Efficacy and Safety of Mupirocin 2% Cream in the Treatment of Primary and Secondary Bacterial Skin Infections in Upper Egypt

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Abstract: Background: Bacterial skin infections are commonly encountered in the community. Topical antibiotics have the advantage of achieving high local drug concentration at target site and less systemic side effects and better compliance with patients. **Objective:** This is the first study in Upper Egypt to evaluate the clinical and bacteriological efficacy and safety of mupirocin® 2% cream in the treatment of different primary and secondary bacterial skin infections. **Methods:** In a prospective, non placebo controlled trial, 70 patients (30 with impetigo, 15 with boils, 10 with folliculitis and 15 with eczema with secondary bacterial infection) received topical mupirocin® 2% cream for 14 days. Patients were attending the clinic for three visits during which clinical and laboratory evaluation were performed. **Results:** Clinical and bacteriological success were obtained in the four groups with statistically significant difference between them considering age, site & severity of lesion and duration of treatment. No side effects were reported. **Conclusion:** Mupirocin® 2% calcium cream proved to be an effective and safe in the treatment of primary and secondary bacterial infections in Upper Egypt.

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Key Words: Mupirocin® , impetigo, boils, folliculitis, eczema, secondry bacterial,treatment

1. Introduction

Bacterial skin infections commonly encountered in the community include impetigo, folliculities, furunculosis, carbuncle, abscesses, erysipelas, cellulites[1], wound infections, scarlet fever, acute paronychea and staphylococcal scalded skin syndrome[2].

Bacterial skin infections are subdivided into superficial and deep infections, the former are often treated locally while the latter may require systemic antibiotic or surgical intervention[3]. They may be localized or spreading[2]. Skin infections may be primary or secondary[4]. Impetigo is the most common primary skin infection[5]. Impetigo can occur as a primary or secondary to pre-existing skin conditions such as eczema or scabies[6]. *Staphylococcus aureus* is the predominant pathogen for impetigo and furuculosis and methicillin resistant strains play a growing role in both diseases[1]. Folliculitis is a pyoderma located within a hair follicle, secondary to follicular occlusion by keratin, over hydration, or either bacterial or fungal infection[7].

Guidelines for treatment of impetigo differ widely, treatment options include many different oral and topical antibiotics as well as disinfectants[5]. If the lesions are not widespread topical mupirocin is the treatment of choice[7].

Mupirocin is a topical antibiotic used to treat superficial skin infections and to control spread of methicillin-resistant *staphylococcus aureus* (MRSA)[8]. It's produced by *Pseudomonas fluorescens* (Pseudomonic acid A) and act by binding competitively to bacterial iso leucyl-t RNA synthetase (IRS) and inhibits bacterial protein synthesis[9, 10].

It has been used successfully to eradicate nasal and hand staphylococcal colonization in patients and healthcare workers[11], to control outbreaks of MRSA, topical mupirocin was shown to be as effective as or slightly superior to oral erythromycin in treatment of impetigo[5]. Mupirocin cream applied three times daily is as effective clinically and superior bacteriologically (against *S. aureus*) compared with oral cephalexin given four times daily in the treatment of 2[ry] infection wounds[12] and secondary infected eczema[13]. Mupirocin cream had a similar efficacy to fusidic acid cream[5].

Aim of the study:

This study aimed to evaluate the clinical and bacteriological efficacy and safety of mupirocin 2% cream in the treatment of different primary and secondary bacterial skin infections in Upper Egypt.

2. Patients and Methods

This study is a prospective, non placebo controlled clinical trial that was carried out at the Dermatology, Venearology and Andrology department, of Assiut University hospitals from July 2011 to May 2012. All patients with primary and secondary superficial bacterial skin infection attending the outpatient clinic were screened for exclusion criteria. The Institutional Review Board of Assiut Faculty of Medicine approved the study. Patients were counseled

about participating in the study, and a written informed consent was taken.

Exclusion criteria

The exclusion criteria were hypersensitivity to mupirocin, patients who had received a topical or systemic antibiotic within the preceding 48 hours, patients on whom the total surface area of the lesion exceeded 50 cm^2, and those with an infection required systemic antibiotic treatment.

The study was started on 85 patients. However only 70 patients were followed up regularly. A written consent was obtained from each enrolled patient or from a parent or legal guardian for each child before treatment. Complete medical history was obtained including age, sex, family history of similar condition, duration, type and extent of lesion. Through physical examination carried out. Six clinical parameters, erythema, oedma, vesiculation, postulation, desquamation and crust formation were evaluated using a 4-point grading system. (0= absent, 1= mild; 2= moderate; 3= severe. The clinical efficacy & outcome was scored as complete or marked improvement (= 3),good (=2), poor (=1),or no response (=0). Enrolled patients were divided into four groups: Group I: include 30 Impetigo cases, Group II: 15 boils cases, Group III: 10 folliculitis cases, and Group IV: 15 patients of eczema with 2^{ry} bacterial infection. They all received topical mupirocin® 2% cream (Probactcin; Kahira Pharm. & Chem. Ind. Co. for Bioxell pharma) twice daily for 7-14 days . Patients were enrolled into study for 14 days and attended the clinic for three visits during which clinical and laboratory evaluations were performed including colored photos before & after treatment in order to assess the degree of response to therapy. On the initial visit, lesions were cultured, complete history , clinical examination & colored photos of the lesions were taken and therapy was begun. Swab cultures were obtained from representative sites after the skin lesions were washed with soap and water to remove any crusts. More than one culture was obtained if multiple body sites were involved. Lesions were counted and mapped to evaluate responses.

