



PIC QUESTION OF THE WEEK: 12/11/06

Q: Can a patient who develops neuroleptic malignant syndrome be re-challenged with another antipsychotic?

A: Neuroleptic malignant syndrome (NMS) is a rare, idiosyncratic drug reaction that occurs in approximately 1% of those administered neuroleptic (antipsychotic) agents. It appears to be related to reduction of dopamine in the CNS and enhanced calcium concentration in peripheral muscle fibers. The majority of cases of NMS have been associated with *older* antipsychotics, predominantly haloperidol, fluphenzine, and chlorpromazine. Other dopamine antagonists such as metoclopramide as well as lithium and anticonvulsants have also been implicated as causes of NMS. Mortality rates have been suggested to range between 4-25%. NMS is usually characterized by hyperthermia, autonomic dysfunction (tachycardia, unstable blood pressure, sweating, incontinence), altered mental status (delirium, stupor, encephalopathy), and muscular rigidity. Rhabdomyolysis has been reported in association with NMS. The syndrome typically begins after the introduction of a neuroleptic drug, an increase in dosage, or addition of another drug in the same class. Onset is generally within the first few weeks of neuroleptic exposure, however, it may be more delayed. Symptoms usually subside within five-ten days after the causative agent is discontinued. Serotonin syndrome presents with many of the characteristics of NMS and must always be considered in the differential diagnosis. The main differences between these two syndromes are the precipitating agents and the more rapid onset associated with serotonin syndrome. Treatment of NMS includes rapid discontinuation of the offending agent followed by temperature reduction, fluid and electrolyte replacement, and pharmacological therapy. Dopamine agonists such as bromocriptine or amantidine and muscle relaxants, particularly dantrolene, have been used successfully in the management of NMS. In most cases, patients with NMS will require continued treatment of their psychiatric disorder. Although a number of factors can contribute to successful re-challenge, delaying initiation of therapy for *at least two weeks* after resolution of signs and symptoms appears to be most crucial. Most authors recommend use of an alternative drug, preferably one of the newer second-generation agents. In addition, the drug should be initiated at the lowest effective dose and gradually titrated. By adhering to the above guidelines, most patients with a history of NMS can be successfully re-challenged with an alternative neuroleptic agent.

References:

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