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Methods: this prospective clinical study included 106 patients with DD diagnosed by ICD 10 criteria for DD, who are randomly divided into control (50 patients) and experimental group (56 patients). Antipsychotic were tested, and patients were observed for 6 months in hospital and extra hospital (outpatients) conditions, according to specially designed protocol, which include Positive and Negative Symptom Schedule Scale (PANSS) and Global Clinical Impression Scale (CGI 1–4). Control group was treated with haloperidol and experimental group was treated with risperidone. Both groups were treated with augmentation therapy of benzodiazepines, valproates, trihexyphenidyl, etc, according to their symptoms.

Results: 32.14% of patients in experimental and 34% in control group were man, and 67.86% of patients in experimental and 66% in control group were women. Middle age was 43.71±11.29 in experimental, and 42.41±10.52 in control group. Patients were hospitalized once (75% in experimental; 66.67% in control group), twice (10.72% in experimental; 13.33% in control group), third or more times (14.28% in experimental; 20% in control group). Average daily dose of antipsychotic were 3.35 mg for risperidone (experimental group), and 8.78 mg for haloperidol (control group). Average pretrial PANSS score was 53.28±13.3 in experimental, and 54.2±13.6 in control group. Average PANSS score after 6 months was 33.42±3.2 in experimental, and 34.92±4.3 in control group. Average pretrial CGI scores and sub scores were: CGI1 (severity of illness sub score) 5.25±0.6, and CGI 58.89±6.4 in experimental group, and 5.18±0.4, and 58.12±12.8 in control group. Average CGI scores and sub scores after 6 months in experimental group were: CGI1 (severity of illness sub score) 3.1±0.1, CGI2 (global improvement sub score) 2.17±0.2, CGI3 (efficacy index) 2.14±0.4, CGI4 (adverse effects sub score) 1.27±0.06, and CGI 37.32±3.4. Average CGI scores and sub scores after 6 months in control group were: CGI1 (severity of illness sub score) 3.52±2.2, CGI2 (global improvement sub score) 2.46±1.2, CGI3 (efficacy index) 2.26±0.7, CGI4 (adverse effects sub score) 2.01±0.8, and CGI 40.84±4.2. Risperidone therapy influenced on PANSS score with statistical significance $p < 0.01$, but not more than haloperidol. Risperidone therapy improves CGI score after 6 months with statistical significance $p < 0.1$, and in comparison to haloperidol therapy with statistical significance $p < 0.01$. CGI4 (adverse effects) sub score turned to be most significantly lower in risperidone group than in haloperidol group with statistical significance $p < 0.1$.Risperidone has the same or slightly better efficacy in treatment of DD comparing with haloperidol. Percentage of adverse effects is significantly lower in RPD than in haloperidol group.

Conclusion: Risperidone has the same or slightly better efficacy in treatment of DD comparing to haloperidol, with significantly lower adverse effects rate.

References

[1] Fear F.C., Libretto E.S. Risperidone for the treatment of delusional disorder. International Journal of Psychiatry in Clinical Practice 2002; 6: 113–116.
[2] Blackwood J.N., Howard J.R., Bentall P.R., Murray M.R. Cognitive Neuropsychiatric Models of Persecutory Delusions. American Journal of Psychiatry 2001; 158: 527–539.
[3] Appelbaum P.S., Robbins P.C., Roth L.H. Dimensional approach to delusions: comparison across types and diagnoses. American Journal of Psychiatry 1999; 156: 1938–1943.

P.3.c.004 Effects of drd3 and dat gene polymorphisms on schizophrenia and response to olanzapine

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Introduction: The dopamine transporter (DAT) and dopamine receptors play a pivotal role in dopaminergic neurotransmission. The association of DAT gene variable number tandem repeat (VNTR) and Dopamin D3 receptor (DRD3) Ser9Gly polymorphisms and schizophrenia and antipsychotic response were studied before [1]. The Ser9Gly polymorphism of DRD3 receptor has been found to be associated with general susceptibility to schizophrenia. Negative studies have also been published, querying the relevance of the Ser9Gly polymorphism in schizophrenia. The majority of data on the VNTR polymorphism of the DAT seem to be consistent, suggesting no association with schizophrenia. Studies on association of these genes with antipsychotic drug response were also conflicting. Some studies revealed an association between these polymorphisms and response to antipsychotics and others do not [2,3]. We aimed to investigate the effects of DRD3 gene and DAT gene polymorphisms on schizophrenia and olanzapine response.

