P.2.117 Antipsychotic agents and serum creatine kinase levels

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Background: Marked elevations of serum creatine kinase (SCK) have been associated with treatment with both typical and atypical neuroleptic agents. In a recent study, relatively massive increases in SCK activity were observed in 10% of patients treated with various atypical antipsychotic agents. The magnitude of these increases were much larger than those previously reported in acutely psychotic patients or patients with NMS. Therefore, the role of atypical antipsychotic agents in producing significant CK elevation in comparison with classical neuroleptics in patients with psychotic disorders needs to be clarified.

Objectives: The purpose of this paper is to report preliminary data concerning the frequency of SCK elevation in patients treated with atypical neuroleptics in comparison with a group receiving typical neuroleptic drugs.

Methods and Subjects: The study group consisted of 90 adult (19–65 years) patients with primary diagnosis of major mental illnesses who had began their oral neuroleptic treatment (clozapine [n=23], olanzapine [n=18], risperidone [n=20], haloperidol [n=13] or perphenazine [n=16]) according to the decision of the treating physician. Patients suffering from any clinically significant physical disorder or receiving parenteral concomitant medication or electroconvulsive treatment were excluded from the study. Blood samples for CK determinations were also collected at weeks: +1, +2, +3, +4, +8, +12 and every 3 months thereafter. Treatment compliance was periodically assessed using the reports of nursing staff and mental status deviations were monitored using the Brief Psychiatric Rating Scale (BPRS).

Results: Within first 6 months of study, 5.5% of evaluated patients (n=5, three with clozapine, one with olanzapine and one with perphenazine) of patients were found to have SCK levels above upper normal limits: 338.7±34.2 IU/L (mean±SD), in range 290–370 IU/L. No correlation between SCK levels and BPRS scoring in these patients was found.

Discussion and Conclusions: The frequency of SCK elevation in patients treated with neuroleptics that was found in our sample is compatible with previous reports (2–10%), however, the magnitude of SCK elevation was less than reported previously (1.000–10.000 IU/L). Most recently, Meltzer hypothesized a possible role of 5-HT2A-receptor blockade, which is common to the atypical antipsychotic agents, in the occasional increases in SCK activity observed with these agents. Fluctuating levels of endogenous 5-HT2A receptor stimulation might cause the increase in SCK activity during psychotic episodes, while additional neuroleptic blockade, in vulnerable individuals, might be a cause of neuromuscular abnormalities. The role of atypical and typical antipsychotic agents in producing SCK elevations, its' frequency, magnitude and pathophysiological significance will be discussed.

References

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P.2.118 How to compare the safety and efficacy of antipsychotic therapies, with a lack of head to head trial evidence; the example of olanzapine versus quetiapine

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Objectives: The aim of this meta-analysis was to directly compare the effects of olanzapine and haloperidol and indirectly compare olanzapine and quetiapine via haloperidol when used for the treatment of schizophrenia. The indirect comparison provides a method to compare the safety and efficacy of different medications in the absence of head to head studies. As many of the trials were fixed in their dosing regimes this analysis examines the effect that varying the dose of all three antipsychotics has on the results.

Methods: Trials of olanzapine versus haloperidol and quetiapine versus haloperidol were identified. Each was compared using all doses of olanzapine, quetiapine and haloperidol. A second comparison looked at clinically relevant doses of the three antipsychotics. Clinically relevant doses were based upon the approved Product Information for each drug.

Results: Both the analysis with all doses of haloperidol and olanzapine and the clinically relevant dose analysis showed that for the efficacy and tolerability outcomes measured, olanzapine was statistically superior to haloperidol.

When comparing olanzapine and quetiapine via haloperidol, the all dose analysis results highlighting the superior efficacy and safety of olanzapine include, more dropouts due to lack of efficacy for quetiapine, greater change in PANSS total for olanzapine and better CGI severity score. The superior efficacy and safety of olanzapine, when analysing trials using clinically relevant doses of olanzapine (10–15mg), quetiapine (300–450mg) and haloperidol (5–15mg), is shown by statistically more dropouts for any reason and due to lack of efficacy for quetiapine, and a higher likelihood of response and a better improvement in PANSS total score for olanzapine.

Conclusions: The analysis of clinically relevant doses is considered to be most informative as it looks at efficacy and safety in patients taking doses of the drugs most likely to be used in clinical practice. In fixed dose trials sub or supra-therapeutic levels of the study drug can be used which could increase or decrease side effects and efficacy of therapy.