Impetigo – review*

Luciana Baptista Pereira[1]

DOI: http://dx.doi.org/10.1590/abd1806-4841.20142283

Abstract: Impetigo is a common cutaneous infection that is especially prevalent in children. Historically, impetigo is caused by either group A β-hemolytic *streptococci* or *Staphylococcus aureus*. Currently, the most frequently isolated pathogen is *S. aureus*. This article discusses the microbiologic and virulence factors of group A β-hemolytic streptococci and *Staphylococcus aureus*, clinical characteristics, complications, as well as the approach to diagnosis and management of impetigo. Topical agents for impetigo therapy are reviewed.
Keywords: Anti-Bacterial agents; Impetigo; *Staphylococcus aureus*; *Streptococcus pyogenes*

INTRODUCTION

Normal skin is colonized by large numbers of bacteria that live as commensals in its surface or in hair follicles. Sometimes, the overgrowth of these bacteria causes skin diseases, and in other occasions, bacteria that are normally found on the skin can colonize it and cause diseases.[1] Skin microflora consists mainly of aerobic diphtheroids (*Corynebacterium spp*.), anaerobic diphtheroids (*Propionibacterium acnes*) and coagulase negative staphylococci (*Staphylococcus epidermidis*). Recent genetic studies have shown a large quantity of *Pseudomonas spp*. and *Janthinobacterium spp*. in disease-free skin.[2] These bacteria form biofilms on the cutaneous surface. Biofilms are complex and sessile aggregates comprising one or more bacterial species associated with an extracellular polymeric substance. Bacteria in biofilms are 50 to 500 times more resistant to antibiotics than bacteria in plankton (organisms that have little or no ability to move). Besides inducing antibiotic tolerance, biofilms can increase bacterial virulence.[2] Newborns are usually aseptic and colonization starts in the first two weeks of life.[1]

Host factors, such as integrity of the skin barrier with its acidic pH, presence of sebaceous secretion (fatty acids, particularly oleic acid), lysozyme and production of defensins and adequate nutritional status, play an important role in resistance to infection.[1,3] The presence of maceration, humidity, previous skin lesions, obesity, corticosteroid or chemotherapy treatments, dysglobulinemias, leukocyte disorders such as leukemia and chronic granulomatous disease, diabetes, malnutrition, other congenital or acquired immunodeficiencies, such as AIDS, are predisposing factors.[4] Most bacteria grow best in a neutral pH and a temperature of 37^0C.[3]

The act of handwashing, with antiseptic soap or even regular soap, especially amongst children caretakers, severely decreased their chance of acquiring infections such as pneumonia, diarrhea and impetigo. In a controlled study, the authors observed a 34% lower incidence of impetigo in the group that underwent an orientation program on the act of handwashing.[5]

STREPTOCOCCI'S CHARACTERISTICS

Lancefield classification of streptococci is based on the cell wall's C carbohydrate antigens, going from A to T. Various streptococci may be commensals on the skin, mucous membranes, and gastrointestinal tract. The isolation of streptococci of groups other than A can mean a secondary infection of preexisting lesions or colonization on cutaneous surface. Group A strepto-

Received on 15.11.2012.
Approved by the Advisory Board and accepted for publication on 08.04.2013.
* Work performed at the Dermatology Service at Minas Gerais Federal University Clinics Hospital (HC-UFMG) – Belo Horizonte (MG), Brazil.

Conflict of interest: None
Financial Support: None

[1] Minas Gerais Federal University (UFMG) – Belo Horizonte (MG), Brazil.

cocci can be subdivided into several serotypes, according to their M protein antigenicity. Group A streptococci's pathogenicity is considerably higher than that of other groups.These are germs with invasive potential, which can reach several tissular planes, such as the epidermis (impetigo), dermis (ecthyma) or deeper subcutaneous tissue (cellulite).[6,7] They can cause localized edema, localized lymphadenopathy and fever. The discovery of these agents in the skin of healthy children precedes the appearance of lesions in about 10 days and they can be isolated from the oropharynx between 14 and 20 days after appearing on the skin. Thus, their path goes from normal skin to injured skin and may subsequently reach the oropharynx.

