

Drug metabolism can be confusing

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TITLE Enzymes of drug metabolism during delirium

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SUMMARY

Drugs have been implicated as the main cause in 11–14% of admissions for delirium in older patients, but alterations in drug metabolism in such delirious patients has been little studied. These researchers selected four esterases for study (acetylcholinesterase, aspirin esterase, benzoylcholinesterase, butyrylcholinesterase), on the basis that the *in vitro* assay is relatively simple, and the enzymes are present in peripheral blood samples. Esterases metabolise such drugs as aspirin, diamorphine, and some anaesthetics, and activate prodrugs such as carbimazole and enalapril.

Two hundred and eighty-three elderly patients were recruited within 24 hours of emergency admission to a Welsh teaching hospital. The mean age was 82.4 years, and 59% were female. Twenty-seven per cent were delirious on admission and 10% became delirious after admission. Esterase activity was significantly lower in patients who were or became delirious, and there was a strong inverse correlation between enzyme activity and mortality, with over 30% dying in the lowest quartile, compared with around 3% in the highest quartile. Delirious patients who recovered were retested a month later; two of the four enzymes tested showed significant improvements in activity. Otherwise, differences between the four enzymes were slight, and all showed similar suppression of activity in delirious patients.

The author concludes that delirious patients are particularly vulnerable to the effects of drugs, and prescription and dosing should be cautious, though the authors point out that esterases are only one group of many involved in drug metabolism.

COMMENT

It is unusual, and refreshing, to see clinical research in elderly, acutely confused patients. These patients have among the highest mortality and morbidity of hospital patients, and are among the least studied. Problems with consent, organisation, heterogeneity and follow-up have probably inhibited research such as this, and it is notable that the Cardiff team has particular expertise in gaining consent or assent in confused patients. They have already demonstrated that drug metabolising enzymes are diminished in patients with fractured femoral neck and community acquired pneumonia, and others have shown reductions in the institutionalised frail elderly. Therefore, it seems that esterase activity is reduced in 'illness', or perhaps frailty, rather than any specific pathology. Perhaps the question to ask is whether low esterase activity is the cause of increased vulnerability, illness and death, or simply a marker of frailty.

Where does one go from here? Doctors will be happier knowing that there is a demonstrated scientific reason for the peculiar sensitivity of some confused patients to sedatives or analgesics: perhaps it is enough that we now have one. However, it would be interesting to know why these enzymes stop working in delirious people, and get closer to the reason patients become confused in the first place.