

Original research article

Assessment of the cost effectiveness and efficacy of fusidic acid and mupirocin for impetigo: a comparative studyDr. Vinay Kumar¹, Dr. Rohit Kumar Singh²¹Tutor, Department of Pharmacology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India.²Associate Professor and HOD, Department of Pharmacology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India.

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Abstract

Aim: to compare the efficacy and cost-effectiveness of topical fusidic acid and topical mupirocin in treatment of impetigo.

Material and methods: This was an open label, prospective study to evaluate efficacy and cost effectiveness of topical 2% fusidic acid cream with topical 2% mupirocin ointment in treatment of impetigo. The study was conducted in Anugrah Narayan Magadh Medical college and Hospital, Gaya, Bihar, India, for 1 year. 120 patients age 1-30 years, either sex and clinically diagnosed as impetigo (bullous and non-bullous) with number of lesions up to 10 (bullous and non-bullous) were included in this study. 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. Scoring was applied to each parameter in the following manner.

Results: 120 patients enrolled in study, 73 were males and 47 were females. 75 patients were of age < 10 years, 29 were of age 10 – 20 years and 16 were of 20 – 30 years of age. 90 cases had non bullous lesions and 30 had bullous lesions. The number of lesions before treatment were 4.59 ± 1.22 and after one week of treatment was 0.31 ± 0.79 with p -value < 0.05 which was statistically significant. The wound area (cm^2) before treatment was 3.54 ± 0.89 and after one week of treatment was 0.38 ± 1.22 with p -value < 0.05 which was statistically significant. The SSI before treatment was 2.43 ± 0.52 and after one week of treatment was 0.17 ± 0.51 with p -value < 0.05 which was statistically significant. While in group II (Mupirocin), the number of lesions before treatment were 4.22 ± 1.22 and after one week of treatment was 0.18 ± 0.82 with p -value < 0.05 which was statistically significant. The wound area (cm^2) before treatment was 3.53 ± 1.18 and after one week of treatment was 0.21 ± 0.88 with p -value < 0.05 which was statistically significant.

Conclusion: Mupirocin is marginally more effective than fusidic acid but this difference was not statistically significant. Cost effectiveness of fusidic acid is less than mupirocin.

Keywords: Fusidic acid, Mupirocin, Impetigo, Cost-effectiveness, Efficacy, Comparison.

Introduction

Impetigo is a superficial bacterial skin infection and highly contagious most commonly affects children.^{1,2} Primary impetigo results from direct bacterial invasion of previously normal skin, by *Staphylococcus aureus* and *Streptococcus pyogenes* and secondary impetigo results from infection of pre-existing skin disease such as eczema etc.^{3,4} Topical antibacterials such as mupirocin, fusidic acid, nadifloxacin etc., are commonly used to accelerate clinical cure, thereby preventing spread of the disease in the individual and in the community.^{5,6} Moreover

affected child will miss less schooling and need not be withdrawn from school in an attempt to limit the spread of the infection.^{7,8} Untreated impetigo will lead to communal outbreaks and also cause significant long term sequelae such as post Streptococcal glomerulonephritis.⁹

Topical agents may be considered more appropriate than systemic antibiotics for the treatment of localised disease (<10 lesions), as the beneficial non-pathogenic bacteria in the gut are unaffected by topical treatment.¹⁰ Most common adverse effects such as nausea, vomiting and diarrhoea associated with systemic antibiotics are thereby avoided by using topical agents. There is a reduced risk of drug- drug interactions, which are most commonly seen with systemic drugs.¹⁰ Mupirocin is available as 2% ointment or 2% cream in mineral oil is bactericidal at concentrations achieved in topical formulations. It acts by inhibiting bacterial isoleucyl t-RNA synthetase, thereby hindering bacterial RNA, protein and cell wall synthesis. Topical absorption and metabolism is minimal. Mupirocin may be less effective on weeping wounds because 95% of the drug is protein bound. Mupirocin resistance encountered in strains of methicillin resistance *Staphylococcus aureus* (MRSA) and methicillin resistance *staphylococcus epidermidis* (MRSE) and prior exposure is a strong predictor of resistance.^{11,12} Fusidic acid is available as sodium fusidate 2% cream/ ointment is bacteriostatic. It acts by inhibiting Elongation factor - G, thereby inhibiting bacterial protein synthesis. It has steroid-like structure, thought to be responsible for high penetration and no cross resistance with other antibiotics. However development of resistance to fusidic acid is low and short lived and is also active against MRSA strains. Both drugs has excellent activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pyogenes* and Beta-hemolytic streptococci and not active against anaerobes or fungi.¹³ In general development of resistance can be minimised by restricting therapy to no more than 14 days at a time.¹³ This study compares the efficacy and cost-effectiveness of topical fusidic acid and topical mupirocin in treatment of impetigo.

