REVIEW ARTICLE

Management of Impetigo in Adults

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Impetigo : An overview

Impetigo is one of the common cutaneous infection of the epidermal layer which is highly communicable and escalate very easily. It is clinically characterized by lesions on the face, arms or legs of the patient that present as erythematous plaques with a yellow crust and may be itchy or painful.[1,2] This disease is known to affect more than 162 million people worldwide.[3] This contagious condition is common amongst the children of two to five years of age. However, persons of any age can be affected by it.[2,4] The risk factors which can accelerate the chances of impetigo are young age, crowding, close contact, and warm humid conditions.[4]

Etiology of Impetigo

Impetigo is caused generally by Gram positive bacteria like the *Staphylococcus aureus* and sometimes by *Streptococcus pyogenes* (group A beta-hemolytic streptococcus) or by both.[1,2]

Classification of impetigo

Impetigo is classified into the following:

- **Primary impetigo:** Direct bacterial invasion over normal skin[1]
- **Secondary impetigo:** Previous skin wound site is affected by infection[1]

Clinical presentation of impetigo

Impetigo is clinically represented into two forms as bullous and non- bullous impetigo or impetigo contagiosa.[4,5] Bullous impetigo represents 30% of cases which is caused by *S. aureus*. Whereas, non- bullous impetigo accounts for 70% of cases which is caused both by *Staphylococcus aureus* and *Streptococcus pyogenes*.[4] These two types of impetigo differ in term of clinical features which is well elaborated in Table 1.

Diagnosis of impetigo

For the diagnosis of impetigo, history and physical examination are essential. During impetigo outbreak or if methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected, bacterial cultures can be used for confirmation of diagnosis.[1]

Bullous impetigo

Non-bullous impetigo

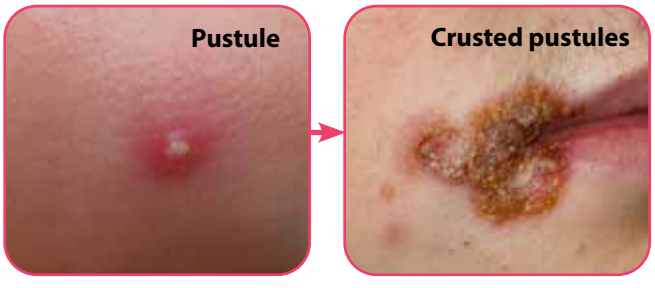
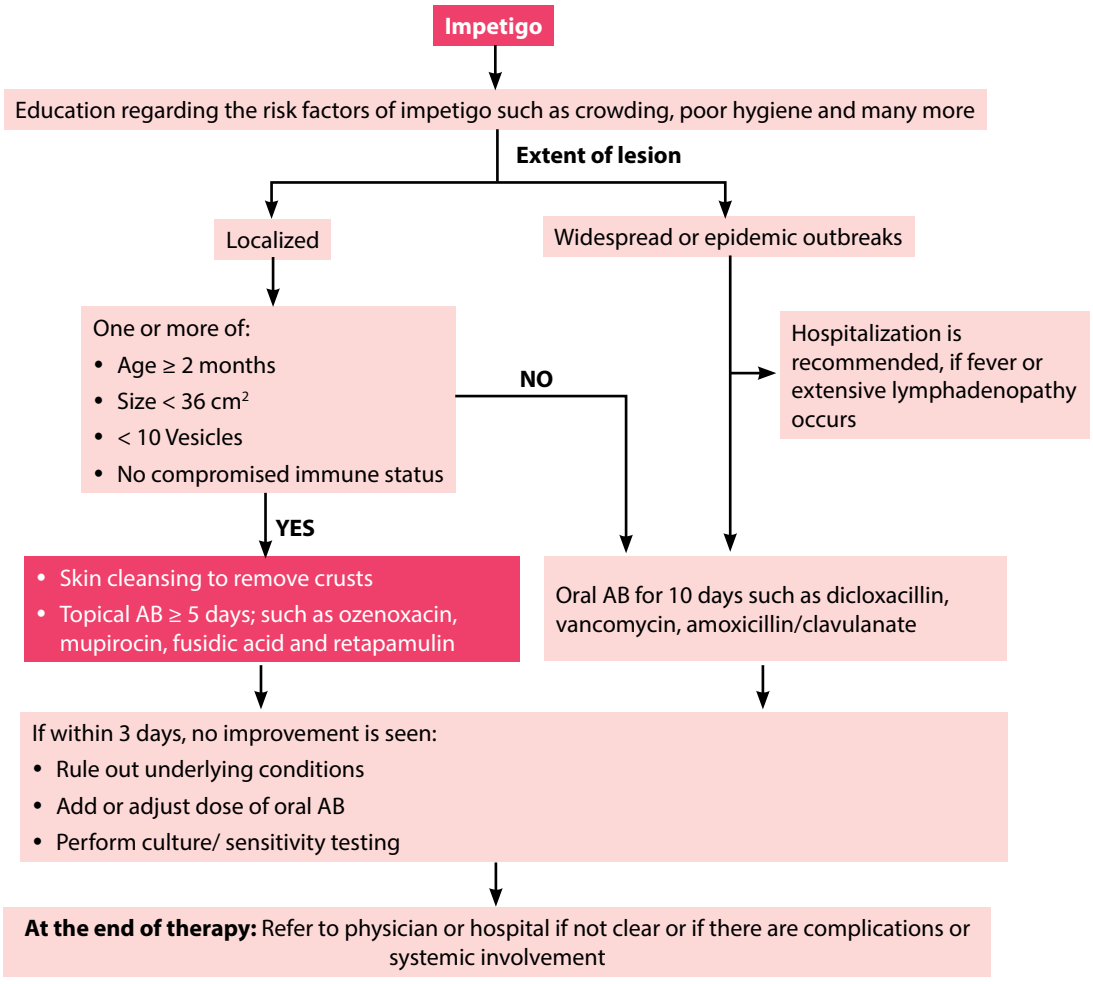