Several decades of epidemiological studies indicate that there are some strains of group A streptococci that elicit oropharyngeal infections, but rarely cause impetigo. On the other hand, there is a distinct group of strains that cause cutaneous infection but that do not affect the throat.[6] Knowingly, a variety of complications can accompany infections caused by group A streptococci, such as rheumatic fever, acute diffuse glomerulonephritis, and erythema nodosum, depending on the strain involved. Rheumatic fever can be a complication of streptococcal pharyngitis or tonsillitis, but it does not occur after skin infections. Rather, glomerulonephritis may result from streptococcal cutaneous or upper respiratory tract infections, but the skin is the main previous site. Treatment of impetigo does not reduce the risk of glomerulonephritis, but it reduces the dissemination of nephritogenic strains in the population.[4,8] The latency period for glomerulonephritis is 7 to 21 days after upper respiratory tract infection and may be longer in the case of impetigo. Beta-hemolytic streptococcus group A is not commonly observed before two years of age, but there is a progressive increase in older children. Glomerulonephritis affects up to 5% of patients with impetigo.[1,4,8]

Streptococci can be retrieved by culture of oropharynx or skin lesion materials. Dosage of antistreptolysin O may not be useful for cutaneous infections since its titles do not increase satisfactorily.[1] The rapid detection test for streptococcus through latex is only used to demonstrate the presence of this agent in the oropharynx. For skin diseases, serological anti-DNA-ase B test, useful to demonstrate a previous streptococcal infection (group A streptococcus), can be performed.[1] However, besides being a high sensitivity and low specificity test, there are few laboratories that have it standardized in their routine.

STAPHYLOCOCCI'S CHARACTERISTICS

A crucial factor to the infection virulence is the ability of these bacteria to produce circulating toxins that act as superantigens.[9] Superantigens are able to skip certain steps of the immune response and promote massive activation of T lymphocytes and also the production of various lymphokines such as interleukin 1 and 6 and tumor necrosis factor alpha. This response may lead to the formation of exfoliative cutaneous eruption, vomiting, hypotension and shock. Bullous impetigo and scalded skin syndrome, caused by staphylococcal toxins and toxic shock syndrome, caused by staphylococcal or streptococcal toxins are examples of toxin-mediated diseases.

Coagulase negative staphylococci are the most common organisms on the normal skin flora, with about 18 different species, and *Staphylococcus epidermidis* being the most common of the resident staphylococci.[1] *S. aureus* (coagulase positive) is often found in the skin, in a transient manner, in healthy children. Carriage status may occur in the nares in 35% of the population, in the perineum in 20%, in the axillae and interdigital regions in 5 to 10%.[10] The condition of staphylococcal nasal carriage was found in up to 62% of patients with impetigo.[11] In patients with atopic dermatitis, it can be found in up to 90% of cases (dry skin and hyperkeratinization would be facilitating adherence factors for staphylococci).[1] Especially in carriers, skin lesions can be explained by self-inoculation secondary to skin excoriation by the patient. The path would be from the nares or perineum to normal skin, and later to injured skin. Host factors seem to determine the onset of disease. Immunosuppression and tissue damage are considered important in the pathological process genesis, since the ability to produce coagulase, leukocidin and toxin appears to be the same in the carrier's normal flora and in bacteria isolated from cutaneous lesions.

Staphylococci are transmitted primarily by hand, particularly in hospital settings. Staphylococcal infections are present in all age groups.

IMPETIGO

BULLOUS IMPETIGO

Bullous impetigo is almost universally caused by a single organism, *S. aureus*, mainly belonging to group II (80%); phage type 71 (60% of cases). Other phage types involved are 3A, 3C and 55.[3,12] There are descriptions, in the literature, of bullous impetigo caused by group A streptococcus.

S. aureus produces exfoliative toxins, which are proteases that selectively hydrolyze one of the intracellular adhesion molecules, desmoglein-1, present in the desmosomes of keratinocytes located in the epidermic granular layer. Toxins are the greatest virulence factor of *S. aureus*, causing dissociation of epidermal cells with blister formation. Blisters are localized in bullous impetigo and disseminated in scalded

skin syndrome. There are at least two different types of exfoliative toxins, so that exfoliative toxin A relates to bullous impetigo and toxin B with scalded skin syndrome. Scalded skin syndrome usually begins after a localized infection on the conjunctiva, nose, navel or perioral region and more rarely after pneumonia, endocarditis and arthritis. Strains of *S. aureus* producing exfoliative toxins are often isolated from patients with impetigo.[13-15]

