

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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SIADH and antidepressants

Syndrome of Inappropriate Antidiuretic Hormone (SIADH) is a well established potential adverse effect of antidepressants. Reports with SSRIs and venlafaxine are particularly predominant, but there have been reports with all other antidepressant classes. The exact incidence of this effect is unclear, but results from observational studies suggest it is common, particularly for SSRIs and venlafaxine amongst elderly patients. The variation in incidence among different antidepressant classes has not yet been well-quantified. The Australian Adverse Drug Reactions Advisory Committee (ADRAC) reported having received 311 reports of hyponatraemia involving SSRIs or venlafaxine in 2003. The SSRIs accounted for about one quarter of these reports.

The risk of antidepressant-induced SIADH appears to be highest during the first weeks of treatment, but SIADH has occurred many months after treatment initiation. Potential risk factors include elderly age, female gender, low body mass index, low baseline plasma sodium level (i.e. ≤ 138 mmol/L) and concomitant use of other drugs that can cause hyponatraemia (e.g. diuretics, other psychotropic drugs). It is unclear whether this reaction is dose dependent.

Initial symptoms of SIADH include lethargy, muscle cramps, anorexia, nausea and vomiting. With more profound or more rapidly developing hyponatraemia, confusion, coma, convulsions and even death may occur. As the early symptoms of SIADH may mimic many of those of depression, awareness of this adverse effect is particularly important. Laboratory abnormalities include low serum sodium concentration, low serum osmolality and high urine osmolality. The serum concentrations of urea, creatinine, albumin and uric acid are usually normal or marginally low.

Definitive guidelines are lacking, but it is reasonable to consider electrolyte monitoring for elderly patients at baseline, and during the first 1–4 weeks after initiation of an antidepressant, particularly for SSRIs and venlafaxine. Frequent monitoring is especially important in the elderly with other risk factors. It is recommended that a serum sodium concentration should be measured in elderly patients who exhibit abrupt changes in mental status (e.g. lethargy or confusion) during treatment with an antidepressant.

In the presence of hyponatraemia, consideration of other potential causes (besides the antidepressant) is essential. Where the antidepressant is thought to be the most likely cause, the following has been suggested. For mild drug-induced hyponatraemia, cease the antidepressant where possible. If the drug is essential, it can be continued with close monitoring of sodium levels. Long term restriction of daily fluid intake (e.g. 800–1000 mL) has been somewhat successful with continued SSRI treatment in hyponatraemic patients, although compliance is often poor. Treatment with demeclocycline could be considered if the antidepressant needs to be continued, although it may not be well tolerated by many patients, and it is only available in Australia via the Special Access Scheme. Where hyponatraemia is more marked, short term fluid restriction and antidepressant cessation is advisable. After correcting the metabolic abnormalities, options for treatment of the depression include rechallenging with the same drug or initiating another antidepressant while carefully monitoring serum sodium levels, or considering electroconvulsive therapy if warranted.

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