

Relative merits of Flucloxacillin versus Amoxicillin in the management of cellulitis in lymphoedema.

Flucloxacillin is commonly recommended as the drug of choice for the treatment of cellulitis (CREST 2005, Eron et al. 2003). The rationale for choosing flucloxacillin is that it has an effect on streptococcal bacteria as well as staphylococcal. However, the general view amongst lymphoedema specialists in the UK is that streptococci are the major cause of cellulitis in lymphoedema and therefore anti-streptococcal antibiotics are preferred (Mortimer 2000, Cox et al 1998).

The decision by the consensus group to recommend amoxicillin as the first line oral antibiotic is based on a combination of the experience of the group and from the available literature.

The main factors considered were:

1. The effectiveness of both antibiotics against streptococcal infections.
 2. Tissue penetration.
 3. The side effect profile.
 4. The reported drug resistance.
1. Although both antibiotics are effective against Group A beta haemolytic streptococci, the minimum inhibitory concentration for amoxicillin is lower than that for flucloxacillin ($\leq 0.03 \mu\text{g/ml}$ for amoxicillin versus $0.1 \mu\text{g/ml}$ for flucloxacillin) (Istre et al 1981, Medsafe, accessed 19.02.2010).
 2. The penetration of different antibiotics into lymphoedematous tissue is not established but evidence would suggest that it is likely to be better for amoxicillin than flucloxacillin. Wise et al (1980) studied the penetration of six antibiotics, including amoxicillin (low protein binding) and flucloxacillin (highly protein bound), into tissue fluid obtained from blisters. The study applied the theory that only the protein-free fraction of an antibiotic can act against bacteria and therefore if other factors are equal, a drug with low protein binding should be superior to one with higher binding. This study concluded that the penetration of antibiotic into the blister fluid was not affected by serum protein binding unless that binding is very high and this difference was demonstrated when amoxicillin was compared to flucloxacillin. The more highly bound flucloxacillin achieved blister fluid levels of about one third of those of amoxicillin.
A contrasting study by Bergan et al (1986) studied the passage of intravenous administration of flucloxacillin into peripheral lymph and skin blisters. This study identified that this highly protein bound antibiotic demonstrated good tissue penetration. It did, however, demonstrate slightly delayed passage into extravascular sites with slightly later peak concentrations and persistently lower levels in extravascular fluid than in serum, as might be expected when compared with an antibiotic that is not protein bound.
 3. Anecdotally, patients seem to tolerate amoxicillin better than flucloxacillin. However, the side effect profile, taken from the electronic Medicines Compendium, for both drugs is similar with common side effects (incidence between 1/100-1/10) including gastrointestinal disorders. Skin rashes have been recognised as a common side effect of oral amoxicillin and an uncommon side effect (1/1000-1/100) of

flucloxacillin. The reported side effects were taken from data collected 6000 patients taking amoxicillin and 929 taking flucloxacillin.

4. The Health Protection Agency's 2008 annual report on antimicrobial resistance and prescribing reported resistance to clindamycin, erythromycin and tetracycline in group A streptococci. However, no resistance to penicillin has been observed in the UK or elsewhere so there is no particular advantage of either amoxicillin or flucloxacillin in this regard.

Conclusion:

Although the consensus group favours amoxicillin as the first line oral antibiotic for treating cellulitis in lymphoedema, flucloxacillin is considered to be an acceptable alternative.

References:

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