All samples were cultured on MacConkey's agar (Himedia – Cat. No. MM081), Mannitol salt agar (Himedia – Cat. No. M118 – 500G), ORSAB (Himedia – Cat. No. M1454 – 500G), Bismuth Sulphide agar (Himedia – Cat. No.MU027 – 500G), Sabouraud's dextrose agar (HiMedia ™ M063) (all the media were provided from Himedia Company – India). Confirmation of the isolated organisms was performed using biochemical reactions (coagulase test, TSI test, Urease test, sugar assimilation test (HiMedia ™ M139), germ tube test, IMVC test for identification of isolated organisms[14].

Staph Aureus and Coagulase negative Staph organisms that grew after 24 hours at 35°C on Mueller-Hinton agar plates containing 6 ug/mL oxacillin and 4% sodium chloride were confirmed as MRSA and MRCNS respectively; while methicillin-sensitive *S. aureus* (MSSA) and MSCNS showed no growth on oxacillin plates. All isolates were tested for susceptibility to mupirocin by agar dilution (MIC) and by Kirby-Bauer method of disk diffusion[15].

Mupirocin resistance was determined initially by a screening method utilizing growth on Mueller-Hinton agar containing 2 ug/mL mupirocin. The minimal inhibitory concentration (MIC) of mupirocin for each isolate was confirmed using a microtiter method. High-level resistance was defined as an MIC greater than 100 ug/mL, low-level resistance as an MIC between 4 ug/mL and 100 ug/mL, and sensitive as less than or equal to 4 ug/mL[16].

Antimicrobial susceptibility tests were carried out using disk diffusion (oxoid, Hamsphire UK), on Muller Hintor agar plate according to the clinical and laboratory standard institute. A strain is considered susceptible to mupirocin if the inhibition zone $\geq$ 14 mm. and resistant if the inhibition zone $\leq$ 13 mm. [17].

All patients were seen again on days 6 to 7 of therapy (second visit) and on day 10 to 14 of therapy (third visit), where clinical &bacteriological evaluation were done. Clinical responses were scored at each visit on the basis of the number of lesions and involved areas. Bacteriologic response was judged by culturing persisting or recurrent lesions at each visit. Compliance was judged by history and by collecting and measuring unused medication.

Statistical analysis:

Statistical analysis was performed using SPSS software version 16 (SPSS Inc., Chicago, USA), and expressed as mean, standard deviation (SD), number and percentage. Statistical methods were applied including descriptive statistics (frequency, percentage, mean and SD) and tests of significance (X2 and Fisher exact tests for categorical variables and Student t test and Mann Whitney tests for continuous variables). Statistical significance was assumed when $P < 0.05$.

3. Results

This study was conducted on 70 patients which were divided into four groups: Group I: 30 impetigo patients, Group II: 15 boils patients, Group III: 10 folliculitis patients, and Group IV: 15 patients of eczema with 2^{ry} bacterial infection.

Table (1): shows the demographic data of all groups; there's significant statistical difference between all groups considering age, site of lesion, severity of lesion and duration of treatment. The cases that required longer duration was that associated with severe lesions and most of them were associated with MRSA.

The study showed that impetigo & multiple boils are more common in females, while folliculitis & eczema with secondary bacterial infection are more common in males. Impetigo was more common in children, while the other three groups were common in young adults. Scalp was the commonest site for impetigo while extremities were the commonest for boils & eczema with secondary bacterial infection. The face was the commonest site for folliculitis.

70% of impetigo cases showed marked cure in ≤7 days while most cases of the other groups were cured in >7 days, which was statistically significant between impetigo and boils (Table 1) & (Figure 3-33).

Marked and complete cure were obtained in most cases of the four groups but with no statistically significant difference (Table 1) & (Figures 3-33).

There is no significant difference between clinical outcome and duration of treatment (Tables, 2 and 3). Marked improvement occurred in chronic and contact eczema with secondary bacterial infection while moderate ones occur in seborrheic eczema with secondary bacterial infection (Table 4).

Figure (1) shows: the positive correlation between the duration of treatment and severity of lesion.

