Penicillins + Tetracyclines

Data from the 1950s suggested that the tetracyclines can reduce the effectiveness of penicillins in the treatment of pneumococcal meningitis and probably scarlet fever. It is uncertain whether a similar interaction occurs with other infections. This interaction may possibly be important only with those infections where a rapid kill is essential.

Clinical evidence

When chlortetracycline originally became available it was tested as a potential treatment for meningitis. In patients with pneumococcal meningitis it was found that intramuscular benzylpenicillin 600 mg every 2 hours was more effective than the same regimen of penicillin with intravenous chlortetracycline 500 mg every 6 hours. Out of 43 patients given penicillin alone, 70% recovered, compared with only 20% in another group of 14 essentially similar patients who had received both antibacterials. 1

Another report about the treatment of pneumococcal meningitis with intramuscular or intravenous penicillin and intravenous tetracyclines (chlortetracycline, oxytetracycline, tetracycline) confirmed that the mortality was much lower in those given only penicillin, rather than the combination of penicillin and a tetracycline. 2 In the treatment of scarlet fever (Group A beta-haemolytic streptococci), no difference was seen in the initial response to treatment with penicillin (oral procaine benzylpenicillin) and chlortetracycline or the penicillin alone, but spontaneous re-infection occurred more frequently in those who had received both antibacterials. 3

Mechanism

The generally accepted explanation is that bactericides such as the penicillins, which inhibit bacterial cell wall synthesis, require cells to be actively growing and dividing to be maximally effective, a situation that will not occur in the presence of bacteriostatic antibacterials, such as the tetracyclines.
Importance and management

Documentation is limited, but this is an apparently important interaction when treating pneumococcal meningitis and probably scarlet fever. However, the use of these **antibacterials** for such severe infections has largely been superseded. It has not been shown to occur when treating pneumococcal pneumonia. It has been suggested that antagonism, if it occurs, may only be significant when it is essential to kill bacteria rapidly, i.e. in serious infections such as meningitis or in neutropenic patients. Any penicillin and any **tetracyclines** (including doxycycline and oxytetracycline) advise that their use with penicillins should be avoided.5-7

Note that, the macrolides, which are also bacteriostatic would be expected to attenuate the action of penicillins, but this does not seem to occur in practice. See ‘**Macrolides + Penicillins**’.

References

7. **Tetracycline (Tetracycline hydrochloride)**. Actavis UK Ltd. UK Summary of product characteristics, March 2007.

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