Anticholinergic Drugs and Cognitive Functions

Since the discovery of the fact that choline acetyltransferase activity and the number of cholinergic neurons are both significantly reduced in the brain of patients with Alzheimer’s disease (1-9), it became well known that the cholinergic system plays an important role in cognitive function of the brain. The effect of blockade of the cholinergic system was examined in normal volunteers (10-12). It has also become recognized that anticholinergic drugs routinely prescribed in Parkinsonian or schizophrenic patients might impair cognitive functions including memory, intelligence or attention. Tune and colleagues tested working and recent memory in 24 schizophrenic patients and found a significant inverse correlation between serum anticholinergic levels and performance on the memory task (13). Memory task did not correlate with the severity of schizophrenic symptoms, verbal IQ, or serum neuroleptic levels. McEvoy and Freter reported dose-responsive relationship between anticholinergic drugs and memory impairment in schizophrenics (14). Similarly, Sadeh and colleagues reported effects of anticholinergic drugs on memory in Parkinson’s disease (15). So far some studies reported that long-term anticholinergic therapy using typical dosage might cause memory disturbances or intelligence impairment (15, 16), while others reported that there was no evidence of memory disturbance caused by long-term anticholinergic therapy (17, 18). Intelligence might be disturbed as well (18-20). Therefore, the issue has not been settled yet nor has it been precisely studied, to determine what kind if any, of the cognitive functions might be impaired. I believe that many neurologists at least have some experience that anticholinergic drugs could cause reversible deterioration of memory or mental state particularly when used in aged patients or patients already with a mild decline of memory. Are these clinical impressions scientifically correct?

In this issue of Internal Medicine, a prospective study done by Nishiyama K and colleagues provides some answers to the questions (21).

They examined 90 patients of Parkinson’s disease with long-term anti-cholinergic therapy with batteries of neuropsychological tests and found that 8 patients exhibited at least one of the following deficits; intelligence impairment, verbal delayed recall impairment, verbal short-term memory disturbance and verbal long-term memory disturbance. The average age was 68.6 in patients with the neuropsychological deficits and 54.7 in patients without deficits suggesting that older patients were more prone to develop cognitive dysfunctions. The deficits were reversible by the cessation of the therapy and appeared again with the resumption of anticholinergic agents. These results are in accordance with our daily experience of Parkinsonian patients on anti-cholinergic therapy.

The paper also gave rise to an intriguing point concerning the relationship between short-term and long-term memory systems although this aspect was already pointed (22). Two out of five patients with short-term memory impairment did not show long-term memory and 2 out of 5 patients with long-term memory impairment did not show short-term memory impairment. This finding indicates that short-term and long-term memory system may be independent.

Anticholinergic drugs which are widely used in clinical practice give an important warning to clinicians as well as a useful hint for neuroscientists for the study of memory systems.

References


