(68.1%) did not differ significantly (60.5%) from the control group. Overall, significantly more adherent patients responded to 80-90% treatment (82.5%) as compared to non-adherent patients (55.8%) (p<0.001). Conclusions This study indicates that treatment adherence increases when using an educational compliance programme. Furthermore there is a strong relationship between treatment adherence and response.

References


P.2. Psychotic disorders and antipsychotics

The effects of antipsychotic agents on skeletal muscle of psychiatric patients as it evidences by their serum creatine kinase activity

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Background: High serum serum creatine kinase (SCK) levels, represented mostly a muscle (MM-fraction) isoenzyme activity, serve as an indicator of the possible skeletal muscle cell membrane damage. Marked elevations of SCK were observed in up to 10% of patients treated with various antipsychotic agents (1-3). It was supposed that ability of antipsychotic agents in producing hyper-CKemia could be a sensible marker of their probable muscular toxicity.

Objectives: The purpose of this study was to estimate prospectively the actual incidence and the range of SCK elevations in psychiatric patients treated with antipsychotic agents (AAA) in comparison with a group receiving typical neuroleptic drugs (TN).

Methods and Subjects: To date, we have screened for this ongoing study 360 adult (19-65 years) outpatients with primary diagnosis of major mental illnesses who had been treated at our clinic according to the decision of their treating psychiatrist. Patients suffering from clinically significant physical disorders, receiving parenteral medication or electroconvulsive treatment were excluded from the study. Blood samples for CK determinations were collected at baseline, weekly during first month and every 3 months thereafter. Treatment compliance was regularly assessed using the reports of nursing staff or family members and mental status alterations were monitored using the Brief Psychiatric Rating Scale (BPRS).

Results: Due to strict inclusion criteria 208 patients were not enrolled to the study. We recruited to the study group 152 eligible patients receiving clozapine [n=33], olanzapine [n=31], risperidone [n=29], quetiapine [n=15], haloperidol [n=19] or perphenazine [n=25]. During the first 12 months of study, 926 blood samples were collected and 8 evaluated patients, treated with clozapine (n=5), olanzapine (n=2), perphenazine (n=1) were found having recurrent SCK levels above upper normal limits: 455.5±48.7 IU/L (mean±SD), in range 280-650 IU/L. No correlation between SCK levels and BPRS scoring changes in these patients was found.

Discussion and Conclusions: The preliminary results of this comparative study indicate that incidence of hyper-CKemia in patients treated with neuroleptics in our sample (5.2%) is compatible with previous reports (2-10%). However, the magnitude of hyper-CKemia is less than reported previously (1000-10000 IU/L). The severity of the psychiatric symptoms do not correlate with the SCK elevations. Of great interest, that the vast majority (seven of the eight) hyper-CKemic patients were treated with AAA (clozapine and olanzapine). We suppose, that 5-HT2A-receptor blockade, which is common to the AAA, may be involved (1-3), and, in some vulnerable individuals, might cause a damage of the skeletal muscle membrane. Further investigation of probable neuroleptic-induced neuromuscular dysfunction and its mechanisms in patients with major mental disorders is certainly warranted.

References


haloperidol. LI was measured in a thirst motivated conditioned emotional response procedure by comparing suppression of drinking in response to a tone in rats which received 9 (nonexposed) or 40 tone presentations (preexposed) followed by either 2 or 5 tone-foot shock pairings. Control rats showed LI with 40 preexposures and 2 conditioning trials, but raising the number of conditioning trials to five disrupted LI. In contrast, NAC-BlA and OFC lesioned rats persisted in exhibiting LI under the latter conditions. Lesion-induced persistent LI was reversed by clozapine but not by haloperidol. These results demonstrate that LI is sensitive to NAC, BlA and prefrontal cortex damage, but that this is manifested in LI perseveration rather than LI disruption. NAC, BlA and OFC induced persistance of LI is consistent with other reports of perseverative behaviors following lesion to these structures. Our finding that this abnormality was normalized by clozapine but not by haloperidol supports the relevance of lesion-induced LI perseveration to negative symptoms. Since these structures are reciprocally connected and reported to be involved in the pathophysiology of schizophrenia, the results may be relevant to the neural circuitry underlying negative symptoms of schizophrenia.

P2.003 Cognitive performance and side effects under clozapine and amisulpride treatment in patients with chronic schizophrenia

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Purpose: To study cognitive performance, quantitative EEG and medication side effects in patients with chronic schizophrenia treated with either clozapine or amisulpride. Clozapine is a multireceptor-antagonist with a potent anticholinergic efficacy, whereas amisulpride is a rather selective D2/D3-antagonist.

