



PIC QUESTION OF THE WEEK: 10/29/07

Q: Is there any association between treatment with SSRIs and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion?

A. Inappropriate secretion of antidiuretic hormone (ADH) alters the regulation of free-water excretion in the kidneys and can result in severe hyponatremia. ADH is normally released from the posterior pituitary and plays a key role in water balance and sodium homeostasis. SIADH impairs urinary dilution resulting in elevated urine osmolality, excessive urine sodium excretion, hyponatremia, and decreased serum osmolality. Relevant laboratory values include urine osmolality and urine sodium levels greater than 150mOsm/kg and 20mEq/L respectively. A serum osmolality less than 280 mOsm/kg and sodium levels below 135 mEq/L suggest possible SIADH. Regardless of actual values, the presence of a *urine osmolality that exceeds the serum osmolality* is indicative of SIADH. Causes of SIADH include CNS disorders, malignancy, drugs, surgery, pulmonary disease, HIV, etc. Those at greatest risk for SIADH are the elderly, hospitalized, volume depleted patients, and those taking diuretics. Symptoms are dependent on serum sodium concentration and are highly variable. Initial symptoms include lethargy, muscle cramps, anorexia, nausea and vomiting, irritability, and headache while severe hyponatremia can present with confusion, depressed reflexes, seizures and coma. Patients may be misdiagnosed since symptoms of hyponatremia coincide with a worsening state of depression. Drugs that stimulate release, enhance action, or are analogs of arginine vasopressin (AVP) can cause SIADH. These consist of antidepressants such as venlafaxine, duloxetine, tranylcypromine, and the tricyclic compounds as well as antipsychotics, NSAIDs, chlorpropamide, carbamazepine, vincristine, opiate analgesics, and several others. There are case reports of SIADH with most available SSRIs. The syndrome commonly develops within the first month of therapy (often within the first two weeks); however, a delayed onset has also been reported. Although actual incidence is difficult to determine, hyponatremia has been reported to occur in approximately 0.06% of patients receiving SSRI therapy. In certain subgroups, the frequency of hyponatremia appears to be much greater. For example, the reported frequency in the elderly population has ranged from 12% to 33%. Limited data is available comparing occurrence rates of SIADH with individual SSRIs; however, one study suggests that incidence is fairly equal within this class of antidepressants. There is little evidence to suggest that use of alternative SSRIs is safe in patients experiencing SSRI-induced SIADH. One case report describes a patient with SIADH secondary to citalopram who was safely re-challenged with mirtazapine. Patients at high risk for SIADH should be closely monitored when prescribed SSRIs and other antidepressants.

References:

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