

The Flucloxacillin / Dicloxacillin Debate

Medical practitioners are being advised by their insurance companies about possible litigation with use of flucloxacillin, due to potential hepatic effects. What implications are there for duty of care and what role is there for alternative drugs such as dicloxacillin?

Flucloxacillin therapy has been associated with cholestatic hepatitis at an incidence variously estimated between 1 in 400 and 1 in 20,000 courses given. The number of serious reactions reported to the Adverse Drug Reaction Advisory Committee (ADRAC) prompted regulatory action. The Australian Drug Evaluation Committee (ADEC), whilst acknowledging the limitations of the available data, approached pharmaceutical companies in June 1994 to encourage registration of alternatives to flucloxacillin, considered less likely to cause hepatitis.¹ Soon after, the Australian Pharmaceutical Benefits Advisory Committee restricted the prescribing of flucloxacillin to "serious" staphylococcal infections.²

Dicloxacillin received marketing approval in Australia in November 1996. It has equivalent antimicrobial actions to flucloxacillin and the oral formulation is similarly absorbed. Cholestatic hepatitis had not arisen as a major clinical problem with dicloxacillin use in North America.³ Doctors in Sweden had been using both antibiotics and a summation of adverse reports⁴ suggested that dicloxacillin caused hepatitis about half as often as flucloxacillin. However, a couple of centres in Sweden were reporting interstitial nephritis occurring more frequently with dicloxacillin than with flucloxacillin. Recent reports to ADRAC⁵ suggest that dicloxacillin use in Australia is also associated less often with cholestatic hepatitis but more often with interstitial nephritis than is flucloxacillin use. Underlying liver disease has not been shown to make cholestatic hepatitis more likely to occur with either drug. Dicloxacillin has been reported to decrease the anticoagulant effect of warfarin when given concurrently.⁶

Dicloxacillin is marketed in Australia in both intravenous and oral presentations, although there is no paediatric oral presentation. Wide post marketing surveillance following intravenous use has shown that it frequently caused thrombophlebitis, especially when given as a bolus injection.

The risk of hepatitis with either drug is increased in people over 55 and with therapy longer than two weeks.⁷ Risk factors for paediatric patients are different: hepatotoxicity in children is extremely rare and has not been reported in Australia.

TAG Member hospitals have endorsed the following strategies:

- Either flucloxacillin or dicloxacillin (or both) may be listed on hospital formularies at the discretion of the individual Drug Committee.
- Flucloxacillin may be used as the intravenous agent of choice to avoid thrombophlebitis.
- Dicloxacillin must not be used in patients who have had cholestatic hepatitis or interstitial nephritis caused by flucloxacillin, nor flucloxacillin used in patients who have had those reactions to dicloxacillin.
- Neither dicloxacillin nor flucloxacillin should be used for minor infections with staphylococci, nor for prophylaxis in adults. A first generation cephalosporin is preferred for surgical prophylaxis where flucloxacillin might formerly have been used.
- Use of flucloxacillin is considered safe in children.

References

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