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Efficacy of fusidic acid and mupirocin in treatment of impetigo: A randomized clinio-pharmacological study

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Abstract
Aim: This study compares the efficacy of fusidic acid and mupirocin in treatment of impetigo.
Materials and Methods: This was an open label; prospective clinical study was carried out among 60 impetigo patients. The primary end points were evaluated at the baseline, and after one week of treatment. In both groups the test drug was applied locally thrice daily. Statistical analysis was done using paired and unpaired t test.
Results: In group I and II; mean number of lesions declined from 4.64 to 0.44 and 4.35 to 0.16 and mean lesion size declined from 3.28 to 0.18 and 3.44 to 0.11 ($p \leq 0.05$) respectively.
Conclusion: Mupirocin is marginally more effective than fusidic acid but this difference was not statistically significant.

Keywords: fusidic acid, mupirocin, efficacy, impetigo

Introduction

Impetigo is the most common skin infection in children; it is caused mainly by *Staphylococcus aureus* and sometimes by *Streptococcus pyogenes* [1, 2], The highly contagious nature of impetigo also allows spread from patients to close contacts. Although impetigo is considered a self-limited infection, antibiotic treatment is often required for quicker cure, to prevent spread to others and to prevent complications [3].

There is some uncertainty regarding the optimal treatment of impetigo. Advice ranges from the use of oral flucloxacillin, erythromycin, penicillin or cephalosporins to topical treatment with fusidic acid, mupirocin, neomycin or bacitracin [4]. The British National Formulary (BNF) recommends topical fusidic acid or mupirocin for limited impetigo and oral flucloxacillin or erythromycin for widespread disease [5].

Mupirocin demonstrated a marked inhibitory effect on multiply resistant strains of S. aureus in an in vitro comparison of a variety of topical formulations currently being used. It Gram-negative organisms have been reported to be generally less susceptible to the activity of mupirocin [6]. Systemic absorption is minimal, and the amount that is absorbed is rapidly and extensively converted to monic acid, an inactive metabolite [7].

Fusidic acid is a bactericidal antibiotic that inhibits bacterial protein synthesis by interfering with amino acid transfer from aminoacyl-sRNA to protein on the ribosomes. Fusidic acid is available in oral and injectable forms and as a 2% topical cream or ointment. Fusidic acid is effective against S. aureus and Streptococcus species [8].

In developing country like India very few studies are available hence the present was under taken with the aim to compare the efficacy and cost-effectiveness of topical fusidic acid and topical mupirocin in treatment of impetigo.

Materials and Methods

Study Design

A Prospective open label study was conducted for the period of jan 2014 to Nov 2014 among patients with the confirmed diagnosis of Impetigo who had attended Out Patient Department of Dermatology, Katihar Medical College and Hospital, Katihar, Bihar, India. The study protocol was reviewed by the Ethical Committee of the Hospital and granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained.

Inclusion criteria

- Patient/Guardians who signed the "informed consent" form
- Patients >10 years of age
- Patients with number of lesions up to 10 (bullous and non-bullous).

Exclusion criteria

- Complicated bacterial skin infections
- Patients with known hypersensitivity to both test drugs
- Pregnant and lactating mothers
- Patients unwilling or unable to comply with the study procedures

Sample selection

The sample size was calculated using a prior type of power analysis by G* Power Software Version 3.0.1.0 (Franz Faul, Universitat Kiel, Germany). The minimum sample size of each group was calculated, following these input conditions: power of 0.80 and $P \leq 0.05$ and sample size arrived were 60 patients i.e 30 per group.

Grouping

Patients were randomly allocated to two treatment groups;
Group I (N=30) -Fusidic acid group
Group II (N=30) - Mupirocin group

In both groups the test drug was applied locally three times a day.

Methodology

At the first visit after obtaining the relevant history, a thorough clinical examination was performed regarding the general condition of the patient, morphological features, distribution of lesions, and involvement of the lymph nodes. The diagnosis of the condition was confirmed clinically. Grading of the lesions was done with reference to parameters such as erythema, edema, vesiculation, pustulation, crusting, and scaling [9]. Apart from that, wound areas were 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.

Assessment of drug efficacy and cost-effectiveness

The primary end points were evaluated two times in the study, at the baseline, and after one week of treatment.

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. 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.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of means. Statistical test applied for the analysis were both paired and un-paired t-test [10]. The confidence interval and p-value were set at 95% and ≤ 0.05 respectively.

Results

Table 1: demographic details of the study subjects

Variables	Group I	Group II
Mean Age	14.17	13.89
Male/Female Ratio	17/13	16/14

Of the 60 patients, 30 patients in each arm completed the protocol defined treatment and follow-up. Mean age of the study subjects in group I and II as follows; 14.17 years and 13.89 years. Majority of the subjects were male in both the groups.

Table 2: comparison of mean number of lesions

Mean Number of lesions	Group I	Group II	p-value
Before Treatment	4.64	4.35	0.619 (NS)
After Treatment	0.44	0.16	0.184 (NS)
p-value	0.001 (Sig.)	0.001 (Sig.)	

Test applied: paired and unpaired t-test. (NS) indicates p≥0.05 (Sig.) indicates p≤0.05

Within the groups before and after treatment; mean number of lesions declined from 4.64 to 0.44 and 4.35 to 0.16 (p≤0.05) respectively but, there is no statistically significant difference observed between the groups (p≥0.05) respectively.

Table 3: comparison of mean lesion size

Mean Lesion size ($cm^{2)}$	Group I	Group II	p-value
Before Treatment	3.28	3.44	0.894 (NS)
After Treatment	0.18	0.11	0.766 (NS)
p-value	0.001 (Sig.)	0.001 (Sig.)	

Test applied: paired and unpaired t-test. (NS) indicates p≥0.05 (Sig.) indicates p≤0.05

Within the groups before and after treatment; mean lesion size declined from 3.28 to 0.18 and 3.44 to 0.11 (p≤0.05) respectively but, there is no statistically significant difference observed between the groups (p≥0.05) respectively.

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 [11, 12]. Indiscriminate and universal use of topical medications including antibiotics has led to widespread resistance (molecular, group, and class) to the same [13].

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. 30 cases were assigned to each group keeping in view the accepted sample size.

Clinical effectiveness of both the study drugs in the present study was found in agreement with study done by Koning *et al*. They found no difference between effectiveness of mupirocin and fusidic acid [14]. Oranje *et al*. in his investigation found that adverse effects were virtually nonexistent with fusidic acid [15]. In the present investigation only 4% of the subjects in fusidic acid group complained of mild adverse effect.

Similar results were observed in terms of clinical effectiveness and cost-effectiveness; recent meta-analysis [16] showed that fusidic acid and mupirocin were equally effective in treating impetigo, but fusidic acid costs less.

Limitations

The limitations of this study were relatively lesser sample size, lack of facilities for complete microbiological analysis of the infecting bacteria with culture, in vitro sensitivity, and determination of minimum inhibitory concentration values.

Follow-up studies for recurrence of the lesions at the same site could not be performed.

Conclusion

Mupirocin is the first new and exclusively topical antibiotic for the treatment of skin infections to emerge in the last 25 years. It has been demonstrated in the present trial mupirocin is marginally more effective than fusidic acid with respect to safety and efficacy but fusidic acid is more costs effective.

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