 20 5	 18 7
No. of Lesions	3 – 5	3 -5
Size of Lesions (cm2)	2.4 – 4.6	2.5 – 4.4

Table 2: Before & After Treatment Observations

Groups	**Group A**		**Group B**	
Administration of	**2% Fusidic acid cream**		**2% Mupirocin ointment**	
	Before Treatment	After Treatment	Before Treatment	After Treatment
No. of Lesions	3 – 5	0 - 1	3 -5	0 – 1
Size of Lesions (cm2)	2.4 – 4.6	0.9 – 1.4	2.5 – 4.4	0.6 – 1.1

Table 3: Efficacy

Groups	Group A	Group B
Administration of	**2% Fusidic acid cream**	**2% Mupirocin ointment**
Cured	22	24
Not Cured	3	1
Total	25	25
Irritation at Application site	2	2

Many topical antimicrobials have been used in past, namely: povidone-iodine, framycetin ointment and neomycin/polymyxin B-bacitracin cream. However, the evidence of efficacy of these agents, compared to Mupirocin and Fusidic acid, is not very supportive. [17] Mupirocin and Fusidic acid are the most commonly used topical antimicrobials for primary pyodermas. Along with treatment of skin infections, they are also used for eradication of nasal carriage of MRSA. The usage of these topical antimicrobials has increased the likelihood of development or transfer of antibiotic resistance. Studies outside India have shown Mupirocin and Fusidic acid resistance to be 14.1% [18] and 11% to 18% [19], respectively.

Topical 2% mupirocin and 2% fusidic acid are well-established in the treatment of uncomplicated bacterial skin infections. There is good evidence that topical mupirocin and topical fusidic acid are equally effective. They are more effective than oral treatment for people with limited disease. There have been reports of resistance to these topical antibiotics hence leading to problems in clinical cure. [20-21]

In Rortviet et al. study, impetigo is a superficial skin infection caused by bacteria and has been shown to be most common infection in children worldwide. [22] Chopra and colleagues reported increased incidence in the paediatric age group, attributing it to poorly developed epidermal barrier in children. [23]

The usage of topical treatment for impetigo, mainly with Mupirocin and Fusidic acid is still prevalent today. It has the advantage of minimizing antibiotic resistance, although recent study done in Greece demonstrated increased resistance to these products among certain staphylococcal clone. The percentage of resistance has increased with the repeated use. When systemic therapy is needed, as in cases of the bullous form or widespread lesions, various options exist, with an average treatment of 10 days. Various studies testing new treatments haven't proven adequate efficacy, and larger studies will need to take place.

Conclusion:

The data generated from the present study concludes that the Mupirocin Ointment had shown more efficacy as compared to Fusidic acid cream in the selected patients. The usage of topical treatment for impetigo, mainly with Mupirocin and Fusidic acid is still prevalent today. It has the advantage of minimizing antibiotic resistance, although recent study done in Greece demonstrated increased resistance to these products among certain staphylococcal clone.

References:

1. Moulin F, Quinet B, Raymond J, Gillet Y, Cohen R. [Managing children skin and soft tissue infections]. Arch Pediatr. 2008 Oct. 15 Suppl 2:S62-7.
2. Moran GJ, Amii RN, Abrahamian FM, Talan DA. Methicillin-resistant Staphylococcus aureus in community-acquired skin infections. Emerg Infect Dis. 2005 Jun. 11(6):928-30.
3. Kuniyuki S, Nakano K, Maekawa N, Suzuki S. Topical antibiotic treatment of impetigo with tetracycline. J Dermatol. 2005 Oct. 32(10):788-92.
4. Cole C, Gazewood J. Diagnosis and treatment of impetigo. Am Fam Physician. 2007 Mar 15. 75(6):859-64.
5. Hirschmann JV. Impetigo: etiology and therapy. Curr Clin Top Infect Dis. 2002. 22:42-51.
6. Gorwitz RJ. Community-associated methicillin-resistant Staphylococcus aureus: epidemiology and update. Pediatr Infect Dis J. 2008 Oct. 27(10):925-6. [Medline].
7. [Guideline] Rush, J and Dinulos JG. Childhood skin and soft tissue infections: new discoveries and guidelines regarding the management of bacterial soft tissue infections, molluscum contagiousum, and warts. Current Opinion in Pediatrics. April 2016. 28(2):250-257.
8. American Academy of Pediatrics. Staphylococcal infections. Pickering LK, ed. Red Book: 2012

Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015. 715-732.
9. [Guideline] Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis. 2014 Jul 15. 59 (2):147-59.
10. Scheinfeld N. A Primer In Topical Antibiotics For The Skin And Eyes. J Drugs Dermatol. 2008. 7(4):409-415.
11. Alsterholm M, Flytström I, Bergbrant IM, Faergemann J. Fusidic acid-resistant Staphylococcus aureus in impetigo contagiosa and secondarily infected atopic dermatitis. Acta Derm Venereol. 2010. 90(1):52-7.
12. Mehta SM, Garg BR, Kanungo R. A clinica-bacteriological study of primary uncomplicated bacterial skin infections of children in Pondicherry. Indian J Dermatol Venereol Leprol 1992;58:183-7.
13. Mehta TK. Pattern of skin disease in India. Indian J Dermatol Venereol Leprol 1962;28:134-9.
14. George A, Rubin G. A systematic review and meta-analysis of treatments for impetigo. Br J Gen Pract 2003;53:480-7.
15. Vos, T (Dec 15, 2012). "Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.". Lancet. 380 (9859): 2163–96
16. Caumes E (2000) Treatment of cutaneous larva migrans. Clinical Infectious Diseases 30: 811-884.
17. Hay R, Bendeck SE, Chen S, Estrada R, Haddix A, McLeod T, et al. Skin Diseases. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al, editors. Disease Control Priorities in Developing Countries. 2nd edition [Internet]. Washington (DC): World Bank; 2006 [cited 2015 October 03]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK11733/.
18. Park SY, Kim SM, Park SD. The prevalence, Genotype and Antimicrobial Susceptibility of High- and Low- Level Mupirocin Resistant MethicillinResistant Staphylococcus aureus. Ann Dermatol., 2012; 24(1): 32-8.
19. Dobie D, Gray J. Fusidic acid resistance in Staphylococcus aureus. Arch Dis Child, 2004; 89: 74-7.
20. Korting HC. Differences in the skin surface pH and bacterial microflora due to the long-term application of synthetic detergent preparations of pH 5.5 and pH 7.0. Results of a crossover trial in healthy volunteers. Acta Derm Venereol 1990;70:429.
21. Koning S, van der Sande R, Verhagen AP, van Suijlekom-Smit LWA, Morris AD, Butler CC, Berger M, van der Wouden JC. Interventions for impetigo. Cochrane Database of Systematic Reviews 2012, Issue 1. Art. No.: CD003261. DOI: 10.1002/14651858.CD003261.pub3.
22. Rortveit S, Rortveit G. Impetigo in epidemic and nonepidemic phases: an incidence study over 4½ years in a general population. Br. J. Dermatol. 157(1), 100–105 (2007).
23. Chopra A, Puri R, Mital RR, Kantha S, Bhatia R. A Clinical and Bacteriological Study of Pyodermas. Ind J Dermatol Venereol Leprol., 1994; 60: 200-2.

Conflict of Interest: Nil
Source of support:Nil