

## Original Research Article

# A randomised open label comparative study evaluating the effectiveness, adherence and safety between 2% mupirocin ointment and 2% fusidic acid cream in children with impetigo

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**Received:** 15 April 2019

**Accepted:** 02 May 2019

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### ABSTRACT

**Background:** Impetigo is a superficial bacterial skin infection that affects mainly children, which is highly contagious. Topical anti-bacterials are most commonly used in both primary and secondary impetigo. Clinical trials have shown high efficacy of these topicals along with systemic antibiotics in both complicated and uncomplicated impetigo. However use of these topical modalities alone in uncomplicated primary impetigo is limited. The aim of the study was to compare the efficacy, safety and adherence to treatment of mupirocin with fusidic acid in primary impetigo.

**Methods:** A total of 60 patients with a clinical diagnosis of primary impetigo, between 2-14 years of age, having <10 lesions, skin infection rating score >4 and pus score equal to or more than one who attended Dermatology OPD, in Chengalpattu Medical College Hospital from February 2018 to March 2019. Study design was a comparative analytical study.

**Results:** Baseline disease characteristics such as number of lesions, the severity of disease (SIRS), and pus scores were statistically similar between the two groups. The clinical improvement observed with mupirocin (25/30) and fusidic acid (24/30) treatment in primary impetigo was not statistically significant ( $p>0.05$ ). Both drugs were tolerated well.

**Conclusions:** Both mupirocin and fusidic acid showed similar clinical success in patients with primary impetigo. Though fusidic acid has additional anti-inflammatory property and its treatment is cost effective, but irritant effects observed in some patients, which reduces the compliance, lead to consider mupirocin as first line treatment in primary impetigo.

**Keywords:** Primary impetigo, Skin infection rating scale, Clinical failure, Anti inflammatory, Adherence

### INTRODUCTION

Impetigo is a superficial bacterial skin infection and highly contagious most commonly affects children.<sup>1,2</sup> Primary impetigo results from direct bacterial invasion of previously normal skin, by *Staphylococcal aureus* and *Streptococcus pyogens* and secondary impetigo results from infection of pre-existing skin disease such as

eczema etc.<sup>3,4</sup> 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.<sup>5,6</sup> Moreover affected child will miss less schooling and need not be withdrawn from school in an attempt to limit the spread of the infection.<sup>7,8</sup> Untreated impetigo will lead to communal outbreaks and also cause significant long

term sequelae such as post *Streptococcal* glomerulonephritis.<sup>9</sup>

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.<sup>10</sup> 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.<sup>10</sup>

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.<sup>11,12</sup>

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.<sup>13</sup> In general development of resistance can be minimised by restricting therapy to no more than 14 days at a time.<sup>13</sup>

Topicals are an empirical therapy, prescribed for impetigo and is cost effective. In this study we compared the efficacy, safety and adherence to treatment of mupirocin with fusidic acid in primary impetigo.

**METHODS**

The study was conducted in a tertiary care centre, Department Of Dermatology, Chengalpattu Medical College Hospital, during the period of April 2018 to March 2019.

**Inclusion criteria**

Inclusion criteria were patients with clinical diagnosis of primary impetigo; age between 2-14 years; afebrile; impetigo lesions <10; skin infection rating score more than or equal to 4; pus score more than or equal to 1; parent/ legal guardian willing and able to comply with the protocol.

**Exclusion criteria**

Exclusion criteria were age <2 years and >14 years; impetigo lesions >10 at baseline and which warrants systemic therapy; secondary impetigo; history of hypersensitivity to fusidic acid or mupirocin; topical/Systemic antibiotic and or corticosteroids within one week before baseline.

**Table 1: Skin infection rating scale.**

Item	Category	Score	Scale
1	Erythema	0	Absent
		1	Minimal
		2	Moderate
		3	Severe
2	Pus	0	Absent
		1	Minimal
		2	Moderate
		3	Severe
3	Crusting	0	Absent
		1	Minimal
		2	Moderate
		3	Severe
4	Pain	0	Absent
		1	Minimal
		2	Moderate
		3	Severe
5	Itching	0	Absent
		1	Minimal
		2	Moderate
		3	Severe

**Study procedures**

In the first visit, patients were screened for study enrolment after taking informed consent from the guardian. Eligible patients were randomly divided into two equal groups and began treatment on the same day. Patients of one group received 2% mupirocin ointment, two times a day for 7 days and another group were given 2% fusidic acid cream, three times a day for 7 days. Follow up was done on 4<sup>th</sup> and 7<sup>th</sup> day of treatment. Further follow up was done on 14<sup>th</sup> day, for those patients who did not have successful clinical response at end of one week. All the patients were followed up for two weeks after clinical cure to look for any recurrence or relapse. Safety was determined by either patient spontaneously reported adverse reactions or adverse findings by the physicians. Adherence to treatment was assessed by the number of missed topical applications and patient who has completed 80% of treatment was considered as compliant.