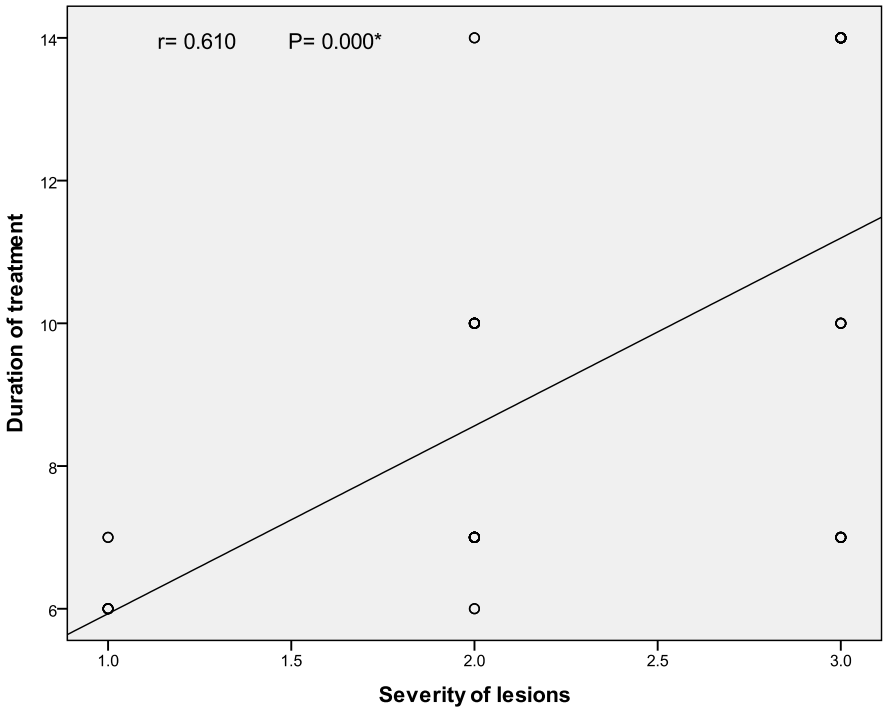
Table (5): shows the distribution of different microorganisms in different patients groups; as a whole, there were significant statistical difference in the distribution of MRSA (Methicillin Resistant Staph Aureus.) and MSCNS (Methicillin Sensitive Coagulase Negative Staph.) in all patients groups.

Figure (2): shows the frequency of different isolates in all groups collectively, MRSA was the most dominant organism isolated in such study, followed by MSSA, MSCNS and MRCNS respectively.

Table (6): shows the MIC for different isolates; MIC for Coryne species was higher than that of MRSA isolates, and then followed by all species. No bacterial isolates were resistant to Mupirocin and all cases responded to treatment and cured completely.

Table (1): shows the demographic data and clinical outcomes

	Impetigo (n= 30)		Boils (n= 15)		Folliculitis (n= 10)		Secondary infected eczema (n= 15)		*P* value
	No.	%	No.	%	No.	%	No.	%	
Sex:									
Male	11	36.7	7	46.7	7	70.0	8	53.3	*P*=0.365
Female	19	63.3	8	53.3	3	30.0	7	46.7	n.s
Age: years									*P*<0.04*
Mean ± SD	6.1 ± 3.0		22.0 ± 11.1		21.8 ± 10.8		29.1 ± 9.2		
Site of lesions:									
Extremities	0	0.0	8	53.3	0	0.0	11	73.3	*P*<
Face	8	26.7	5	33.3	7	70.0	3	20.0	0.001**
Scalp	20	66.7	0	0.0	3	30.0	0	0.0	
Scalp & face	2	6.7	0	0.0	0	0.0	1	6.7	
Trunk	0	0.0	2	13.3	0	0.0	0	0.0	
Severity of lesions:									
Mild	3	10.0	4	26.7	1	10.0	0	0.0	*P*<0.03*
Moderate	12	40.0	7	46.7	7	70.0	8	53.3	
Severe	15	50.0	4	26.7	2	20.0	7	46.7	
Duration of treatment:									
≤ 7 days	21	70.0	5	33.3	4	40.0	6	40.0	*P*<0.02*
> 7 days	9	30.0	10	66.7	6	60.0	9	60.0	
Mean ± SD	8.4 ± 2.8		10.4 ± 3.4		9.6 ± 2.7		9.9 ± 2.9		*P*=0.512 n.s
Clinical outcome:									
Moderate	4	13.3	3	20.0	2	20.0	5	33.3	
Marked to complete cure	26	86.7	12	80.0	8	80.0	10	66.7	*P*=0.284 n.s



Spearman correlation

Fig. (1): Correlation between duration of treatment and severity of lesions

Table (2): The relation between duration of treatment and clinical outcome

Clinical outcome	Mean	±SD	*P*-value
Moderate	8.43	±2.59	0.371
Marked to complete cure	9.54	±3.07	

Mann-Whitney test

Table (3): Clinical outcome versus Duration of treatment

Clinical outcome	Duration of treatment			
	≤ 7 days (n= 36)		> 7 days (n= 34)	
	No.	%	No.	%
Moderate	10	27.8	4	11.8
Marked to complete cure	26	72.2	30	88.2
P-value	0.094			

Chi-square test

Table (4): Type of eczema versus clinical outcome

Type of eczema	Clinical outcome			
	Moderate		Marked to complete cure	
	No.	%	No.	%
Chronic	0	0.0	7	100.0
Contact	1	25.0	3	75.0
Seborrhic	4	100.0	0	0.0
Total	5	33.3	10	66.7

Table (5): Distribution of microorganisms among different lesions.

