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Treatment of serotonin toxicity

by Dr Ken Gillman | Last updated Oct 21, 2021 | Published on Nov 13, 2014 | Serotonin Toxicity, Anti-Depressants

The 'spectrum concept' guides assessment of the likely severity of reactions and therefore the setting for treatment.

Key information is:–

- The quantity and type of drugs ingested.
- The evolution of the symptoms and their rate of change

When both an MAOI and an SRI have been co-ingested (even in low doses) rapid deterioration is likely and early transfer to an medical ITU and consultation with a toxicologist is strongly recommended.

An overdose of an SSRI alone produces serotonin toxicity of only moderately severity in 10% – 20 % of cases (sufficient for admission and active medical treatment), but with no serious sequelae or fatalities (1).

If an MAOI or RIMA + SRI have been ingested then about 50% of such cases experience severe serotonin toxicity (2,3). It is these combinations that are most likely to require active medical intervention including intensive care admission, cooling, 5HT2A antagonists, intubation and neuromuscular paralysis. Details of these treatments are available in medical / toxicology texts. The advice herein is derived from Professor Whyte who is a physician specialising in toxicology (4-7), and from my reviews of other sources, which include an analysis of every known case of ST published since 1955 (8,9).

Cyproheptadine is effective for the milder cases; 12mg orally (or by crushed via nasogastric tube), followed by 4mg – 8mg every six hours.

If charcoal has already been given, the intra-venous route must be used so cyproheptadine is no use and chlorpromazine is used. As yet there is no widely available 5-HT2A antagonist for intra-venous use except chlorpromazine. Olanzapine and ziprasidone are 2A antagonists and are available as short acting IMI preparations in some countries, but there is as yet no direct evidence they are effective. Therefore chlorpromazine remains the only drug for which there is reasonable (in my opinion, strong) evidence of effectiveness, and it is cheap and widely available.

In severe toxicity (MAOI + SRI) intensive care admission, intubation and neuromuscular paralysis (with barbiturate anaesthesia), active cooling, and consideration of 5-HT2A antagonists, cyproheptadine or chlorpromazine will probably be required. Details of these treatments are available in toxicology texts. Chlorpromazine has been used in many cases (~ 20 in the HATS experience) with good effect. Fluid loading is advised before giving chlorpromazine (because of hypotension) – dose in the range of 12.5 to 25 IV initially, followed by 25mg orally or IV every six hours. Chlorpromazine may be best avoided if the drugs inducing serotonin toxicity have marked cardiotoxic, or epileptogenic properties (eg venlafaxine). Contrary to some stated comment there is no evidence this gives rise to risk of exacerbation serotonin toxicity, because fits as part of serotonin toxicity are not epileptic but are severe tremor / clonus (4, 10-16). These references demonstrate

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both the absence of epileptiform EEG changes in serotonin toxicity and some mistaken reports of epilepsy that were serotonin toxicity. I have reviewed all cases treated with chlorpromazine and cyproheptadine (9).

Careful consideration of the need for treatment is particularly important because of the often accepted notion that cessation of drugs and non-specific treatment is all that is likely to be necessary in a majority of cases (9, 17-19). To state that non-specific treatment is adequate, without understanding the spectrum concept and taking the above more complex risk factors into consideration, is a dangerous over-simplification of the issues. The speed with which death can ensue if appropriate treatment is not initiated has been highlighted many times, most recently by the sad case reported by Otte in 2003. Benzodiazepines have also now been demonstrated to reduce temperature in serotonin toxic rats and may be a reasonable adjunctive treatment with 5-HT2A antagonists now GABA has been shown to play a role in lessening symptoms (20-23).

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