**Measures of clinical outcomes**

Skin infection rating scale (SIRS) was used to assess the severity of disease at baseline and 4<sup>th</sup> and 7<sup>th</sup> day of

treatment and day -14 follow up. SIRS evaluates 5 signs and symptoms: pus, crust, erythema, itching and pain on a scale (0-3): 0=absent, 1= mild, 2= moderate, 3= severe.

Clinical success was determined by sufficient resolution of signs and symptoms of infection, as evidenced by the SIRS score of zero each for pus, crust and pain and 0/1 for erythema and itching. Clinical improvement was determined by a SIRS score of 0 for exudates (pus) which does not meet all the criteria for clinical success. Clinical failure is a SIRS score of  $\geq 1$  for pus.

### Statistical analysis

Data were collected in a preformed proforma, and data were entered into Microsoft Excel spreadsheet 2016, and statistics were performed using IBM SPSS statistics for windows, Version 21.0. Tabulations of results were made, data were presented as mean, standard deviation and actual numbers and percentages. Chi-square test was used to draw inferences between two groups on categorical data and unpaired t-test and ANOVA was used to draw inferences on continuous data. A two tailed p value less than 0.05 was used for significance testing.

### RESULTS

A total of 60 patients participated in this study, 30 Patients received 2% mupirocin ointment and 30 patients received 2% fusidic acid cream. The mean age of the patients was  $7.0 \pm 2$  years. The skin infection rating scores were shown in table.1 There were 32/60 (53.4%) male and 28/60 (46.6%) female children. 4/60 (6.8%) were dropped out of the study, the reason for drop out is lost to follow up. we observed that 49/60 (81.6%) of patients had the clinical success of treatment, which is defined as reduction in pus, crust and pain of skin infection rating scale to zero from the baseline. 7/60 (11.6%) of our patients experienced treatment failure after seven days. These patients were given oral antibiotics, based on pus culture and sensitivity for five days along with topical therapy.

All these initial clinical failure patients had complete resolution of signs and symptoms after oral antibiotic therapy. Both mupirocin ointment and fusidic acid cream were tolerated well, with almost 85% of the patients were compliant to therapy. Few patients in fusidic acid arm had complained of irritation following application, which resolved after few applications. No adverse events were observed by the physician during treatment or follow up period. There were no clinical recurrences in any treatment groups.

When we compared the clinical symptoms and signs before and after the treatment between two groups, we found that the number of skin lesions, SIRS, pus score and pain scores were statistically ( $p > 0.05$ ) similar between mupirocin and fusidic acid treatment groups.



**Figure 1: Primary impetigo after treatment with 2% mupirocin ointment (male).**



**Figure 2: Primary impetigo after treatment with 2% mupirocin ointment (female).**



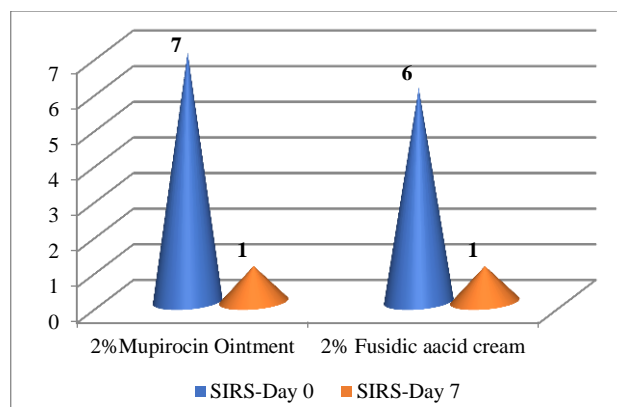
**Figure 3: Primary impetigo after treatment with 2% fusidic acid creams (male).**



**Figure 4: Primary impetigo after treatment with 2% fusidic acid creams (female).**

**Table 2: Clinical outcomes of all patients with primary impetigo.**

Parameters	N	%	
<b>Gender</b>	Female	28	46.6
	Male	32	53.4
	Total	60	100
<b>Clinical success</b>	Yes	49	81.6
	No	7	11.6
	Drop out	4	6.8
	Total	60	100
<b>Compliance</b>	Yes	54	90
	No	6	10
	Total	60	100



**Figure 5: SIRS comparison of topical mupirocin and fusidic acid.**

**Table 3: Clinical characteristics of all patients with impetigo.**

All patients	Count	Mean	SD	Median
<b>Age</b>	60	7	2	7
<b>Treatment duration</b>	60	7	0	7
<b>Number of lesions at baseline</b>	60	6	2	6
<b>Number of lesions at end</b>	60	0	1	0
<b>SIRS at baseline</b>	60	7	3	7
<b>SIRS at end</b>	60	1	2	1
<b>Pus score at baseline</b>	60	2	1	2
<b>Pus score at end</b>	60	0	0	0
<b>Pain score at baseline</b>	60	1	1	1
<b>Pain score at end</b>	60	0	0	0