Organism	Group I 30 cases	Group II 15 cases	Group III 10 cases	Group IV 15 cases	P value
MSSA	5	2	2	3	P=0.476
MRSA	12	6	4	3	P<0.04
MSCNS	3	2	2	4	P<0.02
MRCNS	3	2	1	2	P=0.584
Strept species	1	1	0	1	P=0.727
Coryne species	1	0	0	1	P=0.647
Proteus	3	1	1	0	P=0.538
Mixed Infections	2	1	0	1	P=0.657
Total	30	15	10	15	P=0.583

MSSA: Methicillin Sensitive Staph Aureus. MRSA: Methicillin Resistant Staph Aureus.
MSCNS: Methicillin Sensitive Coagulase Negative Staph. MRCNS: Methicillin Resistant Coagulase Negative Staph.

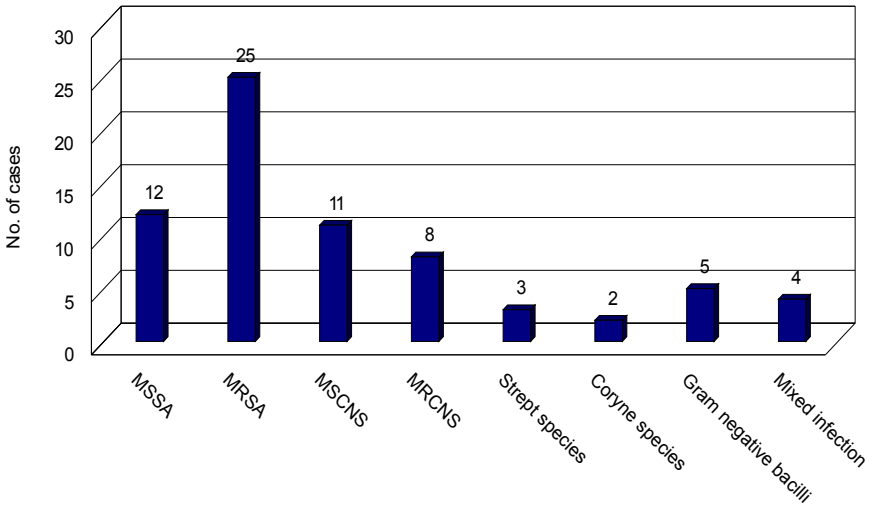


Figure (2): shows the frequency of different isolates in our study.

Table (6) MIC of Mupirocin for different isolates

Organism	MIC for Mupirocin ug/mL
MSSA	2.1 ug/mL
MRSA	4 ug/mL
MSCNS	2.9 ug/mL
MRCNS	3.8 ug/mL
Strept species	2.7 ug/mL
Coryne species	5.1 ug/mL
Gram negative bacilli (Proteus species)	1.9 ug/mL

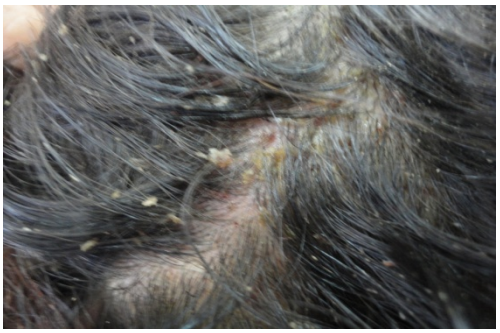


Figure 3: Female child 8 years old with multiple yellowish crusts of scalp impetigo before treatment

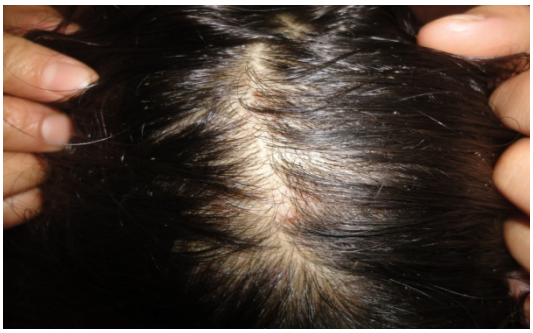


Figure 4: The same child with complete improvement after treatment for 6 days with mupirocin 2% cream (probactcin) alone

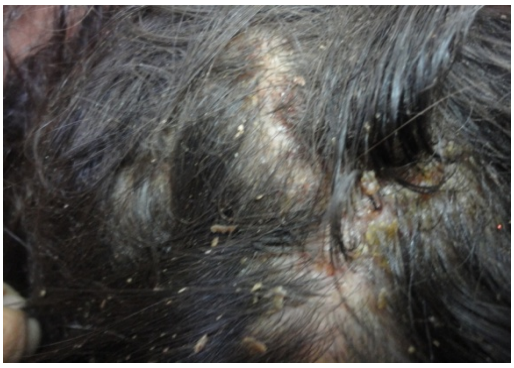


Figure 5: Female child 8 years old with yellowish crusts of scalp impetigo before treatment