Bullous impetigo starts with smaller vesicles, which become flaccid blisters, measuring up to 2 cm in diameter, initially with clear content that later becomes purulent (Figure 1). The roof of the blister ruptures easily, revealing an erythematous, shiny and wet basis. The remainder of the roof can be seen as a collarette at the periphery and the confluence of lesions promotes the appearance of polycyclic figures (Figures 2 and 3). Bullous impetigo occurs most commonly in intertriginous regions such as the diaper area, axillae and neck, although any cutaneous area can be affected, including palms and soles (Figures 1 and 2).[1,13] Regional enlarged lymph nodes are usually absent. It is particularly important in the neonatal period, starting usually after the second week of life, although it can be present at birth in case of premature membranes rupture. Bullous impetigo is most common among children aged two to five years.[13,15-17]

NON-BULLOUS IMPETIGO (CRUSTED)

Non-bullous impetigo represents more than 70% of all cases of impetigo. It occurs in adults and children but rarely in those under two years of age. The main etiological agent has varied over time. *S. aureus* was the predominant agent in the 40s and 50s, with a later increase in the prevalence of streptococcus. In studies conducted over the past three decades, there has been a resurgence of *S. aureus* as the main agent of crusted impetigo.[16-24] *S. aureus*, alone or in combination with group A beta hemolytic streptococci, is responsible for about 80% of the cases, being the most frequently recovered isolated agent. Although we have not found any Brazilian studies conducted in recent decades regarding the epidemiology of impetigo, these data are corroborated in studies conducted in different countries, such as United States, Israel, Thailand, Guyana, India, Chile, and Japan.[16-20,22-25] Some researchers believe in the likelihood that

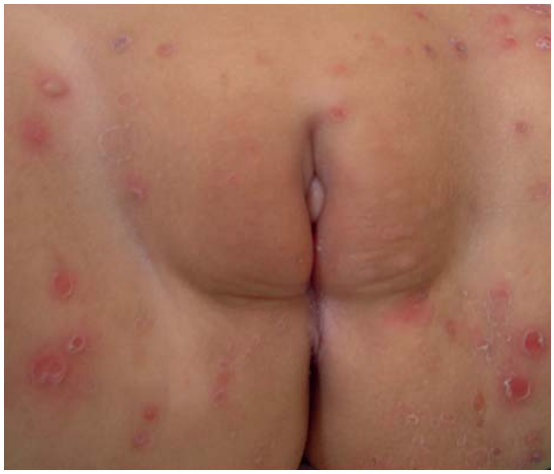

Figure 1: Bullous impetigo in the genital area - intact and flaccid pustules, exulcerations and scaling in collarette

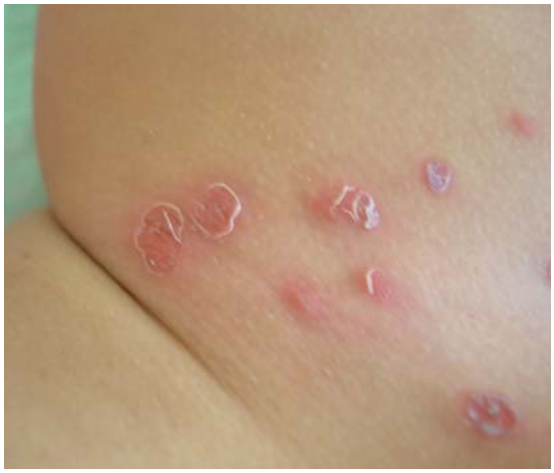

Figure 2: Bullous impetigo –desquamation collarette and flaccid blisters

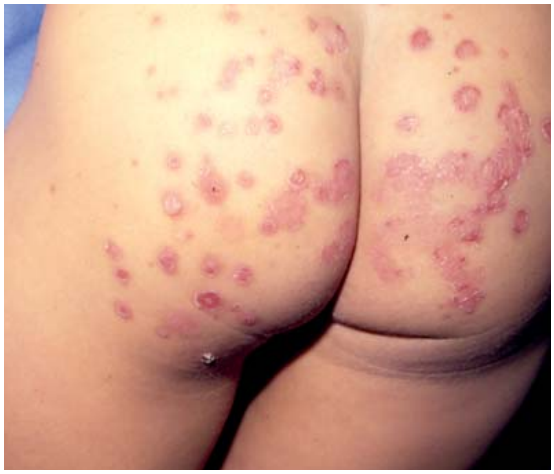

Figure 3: Bullous impetigo in diaper area

*S.aureus*is a secondary invader and not a primary causative agent.