**Table 4: Clinical outcomes of all patients with impetigo.**

Parameters	2% mupirocin	%	2% fusidic acid cream	%	P value
<b>Gender</b>	Male	17	56.6	15	>0.05
	Female	13	43.4	15	
	Total	30	100	30	
<b>Clinical success</b>	Yes	25	83.4	24	>0.05
	No	3	10	4	
	Drop out	2	6.6	2	
	Total	30	100	30	
<b>Compliance</b>	Yes	27	90	25	> 0.05
	No	3	10	5	
	Total	30	100	30	

**Table 5: Comparison of clinical characteristics of patients between 2% mupirocin and 2% fusidic acid cream.**

All patients	2% mupirocin	2% fusidic acid	P value		
<b>Age</b>	7±2	7	7±3	8	>0.05
<b>Number of lesions at baseline</b>	6±3	7	7±3	7	>0.05
<b>Number of lesions at end</b>	0±1	0	0±1	0	>0.05
<b>SIRS at baseline</b>	8±3	8	8±3	8	>0.05
<b>SIRS at end</b>	1±2	1	1±2	1	>0.05
<b>Pus score at baseline</b>	2±1	2	2±1	2	>0.05
<b>Pus score at end</b>	0±0	0	0±0	0	>0.05
<b>Pain score at baseline</b>	3±1	2	3±1	2	>0.05
<b>Pain score at end</b>	0±0	0	0±0	0	>0.05

## DISCUSSION

Impetigo is a superficial bacterial infection of the skin, highly contagious and mostly affects children. Most cases are caused by *Staphylococcus aureus*, *Streptococcus pyogenes*, or mixture of both organisms. The most commonly used topical antibacterials are mupirocin, fusidic acid, nadifloxacin and retapamulin, various meta-analysis showed that there is no difference between their efficacy. We compared the safety and efficacy of mupirocin versus fusidic acid in a total of 60 patients with clinical diagnosis of primary impetigo, between 2-14 years of age, having <10 skin lesions, SIRS >4 and pus score >1. Clinical success was defined as drying up or resolution of the lesion by the end of seven days of treatment.

Mupirocin is a bactericidal topical antibiotic, with minimal systemic absorption, time tested safety preparation used in acute bacterial skin infections, while topical Fusidic acid cream is a bacteriostatic highly active against *Staphylococci*, *Streptococci* and other pathogens known to cause impetigo. Both the drugs have good penetration into the cutaneous surface and high concentration at the site of infection.

The effectiveness of mupirocin and fusidic acid have been assessed in comparison with placebo in various studies.<sup>14-17</sup> A randomised, which compared between mupirocin and fusidic acid cream showed, efficacy of 85% and 84% respectively.<sup>14</sup> These results were almost compatible with our study result of 83.4% and 80%. A similar study by Morley, which compared the efficacy of these two topicals, showed clinical cure of 87%.<sup>15</sup> A randomised study by White, showed similar results as our study.<sup>16</sup> In our study we found that efficacy at the end of 7 days of treatment with mupirocin was 83.4%, and with fusidic acid was 80%. Clinical failure patients, received oral antibiotics for five days along with topical therapy. All these initial clinical failure patients had complete resolution of signs and symptoms after oral antibiotic therapy.

The possible reasons for clinical failure include, non-compliance which is common in school going children, not removing crusts by applying saline soaks before topical applications, oozing nature of lesions, which hamper the time of contact of drugs with lesion. None of our patients had experienced any systemic complications since all our patients had non-bullous impetigo and lower SIRS score at presentation.<sup>18</sup>

This is single centre study with a small group of paediatric population, and treatment outcomes were measured on subjective factors such as erythema, pus, crusting, oedema and pain. Observer blinding was not feasible due to practical reasons. The microbiological response was also not evaluated in our study.

## CONCLUSION

In our study, we observed that both mupirocin and fusidic acid showed similar clinical success in patients with primary impetigo. Though fusidic acid has additional anti-inflammatory property and its treatment is cost effective, but irritant effects observed in some patients, which reduces the compliance, lead to consider mupirocin as first line treatment in primary impetigo.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

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**Cite this article as:** Velappan R, Ramasamy S, Venu S, Chandrasekar M. A randomised open label comparative study evaluating the effectiveness, adherence and safety between 2% mupirocin ointment and 2% fusidic acid cream in children with impetigo. *Int J Res Dermatol* 2019;5:511-6.