Methods: This cross-sectional study was performed in two groups of each 12 patients with chronic schizophrenia, who were matched with respect to age, sex, educational level and disease severity. They had to be in stable psychopathological conditions under maintenance medication with either clozapine or amisulpride; no additional psychotropic medication was allowed. The findings in the patients were compared with those in an age-, sex- and education-matched control group. Cognitive performance was examined by means of the Wisconsin Card Sorting Test (WCST) and the Continuous Performance Test (CPT); working memory was assessed by means of the digit-span subset of the Wechsler Memory Scale, verbal memory by the Auditory Verbal Learning Test (AVLT) and visual memory by the delayed reproduction of the Taylor Figure.

Results: The patients under clozapine treatment had a significantly poorer visual memory measured by number and correctness of the reproduced details of the Taylor Figure (18.7±8.2) than the healthy controls (26.3±6.1; p<0.01, unpaired Student’s t-test) and the patients treated with amisulpride (25.6±6.2; p<0.04). In the EEG spectral analysis, mean alpha power was reduced in the patients under clozapine (28.0±19.9 μV²) compared to healthy controls (67.1±57.9 μV²; p<0.02) and patients treated with amisulpride (56.2±40.7 μV²; p>0.04). With respect to the side-effect profile, the patients treated with clozapine complained more frequently about constipation (6 out of 12) than the patients treated with amisulpride (1 out of 12; p=0.03, chi²-test). Patients treated with clozapine had gained considerable more weight (13.5±13.3 kg) than patients treated with amisulpride (2.3±5.4 kg; p<0.04). However, subjective quality of life was rated similarly high by both patient groups.

Discussion: Patients with chronic schizophrenia treated with clozapine show an impaired visual memory and suffer more frequently from obstipation compared to carefully matched patients treated with amisulpride. These side effects may be attributed to the anticholinergic properties of clozapine. Because of the lack of anticholinergic side effects, amisulpride treatment may be advantageous in this respect.

P2.004 Homocysteine reducing strategies improve symptoms in chronic schizophrenic patients with hyperhomocysteinemia

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Elevated homocysteine levels are a risk factor for Alzheimer’s disease as well as cerebrovascular disease. 1 Homocysteine is neurotoxic in vitro. 2 Recently, markedly elevated homocysteine levels were reported in young male schizophrenia patients 3. Since folic acid, B-12 and pyridoxine have marked homocysteine-reducing properties, we planned a study of these vitamins in schizophrenia patients selected for elevated plasma homocysteine levels. The study was approved by the Helsinki Committee (IRB) of Ben Gurion University. Chronic schizophrenia patients from the Beersheba Mental Center and affiliated clinical facilities were screened for plasma homocysteine. Patients with levels over 15μM were accepted for study after written informed consent. The design was a double-blind crossover with one tablet a day containing 2mg folic acid, 25 mg pyridoxine and 400 mg B-12. After 3 months patients were crossed over from active vitamin to placebo or vice versa. Eighteen patients entered the study, seventeen males and one female. All patients entering the study were highly symptomatic but had shown no major clinical changes for at least one month. Clinical ratings were made monthly using the Positive and Negative Syndrome Scale (PANSS) and Abnormal Involuntary Movement Scale (AIMS). Plasma was taken for homocysteine monthly. Patients improved 7.3 points more on three months of vitamin treatment than on three months of placebo (2.4 points more on the positive symptoms subscale; 1.6 points more on the negative symptoms subscale; 3.4 points more on the general psychopathology subscale). Treatment, time and crossover effects showed a significant three-way interaction (F=6.87; df=3, 48; p<0.001), with a significant main effect of 3 month treatment time (F=20.31; df=1, 16; p<0.001) and 6 month treatment time (F=15.85; df=3, 48; p<0.001). Contrast analysis (with planned comparison between the two periods of treatment) showed significant effect of vitamin treatment (planned comparison between two periods of treatment: for group that starts with placebo, F=9.24; df=1, 16; p<0.008 and for group that starts with placebo, F=11.07; df=1, 16; p<0.005). There was a significant difference between the two groups after 3 months (LSD post hoc test p<0.001). The present study suggests that specific vitamins in a specific clinical population defined by hyperhomocysteinemia may yield measurable clinical benefit. The average benefit on the PANSS compares favorably in this chronic population with, for instance, the benefit of a new atypical antipsychotic over a classic antipsychotic.