Material and methods

This was an open label, prospective study to evaluate efficacy and cost effectiveness of topical 2% fusidic acid cream with topical 2% mupirocin ointment in treatment of impetigo. The study was conducted Department of Pharmacology, Anugrah Narayan Magadh Medical college, Gaya, Bihar, India, for 1 year. after taking the approval of the protocol review committee and institutional ethics committee. 120 patients age 1-30 years, either sex and clinically diagnosed as impetigo (bullous and non-bullous) with number of lesions up to 10 (bullous and non-bullous) were included in this study. Patients with underlying skin diseases such as pre-existing eczematous dermatitis or trauma with clinical evidence of secondary infections. Complicated bacterial skin infections such as those requiring the systemic administration of antibiotics, i.e., those associated with lymphadenitis, signs and symptoms of systemic toxicity, extensive skin lesions, and localized deep infections of skin. Patients with HIV infection, diabetes mellitus, or patients on corticosteroids therapy and known hypersensitivity to fusidic acid and mupirocin were excluded from study.

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. Scoring was applied to each parameter in the following manner.¹⁴ (Table 1)

Table 1: Scoring system of impetigo (SSI)

Score	Comments
0	No parameter noticed
1	Parameter noticed by the patient and the physician, not disturbing the patient
2	Parameter definitely present and interfering with some activity and sleep
3	Parameter marked and disturbing and interfering with some activity and sleep.

Apart from the above parameters, wound areas was also taken as a parameter. Wound area was measured by the greatest length of the wound in two perpendicular dimensions with a standard metric ruler. The two measurements were multiplied together to obtain the overall wound size. The primary end points were evaluated two times in the study, at the baseline, and after one week of treatment.

These end points included:

- Clinical cure assessed by scoring system of impetigo.¹⁴
- Clinical cure defined as the number of lesions before and after treatment.¹⁵
- Clinical cure defined as the approximate size of the lesions before and after treatment.¹⁶
- Cost effectiveness as cost in INR to treat a single case successfully.

Patients were randomly allocated to two treatment groups – fusidic acid group and mupirocin group. In both groups the test drug was applied locally three times a day.

Efficacy assessment

The patients of the two groups were followed up at the end of first week to assess the efficacy.¹⁷ At the end of first week a detailed clinical examination was performed. SSI assessed, number of lesions and size of existing lesions were measured. The clinical outcome was graded as Mild to Moderate (SSI score 1 or 2 and presence of lesions), Good (SSI score 0 and no lesions).

The treatment was considered effective only if at the end of first week the SSI score 0, no. of lesions 0, size of lesions 0 and the lesions were totally improved without appearance of any new lesions from initial visit.^{16,18,19} The patients were asked for any adverse events occurred during the course of treatment.

The cost effectiveness was calculated on the basis of total expenditure on medicine in INR at the end of first week, cure rate and the two drugs were compared on the basis of amount needed to treat one case successfully.¹⁷