Table 1: Cardinal features of bullous and non-bullous impetigo				
Type	**Population affected**	**Areas affected**	**Frequency of lesions**	**Clinical features**
1. Bullous impetigo	It is common in children aged two to five years[5]	• Intertriginous regions such as axillae and neck • Trunk • Buccal membranes[1,5]	Few lesions[1]	• Initiates with small vesicles that become flaccid bullae[1,4,5] • Large, fragile, flaccid bullae that can rupture and ooze yellow fluid[4] • Fever[1] • Ecthyma which is a deep ulcerated infection may occur, which is a complication of bullous impetigo[1]
2. Non- bullous impetigo	Adults and children but rarely in those under two years of age[5]	• Face • Extremities[1]	Multiple lesions[1]	• Initiates as a pustule or a vesicle • Characteristic honey-colored crust • Erythematous base • Associated finding such as mild regional lymphadenopathy[1,4,5]

Figure 1: Treatment algorithm for impetigo[7]



Abbreviation: AB, antibiotics

Box 1: What makes ozenoxacin the ideal topical antibiotic for bacterial SSTIs[9-16]

- Impermeable to efflux pumps that confer resistance to other quinolones in bacteria, possibly due to their high concentration within the bacterial cell.
- Low selection rate for resistant mutants
- Exhibits an antimutagenic concentration lower than the skin concentration of the drug
- Ozenoxacin has shown the lowest minimum inhibitory concentrations (MIC_{90}) (mg/L) for methicillin-sensitive *S. aureus* (MSSA)[0.004 mg/L], methicillin-resistant *S. aureus* (MRSA)[0.12%], and *Streptococcus pyogenes* [0.015mg/L]
- It potrays superior antibacterial activity versus existing topical antibiotics such as mupirocin, fusidic acid and retapamulin
- The dosage regimen of ozenoxacin in patients with impetigo is twice daily for 5 days. Whereas, mupirocin has to be given 3 times a day for 10 days and fusidic acid has to be given 3-4 times a day for 14 days
- Ozenoxacin appears to be superior in therapeutic efficacy to mupirocin and fusidic acid when placebo based trials of individual topical antibiotics are compared
- In Individual placebo based trials, the reported efficacy of ozenoxacin was 92%, mupirocin was 71% and fusidic acid was 55%
- Ozenoxacin may have low rates of anti-bacterial resistance as it is not affected by the bacterial efflux pump which is the main cause of bacterial resistance.

Treatment of impetigo

Impetigo is treated for reasons such as preventing the spread of infection, hastening resolution of symptoms, and improving appearance.[7] The factors on which the treatment depends include extent and site of lesions and presence of systemic symptoms.[8] The treatment of impetigo is illustrated in Figure 1. However, in order to choose the appropriate treatment for impetigo, it is essential to consider local trends in antibiotic resistance in case of other topical antibiotics.[7] Hence, ozenoxacin cream 1% is known to highly effective against *S. pyogenes* and *S. aureus*, including MRSA, and may be a satisfactory option for localized impetigo.[7]

Ozenoxacin for treatment of impetigo

Ozenoxacin (OZ) is a topical quinolone antibiotic approved for the treatment of bullous or non-bullous impetigo in adults and children over 2 months of age.[9] Ozenoxacin appears to be impermeable to efflux pumps that confer resistance to other quinolones in bacteria, possibly due to their high concentration within the bacterial cell. It has a low selection rate for resistant mutants and exhibits an antimutagenic concentration lower than the skin concentration of the drug. Ozenoxacin is the ideal topical antibiotic for bacterial SSTIs including impetigo (Box 1).[9-16] Ozenoxacin exhibits antimicrobial activity against Gram-positive bacteria, especially *S. aureus*, including MRSA, or *S. pyogenes*. It also portrays clinical efficacy against mupirocin-resistant *S. aureus* (MRSA), fusidic acid resistant *S. aureus*, quinolone-resistant *S. aureus* and clindamiycin-resistant *S. aureus*.[7]

