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Medicinal mishap

Tramadol and hyponatraemia

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Case

A 76-year-old woman with a past history of hypertension, compression fracture of the lumbar vertebrae, diverticulitis and leg cramps was admitted to hospital with a Colles' fracture. Her usual medications were perindopril 2 mg in the morning, quinine sulfate 300 mg at night, ranitidine 300 mg at night, calcium carbonate at night and risedronate 5 mg daily. Her sodium on admission was 135 mmol/L.

The fracture was reduced under an arm block and she was commenced on tramadol 50 mg four times daily for pain control.

The patient was transferred to a rehabilitation hospital nine days later. On admission, her sodium was mildly reduced at 129 mmol/L. Her sodium continued to drop over the following seven days, despite fluid restriction, to 122 mmol/L. Her other electrolytes were within normal limits. Clinically she was euvoalaemic. Serum osmolality was low at 256 (280–300), suggesting inappropriate antidiuretic hormone (ADH) secretion. Tramadol was ceased and her sodium returned to normal over four days.

Comment

Tramadol is an analgesic which stimulates the same receptor as morphine and other opioids.¹ It also inhibits noradrenaline and serotonin reuptake potentially resulting in increased concentrations of serotonin and noradrenaline.

It has been well documented that selective serotonin reuptake inhibitors (SSRIs) cause hyponatraemia (defined as a sodium concentration less than 135 mmol/L) particularly in the elderly, females and in the initial stage of therapy.^{2,3} This is thought to be due to increased serotonin levels stimulating the release of

vasopressin (ADH).⁴ Vasopressin causes fluid retention resulting in expansion of extra cellular volume and lowered sodium levels.

Tramadol, by increasing serotonin levels, may result in hyponatraemia through a similar mechanism.

I have had four elderly patients who have taken tramadol for pain control after fractures and have developed hyponatraemia, which has been corrected on cessation of tramadol. One of these cases occurred when tramadol was added to a patient already on citalopram, an SSRI.

Recommendations

Tramadol use should be reviewed and, if possible, the dose reduced or the drug ceased altogether after 48–72 hours. Sodium concentrations should be monitored when prescribing tramadol particularly in the elderly and those taking other medications, such as SSRIs and diuretics, which also predispose to hyponatraemia.

References

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3. Spigset O, Hedenmalm K. Hyponatremia in relation to treatment with antidepressants: a survey of reports in the World Health Organization data base for spontaneous reporting of adverse drug reactions. *Pharmacotherapy* 1997;17:348-52.
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Editor's note:

The Adverse Drug Reactions Advisory Committee has received 14 reports of hyponatraemia in patients taking tramadol.