Results

120 patients enrolled in study, 73 were males and 47 were females. 75 patients were of age < 10 years, 29 were of age 10 – 20 years and 16 were of 20 – 30 years of age. 90 cases had non bullous lesions and 30 had bullous lesions (Table 2). Before starting the treatment, both groups had almost number of lesions, size of lesions and SSI (Table 3). The number of lesions before treatment were 4.59 ± 1.22 and after one week of treatment was 0.31 ± 0.79 with p-value < 0.05 which was statistically significant. The wound area (cm²) before treatment was 3.54 ± 0.89 and after one week of treatment was 0.38 ± 1.22 with p-value < 0.05 which was statistically significant. The SSI before treatment was 2.43 ± 0.52 and after one week of treatment was 0.17 ± 0.51 with p-value < 0.05 which was statistically significant. (table 4.) While in group II (Mupirocin), the number of lesions before treatment were 4.22 ± 1.22 and after one week of treatment was 0.18 ± 0.82 with p-value < 0.05 which was statistically significant. The wound area (cm²) before treatment was 3.53 ± 1.18 and after one week of treatment was 0.21 ± 0.88 with p-value < 0.05 which was statistically significant. The SSI before treatment was 2.52 ± 0.53 and after one week of treatment was 0.11 ± 0.41 with p-value < 0.05 which was statistically significant. The p-value was calculated using student's paired t-test.(table 5).Inter group comparison between these two groups after treatment was similar and not statistically significant (Table 6). Clinical efficacy in group I – fusidic acid group was seen in 54 cases out of 60 while that in group II – mupirocin group was seen in 57 cases out of 60 (Table 7). Only mild adverse events were noted in both groups and they did not require any specific treatment. Irritation at the site of application was observed in three patients in group I and in three patients of group II (Table 8). Cost of one tube of fusidic acid was INR 45.00 and that of mupirocin was INR 70. Overall cure rate in fusidic acid was 90% and that in mupirocin was 95%. Hence cost to treat one case was INR 50 for fusidic acid and INR 73.68 for mupirocin (Table 9).

Table 2: Demographic distribution of the patients in groups I & II

	Group I (Fusidic Acid)		Group II (Mupirocin)	
	N=60	%	N=60	%
Gender				
Male	35	58.33	38	63.33
Female	25	41.67	22	36.67
Age				
Below 10 yrs	35	58.33	40	66.67
10to 20 yrs	16	26.67	13	21.67
20 to 30 yrs	9	15	7	11.66
Type of Lesion				
Non – bullous	47	78.33	43	71.67
Bullous	13	36.67	17	28.33

Table 3: Baseline characteristics of two treatment groups

Parameters	Group I (Fusidic Acid) (n=50)	Group II (Mupirocin) (n=50)	
Age in years (Mean±SD)	11.12±7.96	10.33±7.72	p-value > 0.05
Gender ratio (Male% / Female %)	58.33/41.67	63.33/36.67	
Scoring System of Impetigo	2.43±0.52	2.52±0.53	p-value > 0.05
No. of Lesions (Mean±SD)	4.59±1.22	4.22±1.22	p-value > 0.05
Size of Lesions (cm ²) (Mean±SD)	3.54±0.89	3.53±1.18	p-value > 0.05

Table 4: Clinical Cure for Fusidic acid

Parameter	Before Treatment	After Treatment	p-value
No. of Lesions (Mean±SD)	4.59±1.22	0.31±0.79	< 0.05*
Wound Area (cm ²) (Mean±SD)	3.54±0.89	0.38 ±1.22	< 0.05*
SSI (Mean±SD)	2.43±0.52	0.17±0.51	< 0.05*

Table 5: Clinical cure for mupirocin

Parameter	Before Treatment	After Treatment	p-value
No. of Lesions (Mean±SD)	4.22±1.22	0.18±0.82	< 0.05*
Wound Area (cm ²) (Mean±SD)	3.53±1.18	0.21±0.88	< 0.05*
SSI (Mean±SD)	2.52±0.53	0.11±0.41	< 0.05*

Table 6: Clinical Outcome in two treatment groups at the end of first week

No. of Patients	Group I	Group II	p-value
Cured (SSI = 0 and Absence of lesions)	54	57	>0.05
Not Cured (SSI = 1 – 2 and presence of lesions)	6	3	
Efficacy	90%	95%	

Table 7: Comparison of clinical cure for Group I & II after one week of treatment

Parameter	Group I (Fusidic Acid)	Group II (Mupirocin)	p-value
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No. of Lesions (Mean±SD)	0.24±0.82	0.14±0.70	> 0.05
Wound Area (cm ²) (Mean±SD)	0.34±1.18	0.17±0.85	> 0.05
SSI (Mean±SD)	0.14±0.49	0.08±0.39	> 0.05

Table 8: Adverse events in study groups

	Group I (Fusidic Acid)		Group II (Mupirocin)	
	n	%	n	%
Irritation at the site of application	4	6.67%	4	6.67%