Figure 6: The same child with complete improvement after treatment for 6 days with mupirocin 2% cream (probactcin) alone

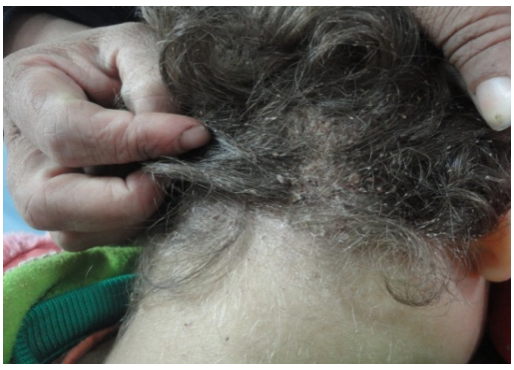


Figure 7: A female child 10 years old with yellowish crusts of scalp impetigo before treatment

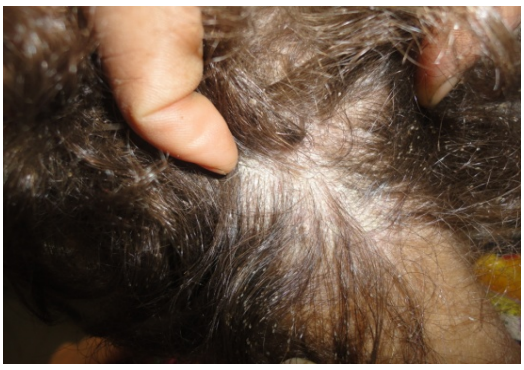


Figure 8: The same patient with complete improvement after treatment for 7 days with mupirocin 2% cream (probactcin) alone

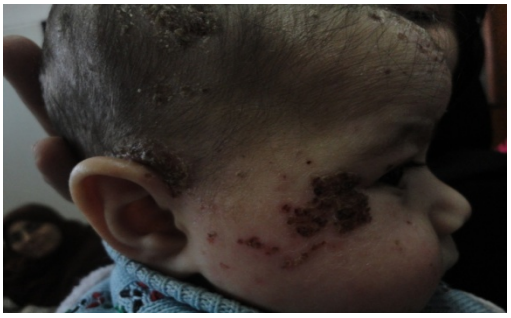


Figure 9: A female baby 6 months old with purulent crusts of ordinary impetigo before treatment

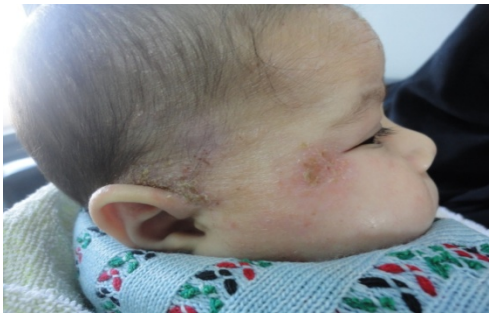


Figure 10:The same baby with marked improvement after treatment for 5 days with mupirocin 2% cream (probactcin) alone

Figure 11: A female child 6 months old with multiple crusts of scalp impetigo before treatment

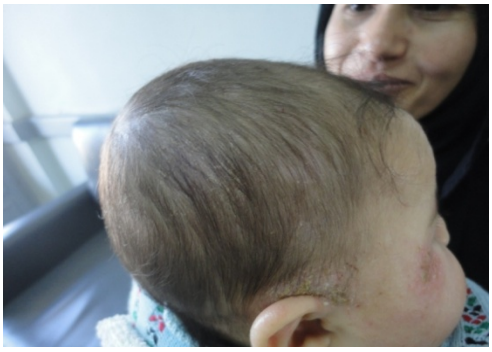


Figure 12:The same baby with complete improvement after treatment for 5 days with mupirocin 2% cream (probactcin) alone

Figure 13:The same baby with complete improvement after treatment for 5 days with mupirocin 2% cream (probactcin) alone