Crusted impetigo can occur in normal skin or impetiginisation may appear over a previous dermatosis such as atopic dermatitis, contact dermatitis, insect bites, pediculosis and scabies. Malnutrition and poor hygiene are predisposing factors. The initial lesion is a vesicle, located on an erythematous base, which iseasily ruptured. The resulting superficial ulceration is covered with purulent discharge that dries as an adhering and yellowish (honey-colored) crust. Each lesion measures 1 to 2 cm in diameter and grows centrifugally (Figure 4). The discovery of satellite lesions, caused by self-inoculation, is frequent. There is a predominance of lesions in exposed areas, especially in the limbs and face (Figures 5 and 6). Regional lymphadenopathy is common and fever can occur in severe cases.[3,26] Non-bullous impetigo may resolve spontaneously without any treatment in 2-3 weeks.[13]

TREATMENT

EVOLUTION OF BACTERIAL RESISTANCE

S. aureus readily acquires antimicrobial resistance, making its treatment difficult.[27,28] For over 60 years, virtually all strains of *S.aureus* are able to produce beta-lactamase (penicillinase), becoming resistant to beta-lactamase sensitive antibiotics. These enzymes hydrolyze the beta lactam ring, and they are, so far, the main mechanism of resistance to betalactam antibiotics.[13]

Methicillin-resistant *Staphylococcus aureus* (MRSA) was first detected in 1961. Cases of infections caused by MRSA in the community were reported in the 80's, but the importance of this group has increased significantly in recent years.[27] MRSA infections are no longer confined to hospital settings, but rates of community-associated MRSA (CA-MRSA) vary widely among studies.[28,29]

The presence of MRSA as impetigo's causative agent in non-hospitalized patients is considered unusual and with heterogeneous distribution. Staphylococcal impetigo is usually caused by *S. aureus* strains that possess the exfoliative toxin gene. On the

