Thus the effectiveness of the alpha-2 adrenoceptor agonists fails to prove the hypothesis that clozapine-induced hypersalivation is due to alpha-2 adrenoceptor blockade. Furthermore, there is evidence indicating that it is unlikely that the hypersalivation caused by clozapine is mediated by alpha-2 adrenoceptors. Firstly, the antidepressant drug mianserin which has a higher affinity for alpha-2 adrenoceptors that clozapine, not only fails to cause hypersalivation, but in fact it causes a significant (60% after a single dose of 20 mg) reduction in salivary output (Ogura et al, 1987). This effect of mianserin cannot be due to muscarinic receptor blockade since mianserin has a much lower affinity of muscarinic receptors than clozapine. Secondly, the atypical antipsychotic drug remoxipride also causes hypersalivation as a side-effect, however, it is a highly selective dopamine D2 receptor antagonist with extremely low affinities for other neurotransmitter receptors, including the alpha-2 adrenoceptor.

Thus, the way in which clozapine causes hypersalivation remains an enigma.


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Influences on cost effectiveness

SIR: Hotopf et al's (1996) review of randomised controlled trials comparing the cost-effectiveness of SSRIs v. tricyclic antidepressants concluded that although SSRIs appeared to be safer and better tolerated, these advantages did not justify their extra costs. However, their review has not considered the fact that the cost of drugs is strongly influenced by regional economic factors such as the differing interpretations of drug patent rules, the production of generic drugs and the variable dose strengths of pharmaceutical preparations. To make this point clearer, I will elaborate from drug experience in India (using figures from Drug Today, January–March 1996). Altogether, there are 16 preparations of fluoxetine available with prices for 10 capsules of 20 mg strength ranging from 12 to 48 Rupees. If one excludes the single preparation costing 48 Rs, the mean cost for 10 capsules is around 20 Rs. Of note, none of the preparations are ‘compound’ i.e. combined with other psychotropic drugs. Two commonly used tricyclics in India are imipramine and amitryptiline. Both are commonly available in 25 mg and 75 mg dosage strengths; many preparations are compound with combinations usually being diazepam and chlordiazepoxide. For the sake of comparison, I only include pure pharmacological preparations of imipramine or amitryptiline. Taking the former, the mean cost of 75 mg preparations (strip of 10) is 13.9 Rs and for 25 mg preparations (strip of 10) is 5.1 Rs; equivalent prices for amitryptiline are 15.7 Rs and 7 Rs. Of note, the minimum price of 75 mg preparations for both tricyclic is 11 Rs.

It is important that any discussion on the cost-effectiveness of interventions (whether pharmacological or psychological) should stress that they are as much influenced by regional political and economic factors as by clinical outcome indicators.

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Cytochromes and psychotropic drug interactions

SIR: Taylor & Lader (1996) have provided a timely editorial on the cytochrome P-450 enzyme system and the practical implications of its role in the metabolism of psychotropic drugs. It should not be overlooked, however, that the cytochrome P-450 enzyme system is also involved in the metabolism of commonly prescribed non-psychoactive drugs such as beta-blockers, type 1C antiarrhythmics and morphine derivatives, and knowledge of their pharmacokinetics is essential to avert adverse cytochrome-mediated drug interactions.

Although the authors rightly recommend the use of alternative drugs which interact to a lesser degree with the cytochrome P-450 system, they state...