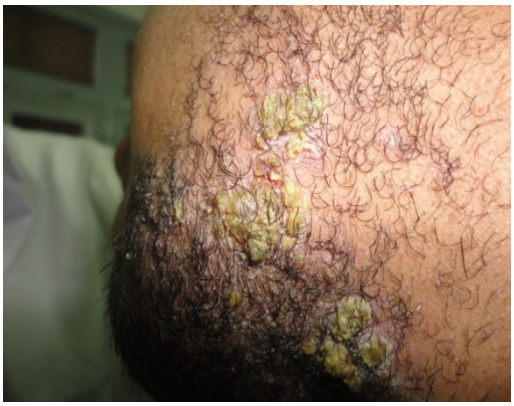


Figure 14: A male 19 years old with marked folliculitis of chin before treatment

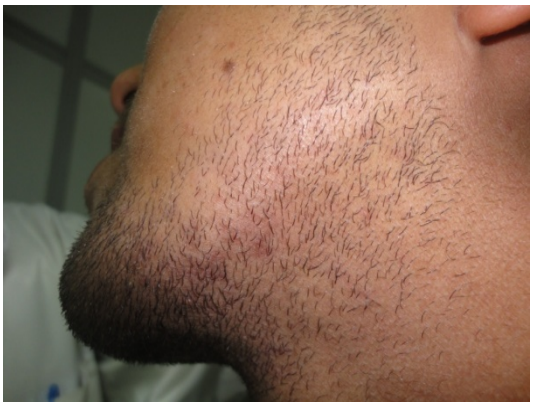


Figure 15: The same patient with complete improvement after treatment for 10 days with mupirocin 2% cream (probactcin) alone

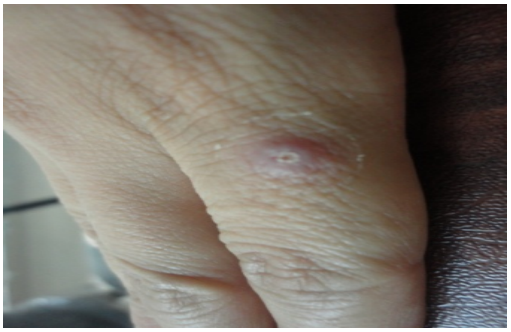


Figure 16:A female 29 years old with Boil of her index finger before treatment

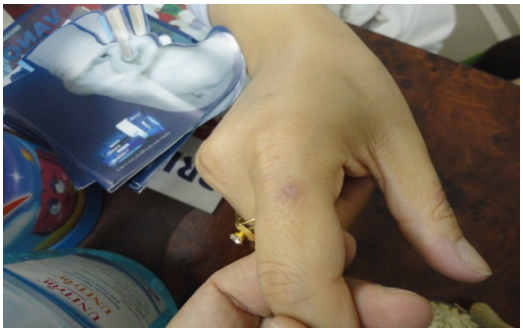


Figure 17:The same patient with marked improvement after treatment for 10 days with mupirocin 2% cream (probactcin) alone

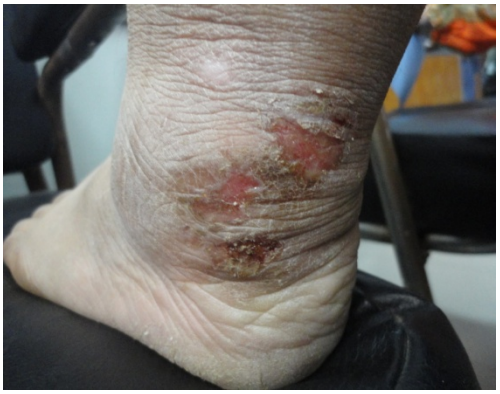


Figure 18:A female 48 years old with marked secondary bacterial infection of eczema of her Lt. leg before treatment

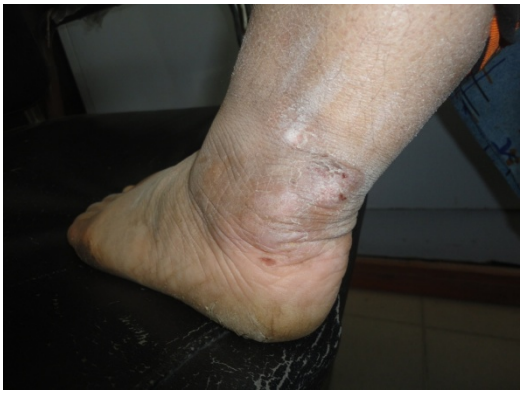


Figure 19:The same patient with marked improvement after treatment for 7 days with mupirocin 2% cream (probactcin) alone

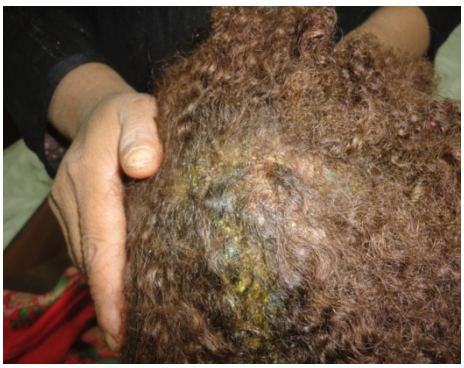


Figure 20: A female child 6 years old with marked purulent crusts of scalp impetigo before treatment

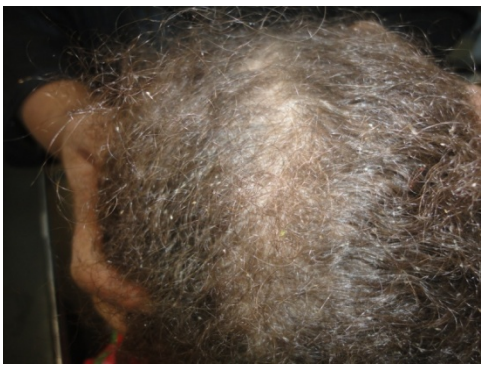


Figure 21:The same patient with complete improvement after treatment for 7 days with probactcin mupirocin 2% cream (probactcin) alone