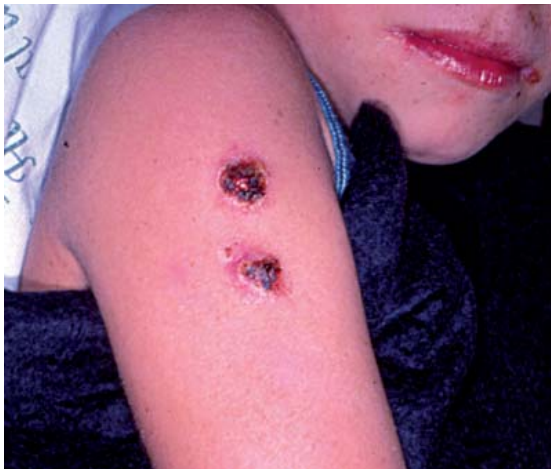

Figure 5: Crusted impetigo located on the arm

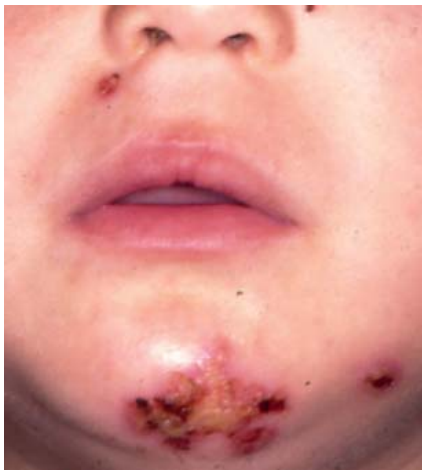

Figure 4: Crusted impetigo–vesicles, honey-colored and hematic crusts

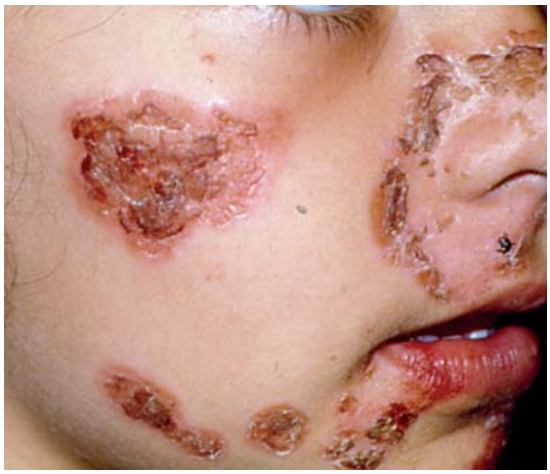

Figure 6: Crusted impetigo(non-bullous) on the face

other hand, community MRSA clones (CA-MRSA) do not have the exfoliative toxin gene, but the Panton-Valentine-Leucodin (PVL) gene. Staphylococci that possess PVL gene cause suppurative cutaneous infections such as abscesses and furuncles. Therefore, concern about MRSA in community-acquired infections, should be greater in the presence of furuncles and abscesses and smaller in impetigo.[30]

GENERAL CARE OF PATIENTS WITH IMPETIGO

In patients with impetigo, lesions should be kept clean, washed with soap and warm water and secretions and crusts should be removed. Common soaps or those containing antiseptic substances such as triclosan, chlorhexidine and povidone iodine, may be used. In the impetigo treatment review performed by the Cochrane Database of Systematic Reviews, the authors report a relative lack of data on the efficacy of topical antiseptics. On the other hand their use is not discouraged, because they do not seem to increase bacterial resistance.[31]

INDICATIONS FOR TREATMENT WITH SYSTEMIC ANTIBIOTICS

Topical antibiotics are the treatment of choice for most cases of impetigo.[8,17] Systemic antimicrobial agents are indicated when there is involvement of deeper structures (subcutaneous tissue, muscle fascia), fever, lymphadenopathy, pharyngitis, infections near the oral cavity, infections on the scalp and / or numerous lesions (more than five) (Figure 6).

SYSTEMIC ANTIBIOTIC THERAPY

The spectrum of the selected antibiotic must cover staphylococci and streptococci, both for bullous impetigo as well as for crusted impetigo. Thus, benzathine penicillin or those sensitive to penicillinases are not indicated in the treatment of impetigo.[31,32] Penicillins that are resistant to penicillinase (oxacillin, cloxacillin, dicloxacillin) can be used, but the difficulty lies in the absence of a specific formulation for oral use in Brazil. The first-generation cephalosporins, such as cephalexin and cefadroxil, may be used, since no differences between them was found in a meta-analysis.[31]

Erythromycin, being less expensive, can become the antibiotic of choice for the most impoverished populations. One should take into account the possibility of resistance to *S. aureus*, which occurs in varying rates, depending on the population studied.

Other macrolides such as clarithromycin, roxithromycin and azithromycin have the advantage of presenting fewer side effects in the gastrointestinal tract, as well as a more comfortable posology, although with a higher cost. Staphylococcal strains that are resistant to erythromycin will also be resistant to clarithromycin, roxithromycin and azithromycin.

The amoxicillin associated with clavulanic acid is the combination of one penicillin with a beta-lactamase inhibiting agent (clavulanic acid), thus enabling adequate coverage for streptococci and staphylococci.

Clindamycin, sulfamethoxazole / trimethoprim, minocycline, tetracycline and fluoroquinolones are the antibiotics of choice for MRSA.

TOPICAL TREATMENT

There is strong evidence on the superiority, or at least the equivalence, of topical antibiotics compared to oral antibiotics in the treatment of localized impetigo. In addition, oral antibiotics have more side effects than topical antibiotics.[31,32]

Mupirocin and fusidic acid are the first choice options. In meta-analyses publications, no difference between these two agents was demonstrated. [31,32] To date, there is only one study comparing retapamulin and fusidic acid, showing no statistical differences between the two products.[31] The combination of neomycin and bacitracin does not lead to bacterial eradication.

TOPICAL ANTIBIOTICS – CHARACTERISTICS
FUSIDIC ACID

Fusidic acid is highly effective against *S. aureus*, with good penetration into cutaneous surface and high concentration at the site of infection. It is also effective, to a lesser extent, against *Streptococcus* and *Propionibacterium acnes*. Gram-negative bacilli are resistant to fusidic acid.[33]

Resistance, in vitro and in vivo, to fusidic acid has been verified but at low levels.[33-36] As it belongs to the fusidanes group, it has a very different chemical structure from that of other classes of antibiotics, such as betalactams, aminoglycosides and macrolides, thereby reducing the possibility of cross-resistance.

