NDPSC Report on topical clindamycin Nov 2001

This report is based on data submitted in response to the NDPSC decision to review the scheduling status of topical clindamycin. The data requirements outlined in the Minutes of the 31st meeting of NDPSC were used to guide this evaluation. It should be noted that the submission makes no reference of support from the other distributors of topical clindamycin containing products used in the treatment of acne.

Recommendations

The committee confirm that topical clindamycin retains its S4/Prescription medicine status, and that it recommend to New Zealand that it reclassifies topical clindamycin to Prescription medicine on the grounds that clindamycin :

- is an essential human antibiotic for the treatment of multi-resistant bacterial infections,
- resistance is associated with cross-resistance to other lincosamide, macrolide and streptogramin antibacterials which are deemed essential human antibiotics by Jetacar;
- resistance occurs with prolonged topical use in both propionibacterium acne, and gram-negative cutaneous staphylococci which can cause opportunistic infection in immune-compromised individuals;
- transmission by plasmid transfer of clindamycin resistance from gram-negative streptococci to pathogenic staphylococci including staph aureus has been recorded;
- rates of resistance to clindamycin in skin bacteria of both treated patients and their close contacts is increasing.

Therapeutic Class

Clindamycin belongs to a group of lincosamide antibacterials which can be either bacteriostatic or bactericidal, dependant on concentration and bacterial sensitivity. Clindamycin is active against a wide range of bacteria including most aerobic gram-positive cocci and several anaerobic gram negative and positive organisms.

Therapeutic importance

Oral and parenteral clindamycin are regarded by Jetacar as Group B antibiotics i.e. antibiotics used in infections for which other treatment options are limited. Use of oral/parenteral clindamycin is severely restricted due to attempts to delay the emergence of resistance to this important antibacterial.

While the therapeutic range and usefulness of clindamycin and the lincosamides is similar to that for the macrolide antibiotics, other than when used as a topical treatment for acne, the lincosamide group of antibiotics are used infrequently and nearly always by specialists to manage severe infections such as endocarditis, or infections caused by multi-resistant staphylococci.

Antibacterial resistance

Rates of resistance to clindamycin in the target species of propionibacterium acne, and gram-negative cutaneous staphylococci are increasing from very

low background levels to 60% of isolates taken from patients who have used topical clindamycin over prolonged periods. Increased rates of carriage of resistant strains have been documented not only in treated patients but also in close contacts of treated patients. Several papers have been published linking previous treatment with clindamycin or erythromycin and presence of resistant strains on the skin of patients with treatment failure and generally poor treatment outcomes. Background rates of clindamycin resistance in Australia are low, compared to Europe and the USA, due to the late arrival of the treatment option. Rates in NZ are only documented for 1995 where the rate was 14%, however, given the widespread availability and use of the agent in NZ, the resistance rate is now likely to be similar to those found in European markets i.e. >40%.

Mechanism of resistance

Several papers in the submission analyze resistant isolates from around the world demonstrating that clindamycin resistance in propionibacteria is predominately due to point mutations at a specific site in microsomal dna. Plasmid transfer of resistance from propionibacteria species, and other cutaneous bacterial species such as staphylococci epidermis (a potential cause of infection in immune compromised individuals), to pathogenic staphylococci has already been documented. Many of the current strategies to reduce antibiotic use are aimed specifically at decreasing, or delaying, the emergence of multiple-resistant staphylococci. In this respect, lowering rates of clindamycin resistance in common skin commensals and pathogens is crucial as it will decrease the pool of potential sources of plasmid transfer of resistance genes which leads to multiple-resistance in staphylococci. Limiting use of topical clindamycin may also relieve some of the selective pressure on staphylococci which results from increased antibiotic use generally.

Use of dual therapy, clindamycin and benzoyl peroxide, may further decrease selective pressure as there is some evidence that resistance rates in skin bacteria can be reduced by concomitant use of these two products. Even with concomitant use, however, the rates of resistance found are still substantially higher than those in untreated patients.

As with nearly all antibiotics, however, it is not yet certain that decreased pressure of use will definitely reduce the prevalence of development and carriage of resistant strains of propionibacteria or staphylococci.

Cross-resistance

As the mode of action of the lincosamide and macrolide antibiotics is similar, i.e. they both inhibit protein synthesis at the same site, resistance to clindamycin is linked to cross-resistance to erythromycin and other macrolides. In addition, the point mutations associated with clindamycin resistance also confer cross-resistance to the beta streptogramin antibacterials such as quinupristin and dalfopristin, new human antibacterial agents that are hoped to be the solution to treating multi-resistant bacteria.

Discussion

Acne, while it can be a severe and soul-destroying condition, is usually a minor medical problem in most patients. Current dermatology guidelines are moving away from prolonged oral use of antibiotics such as the tetracyclines and erythromycin, towards shorter treatments with topical antibacterial agents such as benzoyl peroxide as a first line choice, followed by the additional of topical clindamycin in cases where response is unsatisfactory. Oral antibiotics, for up to 6 months, and oral isotretinoin are held for severe and resistant cases.

The potential consequences of very high rates of clindamycin resistance in common skin bacteria are severe, and steps to minimise resistance developing should be encouraged. The increasing rates of clindamycin resistance, the ability to disseminate resistance across commensal, opportunistic pathogens and active pathogenic bacteria and the proven cross-resistance conferred by the gene mutations associated with clindamycin resistance are potent arguments for maintaining a tight control over access to this antibiotic.

In addition to maintaining all forms of clindamycin as a Prescription only antibiotic, the committee should consider requesting changes be made to the prescribing and patient information to bring it into line with latest dermatological guidelines namely that topical clindamycin:

- treatment of acne needs careful assessment and monitoring by a doctor;
- is second-line therapy; and
- should be used for no more than 3 to 6 months at a time and always in conjunction with benzoyl peroxide