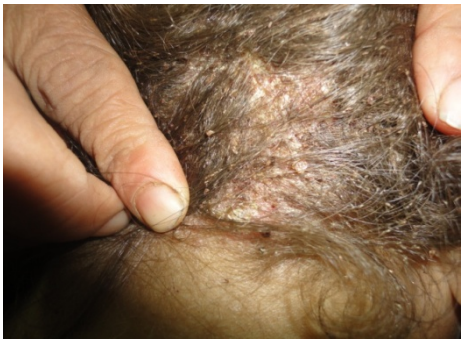


Figure 22: A female child 6 years old with marked purulent crusts of scalp impetigo before treatment

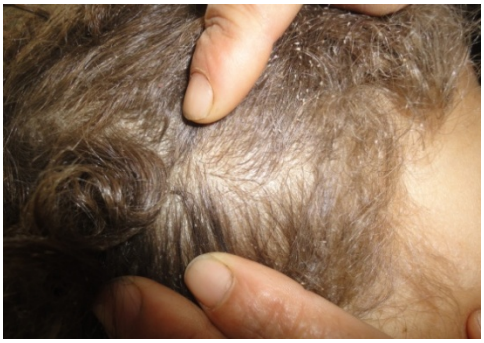


Figure 23:The same patient with complete improvement after treatment for 6 days with mupirocin 2% cream (probactcin) alone

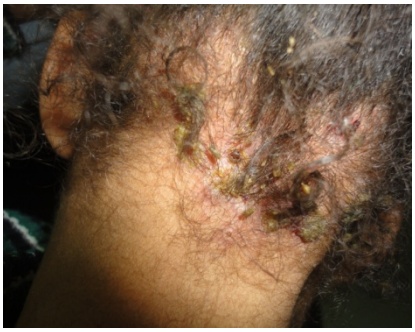


Figure 24: A female child 7 years old with purulent crusts of scalp impetigo before treatment

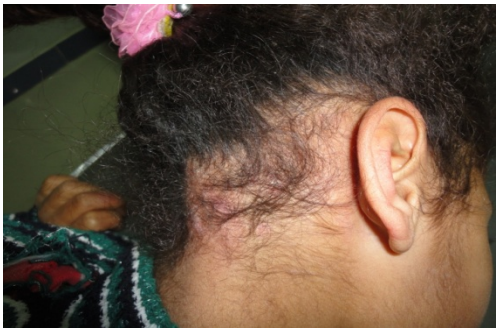


Figure 25:The same patient with complete improvement after treatment for 7 days with mupirocin 2% cream (probactcin) alone

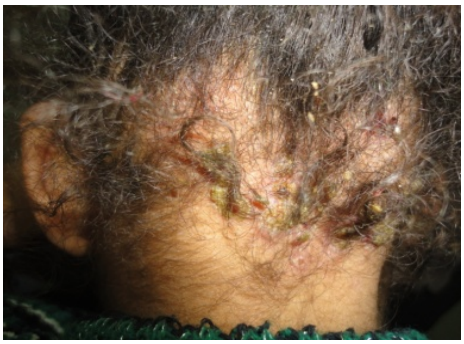


Figure 26: A female child 7 years old with purulent crusts of scalp impetigo before treatment

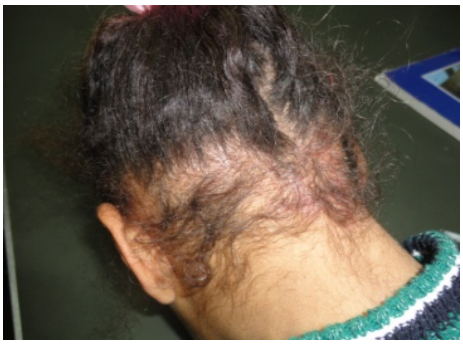


Figure 27:The same patient with complete improvement after treatment for 7 days with mupirocin 2% cream (probactcin) alone

Figure 28: A female child 7 years old with marked purulent crusts of scalp impetigo before treatment

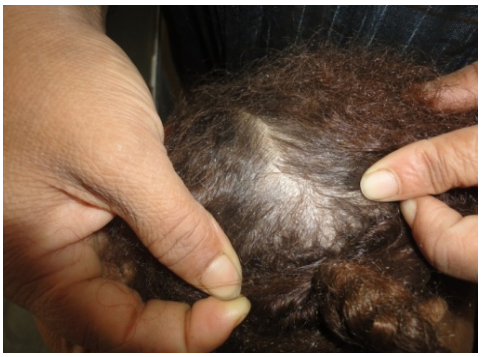


Figure 29: The same patient with complete improvement after treatment for 7 days with mupirocin 2% cream (probactcin) alone