The incidence of allergic reactions is low and cross-allergy has not been seen. This antibiotic is not marketed in the United States. Unlike in Europe, in Brazil it can only be found as 2% cream, being thus unavailable for oral use.

MUPIROCIN

Mupirocin (pseudomonic acid A) is the major metabolite of *Pseudomonas fluorescens* fermentation.[37] Its chemical structure is not related to antibacterial agents and due to its unique mechanism of action there is no cross-resistance with other antibiotics. Mupirocin acts by inhibiting bacterial protein synthesis, by binding with isoleucyl-tRNA synthetase enzyme, thus preventing the incorporation of isoleucine into protein chains. It is highly effective against *Staphylococcus*

aureus, *Streptococcus pyogenes* and all other species of streptococci except those of group D. It is less effective against Gram-negative bacteria, but exhibits in vitro activity against *Haemophilus influenzae*, *Neisseria gonorrhoeae*, *Pasteurella multocida*, *Bordetella pertussis*, and *Moraxella catarrhalis*. It is not active against bacteria of the normal cutaneous flora and therefore does not alter the skin's natural defense. Mupirocin's bactericidal activity is increased by the acidic pH on the skin. It can eradicate *S. aureus* on the skin.

Bacterial resistance rate is low, around 0.3% for *S. aureus* strains. MRSA resistance to mupirocin has already been described.[8]

Adverse reactions are reported in 3% of patients, with itching and irritation at the application site being the most common ones. Photoreactions are unlikely, because the range of ultraviolet light that is absorbed by the product does not penetrate the ozone layer. Systemic absorption is minimal and the little that is absorbed is rapidly converted to inactive metabolite, hence the reason why there are not oral or parenteral formulations available. The use in extensive area or in patients with burns aren't recommended, because of the risk of nephrotoxicity and absorption of the drug's vehicle, polyethylene glycol, especially in patients with renal insufficiency. In the United States there is already a formulation of mupirocin ointment without polyethylene glycol. It is considered safe and effective in patients over two-months old. It is listed in category B for use in pregnant and lactating women.[38]

The product is found in Brazil as 2% cream.

NEOMYCIN AND BACITRACIN ASSOCIATION

Aminoglycosides exert their antibacterial activity by binding to the 30S ribosomal subunit and interfering with protein synthesis. Neomycin sulfate is an antibiotic of the aminoglycoside group most commonly used in topical form. It is the result of *Streptomyces fradiae* fermentation. The commercially available formulation is a mixture of neomycin B and C, while framycetin, used in Canada and several European countries, is composed of pure neomycin B. Neomycin sulfate is active mainly against aerobic Gram-negative bacteria (*Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Proteus vulgaris*). Most species of *Pseudomonas aeruginosa* are resistant to it. Its actions against most Gram-positive bacteria are limited. *Streptococcus pneumoniae* and *Streptococcus pyogenes* are highly resistant to neomycin, which is why the drug is usually associated with bacitracin to treat cutaneous infections. Although *S. aureus* is a Gram-positive bacteria inhibited by neomycin, topical use of the drug is not able to eradicate it from the skin, hence its inferiority compared to fusidic acid and mupirocin. The association is not effective against MRSA.[13]

The incidence of contact dermatitis by sensitization is relatively high, occurring in 6-8% of patients who use this medication in the topical form. Sensitized patients may cross-react when exposed to other topical or systemic aminoglycosides.

It is available in Brazil in the form of ointment, alone or in combination with bacitracin. The use of associations with topical corticosteroids and/or antifungal agents is not recommended.

Bacitracin is a topical antibiotic originally derived from the bacterium *Bacillus subtilis* that was first isolated from a patient who had a bone fracture contaminated by soil ("baci", bacillus + "tracina", derived from the patient's name Tracy). It is a polypeptide formed by multiple components (A, B and C). Bacitracin A is the main component of commercial products and is generally formulated as a zinc salt. It works by interfering with bacterial cell wall formation. It is active against Gram-positive cocci such as staphylococci and streptococci. Most Gram-negative microorganisms and yeasts are resistant to it.

As side effects, contact dermatitis and more rarely, anaphylactic shock have been reported.

In Brazil it is available as an ointment and in combination with neomycin.

