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Overdose Risk with Selective Serotonin Reuptake Inhibitors

The article in the April issue of *Drugs* by Edwards and Anderson[1] on the selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors (SSRIs) uses the technique of meta-analysis to compare a set of very disparate papers and comes up with some very broad generalisations. An important paper by Barbey and Roose,[2] which was not cited by Edwards and Anderson,[1] reviews much of the same data and reaches very different conclusions. I would like to outline some general themes before dealing with the specific statements made about overdoses with one of the SSRIs, citalopram.

Any depressed patient is at potential risk of suicide. This is particularly so if their depression is severe (a patient population in whom Edwards and Anderson[1] admit citalopram is often favoured). The risk is greatest at the start of therapy, where Edwards and Anderson[1] suggest that fluoxetine may be at a disadvantage due to a slower onset of action.

Treatment guidelines from standard works[3] warn of the need for caution when dealing with depressed patients:

- it is advisable to limit the initial supply of drug given to the patient. Some of the citalopram overdoses are with 40 to 200 times the recommended daily dose
- where possible, therapy should be supervised to ensure that it is actually taken (and overdose avoided)
- the least toxic group of drugs should be prescribed. This would rule out tricyclic antidepressants (TCAs); any doctor who has had experience of a casualty department knows that the cardiac arrhythmia induced by a TCA overdose is very serious indeed.

The paper by Edwards and Anderson[1] contains no new data relating to overdose with citalopram. The 6 cases mentioned are those first reported in August 1996 by Öström et al. in the *Lancet*.[4] The correspondence that followed the original paper[5-8] applied perspective to these cases and confirmed the issue was wider than just an effect of citalopram, as several patients had survived overdoses with greater quantities of the drug than reported by Öström et al.[4]. Under-treatment in depression remains a major risk in determining suicide attempts.

Personne et al.[9,10] cite Scandinavian cases, reviewing overdose data received by the Swedish Poisons Information Centre, and conclude that overdose risk with SSRIs is less than with TCAs, but that serious symptoms may still develop. Interestingly, in 108 cases of 'pure' citalopram overdose (140mg to 5.2g) ECG aberrations such as nonspecific changes in the ST-T region and moderate widening of the ECG complexes occurred in about 25% of all patients, but clinically significant arrhythmias were not seen. There were no deaths. Convulsions were seen in 6 of 34 patients who had taken 600mg to 1.9g of citalopram and in 9 of 10 patients after doses of 1.9 to 5.2g. Despite the case reports, SSRIs are much less dangerous in overdose than other groups of drugs used to treat depression.[11]

Edwards and Anderson[1] suggest that the causes of death in the 6 patients described in the paper of Öström et al.[4] were cardiac arrhythmias or seizures, which echoes the original paper. However, the causes of death for the 6 patients are unknown; thus, this is pure speculation and not very likely in view of the more recent overdose data reported by Personne et al.[9,10]

Another factor which could have contributed to the deaths is co-ingested drugs, which may add to the potential toxicity of any drug, not just citalopram. In the paper of Öström et al.,[4] only one patient took citalopram alone (200 times the recommended daily dose), although we are aware of 108 cases of 'pure' citalopram overdose from Personne et al.[9,10] In their paper, Edwards and Anderson[1] discuss the original 6 cases, only one of

which involved the ingestion of citalopram alone, but come up with no new data.

We believe that the paper of Edwards and Anderson[1] does not add to the understanding of overdose risk with SSRIs. We would also reiterate the findings of Barbey and Roose[2] who describe fatal overdoses involving all SSRIs when taken alone, concluding 'There is no apparent difference between SSRIs with respect to overdose safety'.

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References

1. Edwards JG, Anderson I. Systematic review and guide to selection of selective serotonin reuptake inhibitors. Drugs 1999; Apr 57 (4): 507-33
2. Barbey JT, Roose SP. SSRI safety in overdose. J Clin Psychiatry 1998; 59 (Suppl. 15): 42-8
3. Cowen PJ. Psychopharmacology in medical practice. In: Weatherall DJ, Ledingham JGG, Warrel DA, editors. Oxford textbook of medicine. 3rd ed. Oxford: Oxford University Press, 1996
4. Öström M, Eriksson A, Thorson J, et al. Fatal overdose with citalopram. Lancet 1996 Aug 3; 348: 339-40
5. Isacsson G, Bergman U. Risks with citalopram in perspective [letter]. Lancet 1996 Oct 12; 348: 1033
6. Brion F, Brion N, Durigon M. Fatal overdose with citalopram [letter]? Lancet 1996 Nov 16; 348: 1380
7. Grundemar L, Wohlfart B, Lagerstedt C, et al. Symptoms and signs of severe citalopram overdose. Lancet 1997 May 31; 349: 1602
8. Glassman AH. Citalopram toxicity [letter]. Lancet 1997 Nov 13; 350: 818
9. Personne M, Sjöberg G, Persson H. Citalopram overdose: review of cases treated in Swedish hospitals. Clin Toxicol 1997; 35 (3): 237-40
10. Personne M, Persson H, Sjöberg G. Citalopram toxicity [letter]. Lancet 1997 Aug 16; 350: 518-9
11. Henry JA. Epidemiology and relative toxicity of antidepressant drugs in overdose. Drug Saf 1997; 16 (6): 374-90