Plasma concentrations of trifluoperazine following single low doses

Curry and associates[1] have noted that there is little in the literature on the levels of trifluoperazine in plasma because suitably sensitive and specific analytic procedures have not been available until recently. Curry and associates used a high-pressure liquid chromatographic method sensitive to 1 ng/ml to measure the plasma concentrations of trifluoperazine in a patient receiving high-dose therapy (80 mg/d).

Our group has now developed two types of analytic procedures for this purpose, one based on an immunoresponse[2] (with a sensitivity of 0.05 ng in 200 μl of plasma) and the other based on gas–liquid chromatography with either nitrogen–phosphorus (GLC-NPD)[3] or mass spectrometric (GLC-MS)[4] detection (sensitivities of 0.5 and 0.078 ng/ml respectively). In a study in which trifluoperazine (5 mg) was administered orally to five healthy male volunteers, we were able to detect trifluoperazine at the first sampling point, as well as in the specimen collected as late as 24 hours after administration, by means of the radioimmunoassay[5] or the GLC-MS[6] procedure. With GLC-NPD, however, we could only measure the drug's plasma concentration around the peak level. The maximum concentration and the time taken to reach this concentration were 0.5 to 3.0 ng/ml and 1 to 4 hours respectively according to GLC-MS. The area under the concentration–time curve as determined by radioimmunoassay was higher than that determined by GLC-MS because the antibody used in the radioimmunoassay cross-reacted with the *N*-desmethyl and 7-hydroxy metabolites to the extent of 26% and 24% respectively. The plasma elimination half-life ranged between 6 and 12 hours.

It is important to study carefully the disposition of trifluoperazine in patients because this drug has been employed in the management of schizophrenia for more than 20 years without any knowledge of its pharmacokinetics. The availability of sensitive and specific procedures for the trace analysis of this drug in plasma means that patients receiving normal therapeutic doses can be studied. Plasma concentrations of the drug are certainly very low. For example, in one patient receiving 1.0 mg of trifluoperazine three times a day the steady-state plasma concentrations were 0.4 ng/ml as determined by GLC-MS, yet this patient's symptoms were judged to be under good clinical control.

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Neonatal circumcision

In his discussion of factors that influence the decision about circumcision of the newborn, Dr. Paul G. Taylor mentioned those relating to physicians and family members but none relating to the newborn (*Can Med Assoc J* 1983; 128: 814–817). In my 1980 study of neonatal circumcision at the Royal Inland Hospital in Kamloops, BC, the proportion of circumcised newborns who spent part of their hospital stay in the neonatal intensive care unit was one half the overall proportion of circumcised newborns (13.6% v 26.8%). Therefore, illness or prematurity may have an over-riding influence on the decision about circumcising newborns.

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Triazolam abuse

Each day, throughout the world, 40 billion doses of benzodiazepines are consumed.[1] Despite this widespread use the reported incidence of dependence remains low: one case per 5 million patient-months for all forms of dependence, and one case per 50 million patient-months for dependence arising from prescribed drug treatment.[2]

Hollister[3] warned that the newer, short-acting benzodiazepines lend themselves to the type of intoxication favoured by abusers of sedative drugs. He noted that when barbiturates were in vogue the short-acting drugs secobarbital and pentobarbital sodium were abused rather than the longer-acting phenobarbital. A recent report supports this concern by concluding that primary benzodiazepine dependence is increasing and that the short-acting drug lorazepam appears to have a high potential for addiction.[4] Crawford[5] predicted that "triazolam will have the highest abuse potential of all the benzodiazepines yet marketed".

Case report

A 28-year-old single man was referred for outpatient assessment of a sleep disturbance. His general practitioner had noted an escalation in requests for repeat prescriptions of triazolam. The patient complained that he was unable to sleep without triazolam and that even when using the drug he took 2 to 3 hours to fall asleep and often awoke for short periods throughout the night. Early morning awakening was absent, but he awakened feeling drowsy and unrefreshed.

His sleep disturbance, of 9 years' duration, had been precipitated by a