RETAPAMULIN

Retapamulin is a semi-synthetic agent derived from an edible mushroom called *Clitopilusscyphoides*. Its antibacterial action occurs through the inhibition of protein synthesis by binding selectively to bacterial ribosomes. It is effective against *S. aureus* and *S. pyogenes*.[39,40]

Clinical cure of impetigo with retapamulin is well defined, when compared with placebo. Being a bacteriostatic drug, bacterial eradication may not occur, even after the clinical cure of impetigo.[39,40] Retapamulin is not indicated for MRSA infections. It is less effective in traumatic lesions and those with abscess formation (usually caused by anaerobic bacteria and MRSA).[39,40]

Available as a 1% ointment, it can be used in children older than 9 months.[39] ❑

REFERENCES

1. Oumeish I, Oumeish OY, Bataineh O. Acute bacterial skin infections in children. Clin Dermatol. 2000;18:667-78.
2. Vlassova N, Han A, Zenilman JM, James G, Lazarus GS. New horizons for cutaneous microbiology: the role of biofilms in dermatological disease. Br J Dermatol. 2011;165:751-9.
3. Chiller K, Selkin BA, Murakawa GJ. Skin microflora and bacterial infections of the skin. J Investig Dermatol Symp Proc. 2001;6:170-4.
4. Carrol JA. Common bacterial pyodermas. Postgrad Med. 1996;100:311-3, 317-22.
5. Luby SP, Agboatwalla M, Feikin DR, Painter J, Billhimer W, Altaf A, et al. Effect of handwashing on child health: a randomized controlled trial. Lancet. 2005;366:225-33.
6. Scaramuzzino DA, McNiff JM, Bessen DE. Humanized in vivo model for streptococcal impetigo. Infect Immun. 2000;68:2880-7.
7. Lin JN, Chang LL, Lai CH, Lin HH, Chen YH. Clinical and molecular characteristics of invasive and noninvasive skin and soft tissue infections caused by group A streptococcus. J Clin Microbiol. 2011;49:3632-7.
8. Brown J, Shriner DL, Schwartz RA, Janniger CK. Impetigo: an update. Int J Dermatol. 2003;42:251-5.
9. Manders SM. Toxin-mediated streptococcal and staphylococcal disease. J Am Acad Dermatol. 1998;39:383-98.
10. Noble WC. Skin bacteriology and the role of Staphylococcus aureus in infection. Br J Dermatol. 1998;139:9-12.
11. Durupt F, Mayor L, Bes M, Reverdy ME, Vandenesch F, Thomas L, et al. Prevalence of Staphylococcus aureus toxins and nasal carriage in furuncles and impetigo. Br J Dermatol. 2007;157:1161-7.
12. Araújo T, Schacner L. Benign vesicopustular eruptions in the neonate. An Bras Dermatol. 2006;81:359-66.
13. Bangert S, Levy M, Hebert AA. Bacterial resistance and impetigo treatment trends: a review. Pediatr Dermatol. 2012;29:243-8.
14. Kato F, Kadomoto N, Iwamoto Y, Bunai K, Komatsuzawa H, Sugai M. Regulatory mechanism for exfoliative toxin production in Staphylococcus aureus. Infect Immun. 2011;79:1660-70.
15. Nishifuji K, Shimizu A, Ishiko A, Iwasaki T, Amagai M. Removal of amino-terminal extracellular domains of desmoglein 1 by staphylococcal exfoliative toxin is sufficient to initiate epidermal blister formation. J Dermatol Sci. 2010;59:184-91.
16. Barton LL, Friedman AD. Impetigo, a reassessment of etiology and therapy. Pediatr Dermatol. 1987;4:185-8.
17. Rhody C. Bacterial infections of the skin. Prim Care. 2000;27:459-73.
18. Schachner L, Gonzalez A. Diagnosis and treatment of impetigo. J Am Acad Dermatol. 1989;20:132.
19. Dagan R. Impetigo in childhood: changing epidemiology and new treatments. Pediatr Ann. 1993;22:235-40.
20. Pruksachatkunakorn C, Vaniyapongs T, Pruksakorn S. Impetigo: an assessment of etiology and appropriate therapy in infants and children. J Med Assoc Thai. 1993;76:222-9.