Clinical evidences:

1. Effectiveness and safety of ozenoxacin in management of impetigo

Rosen et al. conducted a clinical trial[10] amongst 411 patients with impetigo to examine the efficacy, safety, and tolerability of ozenoxacin cream, 1%, after 5-day twice-daily topical treatment. In this study, patients were randomized 1:1 to receive ozenoxacin and placebo control. The results revealed that ozenoxacin showed superior clinical success after 5 days of treatment in comparison to placebo (54.4% vs. 37.9%; Figure 2). Moreover, ozenoxacin exhibited superior microbiological success compared with placebo after 2 days of therapy (87.2% vs. 63.9%; p=0.002). In terms of safety, there were no ozenoxacin associated adverse effects. Conclusively, ozenoxacin is a safe and well tolerated option for treatment of impetigo amongst patients of 2 months and older.

Figure 2: Clinical success of ozenoxacin and placebo group after 5 days of treatment amongst patients with impetigo

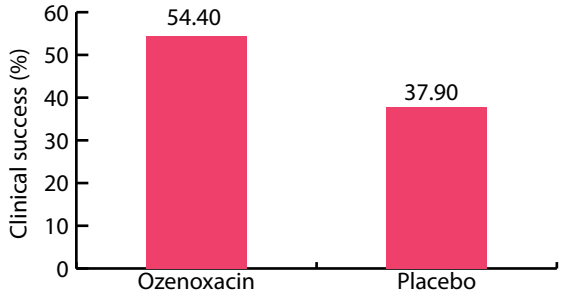


Figure 3: Proportion of patients with impetigo terminating their treatment in mupirocin, fusidic acid and ozenoxacin group after 2 weeks of treatment

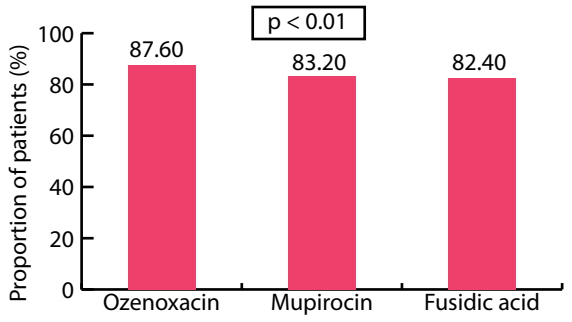
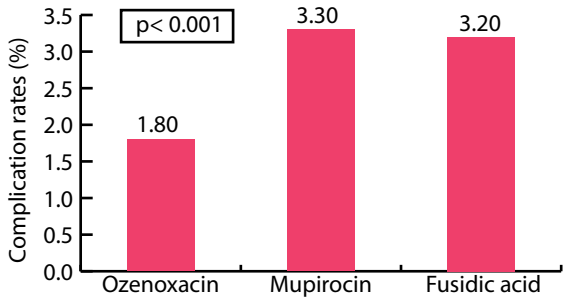


Figure 4: Rate of complications among patients with impetigo in mupirocin, fusidic acid and ozenoxacin group



2. Ozenoxacin is a clinically effective alternative for impetigo

A study[2] was conducted to evaluate the clinical consequences of the use of OZ vs. mupirocin (MUP) and vs. fusidic acid (FA) for the treatment of impetigo. In this study, treatment duration, comorbidities, use of systemic medication, complications and utilization of resources across treatments were compared. The effectiveness measures were complication rates and treatment duration. The results of the study showed that the proportion of patients ending treatment after 2 weeks was 87.6% (OZ) vs. 83.2% (MUP) vs. 82.4% (FA) (Figure 3); and the complication rates were 1.8% (OZ), 3.3% (MUP) and 3.2% (FA), p<0.001 (Figure 4). It was concluded that ozenoxacin is a dominant treatment of impetigo.

Conclusion

Impetigo is clinically characterized by lesions on the face, arms or legs of the patient that present as erythematous plaques with a yellow crust and may be itchy or painful. It is caused generally by Gram positive bacteria like the *Staphylococcus aureus* and sometimes by *Streptococcus pyogenes*. The factors on which the treatment of impetigo depends include extent and site of lesions and presence of systemic symptoms. In order to choose the appropriate treatment for impetigo, it is essential to consider local trends in antibiotic resistance in case of other topical antibiotics. Ozenoxacin can be considered as a front-line topical antibiotic for treatment of impetigo in adults as it is highly effective against *S. pyogenes* and *S. aureus*, including MRSA, and may be a satisfactory option for localized impetigo.

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