Methods: Our study comprised 95 unrelated subjects who strictly met DSM-IV criteria for schizophrenia and 186 controls and all were of Turkish origin. All patients were evaluated with SAPS, SANS and BPRS at the beginning of the study and at the end of six weeks. Patients were taking olanzapine 5–30 mg/day. Blood for DNA analysis were obtained and analyzed as mentioned in literature. SPSS 13.0 program was used for evaluation of data.

Results: 45 patients had ser/ser (%47.9), 37 patients had ser/gly (%39.4) and 13 patients had gly/gly (%12.8) polymorphism of DRD3 gene. 82 of the controls had ser/ser (%44.1), 85 of controls had ser/gly (%45.7) and 19 of controls had gly/gly (%10.2) polymorphism of DRD3 gene. 27 patients had 9/10 (%28.4), 56 patients had 10/10 (%58.9), 4 patients had 10/11 (%4.2), 7 patients had 9/9 (%7.4) and 1 patient had 6/9 (%1.1) tandem repeat polymorphism of DAT gene. 55 of controls had 9/10 (%44.7), 56 of controls had 10/10 (%45.5), 5 of controls had 10/11 (%4.1), 2 of controls had 9/9 (%1.6) and 2 of them had 6/9 (%1.6) tandem repeat polymorphism of DAT gene. No association was found between DAT gene VNTR and DRD3 Ser9Gly polymorphisms and schizophrenia. We also couldn't find statically significant association between response to olanzapine and DAT and DRD3 polymorphisms.

Conclusion: Recent studies have focused on the Ser9Gly polymorphism of the DRD3 gene and VNTR polymorphism of DAT gene but the results were inconclusive. DRD3 Ser9Gly polymorphism was associated with response to clozapine and risperidone. Some of the studies were mentioning that Ser9Gly polymorphism of the DRD3 gene was associated with response to negative symptoms [2,3]. Our study findings couldn't show an association between schizophrenia and olanzapine response with these polymorphisms. Despite our negative result, Ser9Gly polymorphism of the DRD3 gene and VNTR polymorphism of DAT gene might be a useful genetic marker but there is a need of studies with larger samples and longer duration.

References

[1] Arranz MJ, de Leon J. Pharmacogenetics and pharmacogenomics of schizophrenia: a review of last decade of research. Mol Psychiatry. 2007;12:707–747.
[2] Szekeres G, Kéri S, Juhász A, Rimanóczy A, Szendi I, Czimmer C, Janka Z. Role of dopamine D3 receptor (DRD3) and dopamine transporter (DAT) polymorphism in cognitive dysfunctions and therapeutic response to atypical antipsychotics in patients with schizophrenia. Am J Med Genet B Neuropsychiatr Genet. 2004;124:1–5.
[3] Xuan J, Zhao X, He G, Yu L, Wang L, Tang W, Li X, Gu N, Feng G, Xing Q, He L. Effects of the dopamine D3 receptor (DRD3) gene polymorphisms on risperidone response: a pharmacogenetic study. Neuropsychopharmacology. 2008;33:305–11.

P.3.c.005 Prolactin variations during screening for hyperprolactinaemia in patients taking antipsychotic medication

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Purpose of the study: Prolactin is elevated by antipsychotics in about a third of patients [1]. Elevated serum prolactin levels can vary by 2–3 times over periods as short as two hours [2]. There is a diurnal pattern too. External stress and physiological conditions also affect circulating prolactin. Dopamine blockade by antipsychotics stimulates prolactin release and this has been linked to sexual dysfunction, osteoporosis, hip fracture and breast cancer. This study assessed the variation in prolactin levels in a clinical sample of patients taking antipsychotics.