21. Brook I, Frazier EH, Yeager JK. Microbiology of non-bullous impetigo. Pediatr Dermatol. 1997;14:192-5.
22. Couppié P, Sainte-Marie D, Prévost G, Gravet A, Clyti E, Moreau B,et al. L' impetigo en Guyane Française. Etudes clinique, bactériologique, toxicologiqueet de sensibilité aux antibiotiques. Impetigo in the French Guiana. Clinical, bacteriological, toxicological and sensitivity to antibiotics studies. Ann DermatolVenereol. 1998;125:688-93.
23. Kakar N, Kumar V, Mehta G, Sharma RC, Koranne RV. Clinico-bacteriological study of pyodermas in children. J Dermatol. 1999;26:288-93.
24. Pérez LC, López PB, Barrios M, Ulloa SR, Aguileira OS, Perfaur MC, et al. Etiología del impétigo infantil. Etiology of impetigo in children. Rev Chil Pediatr. 2001;72:199-203.
25. Akiyama H, Yamasaki O, Kanzaki H, Tada J, Arata J. Streptococci isolated from various skin lesions: the interaction with Staphylococcus aureus strains. J Dermatol Sci. 1999;19:17-22.
26. Mancini AJ. Bacterial skin infections in children: the common and the not so common. Pediatr Ann. 2000;29:26-35.
27. Nagaraju U, Bhat G, Kuruvila M, Pai GS, Jayalakshmi, Babu RP. Methicillin-resistant Staphylococcus aureus in community-acquired pyoderma. Int J Dermatol. 2004;43:412-4.
28. Petry V, Bessa GR, Poziomczyck CS, Oliveira CF, Weber MB, Bonamigo RR,et al. Bacterial skin colonization and infections in patients with atopic dermatitis. An Bras Dermatol. 2012;87:729-34.
29. Kluytmans-Vandenbergh MF, Kluytmans JA. Community-acquired methicillin-resistant Staphylococcus aureus: current perspectives. Clin Microbiol Infect. 2006;12:9-15.
30. Del Giudice P, Hubiche P. Community-associated methicillin-resistant Staphylococcus aureus and impetigo. Br J Dermatol. 2010;162:905.
31. Koning S, van der Sande R, Verhagen AP, van Suijlekom-Smit LW, Morris AD, Butler CC, et al. Interventions for impetigo. Cochrane Database Syst Rev. 2012;1:CD003261.
32. George A, Rubin G. A systematic review and meta-analysis of treatments for impetigo. Br J Gen Pract. 2003;53:480-7.
33. Spelman D. Fusidic acid in skin and soft tissue infections. Int J Antimicrob Agents. 1999;12:S59-66.
34. Wilkinson JD. Fusidic acid in dermatology. Br J Dermatol. 1998;139:37-40.
35. Tveten Y, Jenkins A, Kristiansen BE. A fusidic acid-resistant clone of Staphylococcus aureus associated with impetigo bullosa is spreading in Norway. J Antimicrob Chemother. 2002;50:873-6.
36. Rørtveit S, Skutlaberg DH, Langeland N, Rortveit G. Impetigo in a population over 8.5 years: incidence, fusidic acid resistance and molecular characteristics. J Antimicrob Chemother. 2011;66:1360-4.
37. Booth JH, Benrimoj SI. Mupirocin in the treatment of impetigo. Int J Dermatol. 1992;31:1-9.
38. Eichenfield LF, Carney PS, Chow MJ, Tal A, Weinberg JM, Yurko M. Unique approaches for the topical treatment and prevention of cutaneous infections:report from a clinical roundtable. Cutis. 2004;74:2-23.
39. Yang LPH, Keam SJ. Retapamulin. A review of its use in the management of impetigo and other uncomplicated superficial skin infections. Drugs. 2008;68:855-73.
40. Koning S, van der Wouden JC, Chosidow O, Twynholm M, Singh KP, Scangarella N, et al. Efficacy and safety of retapamulin ointment as treatment of impetigo: randomized double-blind multicentre placebo-controlled trial. Br J Dermatol. 2008;158:1077-82.

MAILING ADDRESS:
Luciana Baptista Pereira
Av. Prof. Alfredo Balena,189 sala 602 Santa Efigênia
Belo Horizonte
CEP 30130-100
E-mail: lucianabpereira@terra.com.br

How to cite this article: Pereira LB. Impetigo - review. An Bras Dermatol. 2014;89(2):293-9.