Figure 30: A female child 7 years old with marked purulent crusts of scalp impetigo before treatment

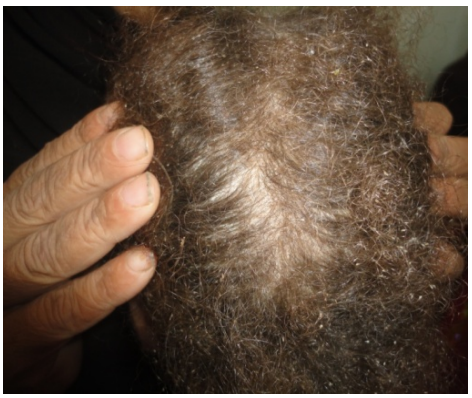


Figure 31:The same patient with complete improvement after treatment for 7 days with mupirocin 2% cream (probactcin) alone

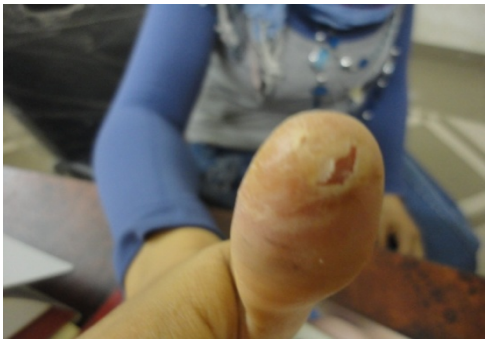


Figure 32: A female 29 years old with marked bacterial infection of tip of her Rt. Thumb (felon) before treatment

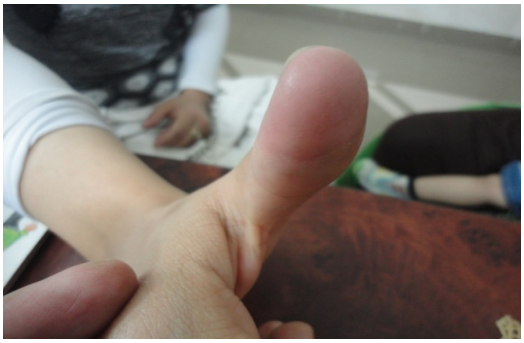


Figure 33: The same patient with marked improvement after treatment for 14 days with mupirocin 2% cream (probactcin) alone

4. Discussion

This is the first study in Upper Egypt to evaluate the clinical and bacteriological efficacy of mupirocin 2% cream in the treatment of different primary and secondary bacterial skin infections. Impetigo is the most common primary skin infection; it's highly contagious and occurs mainly in children. While changes in the etiology of impetigo have been reported, with approximately one half of infections now being caused by *Staph aureus*, Group A streptococci remain important pathogen in over a third of cases of impetigo, and in infections such as boils, folliculitis and eczema with 2^{ry} bacterial infection.[18]

The present prospective study confirmed the efficacy and safety of mupirocin 2% cream in patients presenting with a variety of primary & secondary bacterial skin infection in Upper Egypt. Marked and complete cure were obtained in most patients of the four groups which was concomitant with other studies.[6,13,19,20,21]

Most patients with impetigo were markedly improved in $\leq$7 days which agree with other studies[5,19].

No side effects as irritation, dryness or photosensitivity were reported which were concomitant with other studies.[18,19,20,21]

An important finding of our study was the greater and faster improvement of all evaluated clinical parameters with mupirocin® 2% cream in the four groups. It was noticed that Mupirocin has very effective role, with statistical significant difference in the site of lesion, severity of lesion and duration of treatment between all groups. This is concomitant with other studies[13,21] that demonstrated similar effective role for Mupirocin in their study.

In our study; Staph species were the dominant isolate in different patient groups, with high percent in group I and II and significant difference in MRSA and MSCNS distribution. This is concomitant with different studies[9, 22] that demonstrates that Staph species is the dominant isolate in such lesions. MRSA was the most dominant isolate, but all of them cured completely and were all sensitive to Mupirocin. This is concomitant with similar studies [3] that demonstrates similar results.

In our study, all isolates were sensitive to Mupirocin, no single isolate was resistant. This is in contrast of some studies[10] that detected some resistant strains of *Staph aureus* to Mupirocin. Although other studies found similar results[8].

Measuring the MIC of Mupirocin for different bacterial isolates; we found that Coryne species required higher MIC than MRSA than MRCNS than MSCNS than *Strept pyogens* than MSSA. This is concomitant with other studies[8, 23] that found similar figures for MIC of Mupirocin against different bacterial isolates.

Limitations of the study:

Our study was a prospective, non placebo controlled clinical trial that did not contain a formal control arm, although one could argue that each patient served as their own control. Our follow-up period was short and patients were assessed immediately after the cessation of their treatment. We therefore are unable to comment on the longevity of clinical improvement.

Conclusion:

This study demonstrates that mupirocin® 2% cream was an effective and safe topical antibiotic in the management of primary and secondary bacterial skin infection in Upper Egypt.

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