Methods: 13 people with clinically diagnosed schizophrenia or severe affective disorders (bipolar affective disorder, depression with psychotic symptoms) were treated with risperidone antipsychotic mono-therapy (sometimes in combination with other types of medication including antidepressants and mood stabilisers). This occurred as part of a programme of physical health assessment in which patients had routine screening for prolactin over a period of up to 2 years. There was no other reason for testing, such as pre-exiting pituitary disease, or symptoms of hyperprolactinaemia.

Blood was taken between 9am and 5pm without regard to medication dosing.

Results: There were 6 males and 7 females. All took risperidone and attended a community mental health clinic. Three took Risperdal Consta long acting injection. Oral doses ranged from 1–6 mg daily. Consta injection doses ranged from 25–50 mg fortnightly (see table 1.) 7 patients had normal prolactin tests (local prolactin upper limit of normal concentrations were 550mIU/l for males and 600mIU/l for females on a Siemens Advia Centaur with inter-assay coefficient of variation of 5% at mean prolactin concentration of 510mIU/l). 6 patients had hyperprolactinaemia. 2/3 patients on Risperdal Consta had hyperprolactinaemia. All patients with hyperprolactinaemia and more than one prolactin result showed variability of hyperprolactinaemia with at least one normal prolactin result.

Conclusions: This study reveals heterogeneity over time for prolactin results in a clinical sample of people taking risperidone for severe mental illness. Patients with a normal initial prolactin were less likely to have measures repeated. Patients with repeated testing were more likely to display hyperprolactinaemia (5/8) than those with a single test (1/5). This suggests that repeat testing of prolactin may be necessary to identify all patients with hyperprolactinaemia. Early morning samples prior to medication and with minimum stress from the sampling procedure may produce more consistent results. However, variations of up to 300% in 2 hours have been found in hyperprolactinaemic patients [2]. Compliance might be considered to be important too, but 2 patients known to be compliant with depot Consta also showed variation between hyperprolactinaemia and normal results.

Medication induced hyperprolactinaemia has been reported as a risk factor in sexual dysfunction, osteoporosis and breast cancer. A single prolactin result is insufficient to help clinicians assess the individual risk of hyperprolactinaemia in patients and repeated testing is more likely to represent the existence and degree of medication-induced hyperprolactinaemia. The variation in prolactin over time may be relevant to the prediction of long-term side effects and should be considered in future research.

Table 1. 13 patients and prolactin results. High prolactin results in bold type.

No./sex	Dose oral, mg/d	Dose Consta, mg/14 d	High/normal	Variable	result 1, mIU/l	result 2, mIU/l	result 3, mIU/l	result 4, mIU/l	result 5, mIU/l
1 M	4	25	H	V	**920**	422	**720**	274	**637**
2 F	4		H	V	**735**	**1680**	206		
3 M	4		H	V	**739**	516	**677**		
4 F	6		H	V	**1159**	52			
5 F	1		H		**7211**				
6 M	0	37.5	H	V	**736**	495			
7 M	4		n		370	497			
8 F	0.5		n		93				
9 M	3	50	n		161	262			
10 F	2		n		262				
11 F	4		n		277				
12 M	6		n		498	389			
13 F	4		n		225				

References

[1] Bushe, C., Yeomans, D., Floyd, T., Smith, S., 2008, Categorical prevalence and severity of hyperprolactinaemia in two UK cohorts of patients with severe mental illness during treatment with typical and atypical antipsychotics. J Psychopharmacol Suppl (in press).
[2] Boyar, R.M., Kapen, S., Finkelstein J.W., Perlow, M., Sassin J.F., Fukushima, D.K., Weitzman, E.D., Hellman, L., 1974, Hypothalamic-pituitary function in diverse hyperprolactinemic states. J Clin Invest 53, 1588–1598.

P.3.c.006 Cognitive function and antipsychotic treatment in chronic schizophrenia

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Background: Many research in field of neuropsychopharmacology in schizophrenia indicated beneficial influence of atypical antipsychotic treatment on cognitive function [1], however latest CATIE study showed that differences between influence of typical and atypical antipsychotics on patients cognitive and psychosocial outcome is not as significant as described in previous works [2].

Purpose of the study: The aim of this study was to assess the relationship between type of current antipsychotic treatment (typical or atypical antipsychotics) and cognitive, clinical and