Table 9: Cost effectiveness of each study drug at the end of first week based on overall cure rate

Parameters	Fusidic Acid	Mupirocin
Cost in INR for 100 participants	45×100=4500	70×100=7000
Overall Cure rate (%)	90	95
Cost effectiveness	4500 for 90 participants	7000 for 95 participants
Cost in INR to treat one case	50	73.68

Discussion

Impetigo is a common, highly contagious superficial bacterial skin infection caused by either *Staphylococcus aureus* or *streptococcus* or both. *Staphylococcus* is the most common agent in temperate climates, whereas streptococcal impetigo is more often seen in hot, humid areas. All ages can contract the infection but non-bullous disease particularly affects young children, often in late summer.^{20,21} It can be sporadic, although outbreaks can arise in conditions of overcrowding and poor hygiene or in institutions. A widespread form can occur in neonates. Predisposing factors are minor skin abrasions and the existence of other skin conditions, such as infestations or eczema.²² The diagnosis of non-bullous and bullous impetigo is nearly always clinical. Treatment options for impetigo include topical antibiotics, systemic antibiotics and topical disinfectants depending on the severity.²³ Among the topical antibiotics, fusidic acid and mupirocin are quite commonly used.²⁴ In group I (Fusidic acid) the clinical cure parameters were assessed before and after treatment for one week.

The number of lesions before treatment were 4.59±1.22 and after one week of treatment was 0.31±0.79 with p-value < 0.05 which was statistically significant. The wound area (cm²) before treatment was 3.54±0.89 and after one week of treatment was 0.38±1.22 with p-value < 0.05 which was statistically significant. The SSI before treatment was 2.43±0.52 and after one week of treatment was 0.17±0.51 with p-value < 0.05 which was statistically significant. While in group II (Mupirocin), the number of lesions before treatment were 4.22±1.22 and after one week of treatment was 0.18±0.82 with p-value < 0.05 which was statistically significant. The wound area (cm²) before treatment was 3.53±1.18 and after one week of treatment was 0.21±0.88 with p-value < 0.05 which was statistically significant. The SSI before treatment was 2.52±0.53 and after one week of treatment was 0.11±0.41 with p-value < 0.05 which was statistically significant. The p-value was calculated using student's paired t-test.

Clinical efficacy was defined as no lesions and SSI score zero after one week of treatment along with no appearance of any new lesions from initial visit. Percentage of patients cured to the total number of patients in the study group was taken as clinical efficacy. The efficacy of group I (Fusidic acid) was 90% while that of group II (Mupirocin) 95%. Clinical outcome after one week in both groups was similar and not statistically significant. Student's unpaired t test was used to calculate p value.

Adverse effects reported in this study were mild and did not require any specific treatment or discontinuation of drug. 4 cases in each group complained of skin irritation at site of application.

Cost effectiveness of each study drug at the end of first week based on overall cure rate was calculated in INR (Indian National Rupee). The cost incurred to treat one case successfully was INR 50 for fusidic acid and INR 73.68 for mupirocin. So fusidic acid was more cost effective than mupirocin in treatment of impetigo.

Results of our study with regard to clinical effectiveness are consistent with study done by Koning et al. They found no difference between effectiveness of mupirocin and fusidic acid.²⁵ Chosidow et. al. compared retapamulin with fusidic acid and found that adverse effects were virtually nonexistent with fusidic acid.²⁶ In our study too only 6.67% cases in fusidic acid group complained of mild adverse effect. We could not find any study that compared cost effectiveness of mupirocin and fusidic acid.

In our study proper randomization was used to allocate a patient to a treatment group. Care was taken to maintain similar demographics in both groups. 60 cases were assigned to each group keeping in view the accepted sample size. Cost effectiveness was also compared in this study which was not done in any previous studies.

However, our study was limited to mild – moderate cases of impetigo having ≤ 10 lesions. Impetigo with secondary bacterial infections were excluded here and the outcome may vary in such cases. Further studies are required in various subsets of impetigo cases.

Conclusion

Mupirocin is marginally more effective than fusidic acid but this difference was not statistically significant. Cost effectiveness of fusidic acid is less than mupirocin.

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