elevated waist circumference (male ⩾ 102 cm; female ⩾ 88 cm) for Ccaucasians, elevated triglycerides ⩾150 mg/dL or receiving drug treatment, decreased high-density lipoprotein cholesterol Male <40 mg/dL, female <50 mg/dL or receiving drug treatment, elevated blood pressure ⩾130/⩾85 mm Hg ⩾130/⩾85 mm Hg or receiving drug treatment, elevated fasting plasma glucose ⩾100 mg/dL or receiving drug treatment.

Results: Prevalence of MS was 48%. MS was associated with body mass index (BMI) and there were no association with age, duration of disease and another parameters.

Conclusion: Prevalence of MS was high in our sample. Regular monitoring and treatment of metabolic abnormalities are essential in patients treated with clozapine. Further studies with larger samples are necessary to replicate this findings.

P-02.18 A comparison of the effect of proton pump inhibitors (PPIs) omeprazole and rabeprazole on plasma clozapine concentrations in patients with schizophrenia.

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Objective: The aim of this study was to compare the effects of rabeprazole and omeprazole on the CYP1A2-mediated clearance of clozapine.

Methods: A cross-over study design was used for this study. 20 patients from Macquarie hospital who were receiving clozapine and rabeprazole (with no other interacting medications) for at least 3 weeks were recruited into this study. Blood samples were taken at 30 min, 1 hr, 2 hr and 12 hr after a dose of clozapine. Rabeprazole was then changed to omeprazole. After at least 1 month blood samples were again collected at the above corresponding intervals after clozapine. The plasma concentrations of clozapine and norclozapine were determined by HPLC. Abbottbase Pharmacokinetic Systems (PKS) Software, which utilises Bayesian forecasting, was used to estimate pharmacokinetic parameters of clozapine. The ratio of norclozapine/clozapine at trough level was used to reflect CYP1A2 activity.

Results: No difference was observed in clozapine clearance and CYP1A2 activity during concurrent therapy with either rabeprazole or omeprazole.

Conclusion: Omeprazole and rabeprazole do not induce the CYP1A2-mediated clearance of clozapine when used at conventional therapeutic dosage (<40 mg/day) and that switching from omeprazole to rabeprazole or vice versa does not require that the dose of clozapine to be adjusted.

P-02.19 A two-year prospective follow-up study of lower urinary tract symptoms in patients treated with clozapine

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Objective: Urinary incontinence and nocturnal enuresis are well-known side effects of clozapine medication. However, clinical experience has shown that patients also suffer from diverse lower urinary tract symptoms (LUTS). The natural course of clozapine-related LUTS is quite unclear. Thus, a longitudinal follow-up study of the wide range of LUTS is needed.

Methods: A total of 101 subjects who was taking clozapine initially participated. Their LUTS were evaluated with the International Prostate Symptom Score (IPSS), other questionnaires and the medical records review. After two years, 87 of the original subjects could be contacted and the status of their LUTS was re-evaluated.

Results: The average IPSS total was 7.4±5.9 at the initial evaluation. Though only 11 subjects (10.9%) reported actual incontinence of the urge type, 42 subjects (41.6%) were found to have clinically significant LUTS (IPSS total score ⩾ 8). No influencing factors could be found among the demographic and clinical variables. At the follow-up, the average IPSS total (7.9±6.0) and the percentage of subjects with clinically significant LUTS (43.7%) had both increased, though not statistically significantly so. About two-thirds of the subjects with significant LUTS at the initial evaluation still had similar symptoms two years later.

Conclusion: The prevalence of LUTS in clozapine-medicated patients was higher than in the general population of the same age. However, the prevalence of actual incontinence was only a quarter of that of LUTS. If the clinicians focus only on incontinence, distress from other LUTS will not receive appropriate attention. Furthermore, contrary to literature observations, clozapine-related LUTS did not remit easily but, rather, persisted even into the long-term maintenance phase. More concern and active research efforts should be directed at these troublesome and often neglected side effects.

P-02.20 Amisulpiride for the treatment of clozapine-induced hypersalivation: A preliminary study

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Objective: Sialorrhea (hypersalivation) is a common side effect occurring in 31–54% of patients receiving clozapine therapy. It usually develops early in the course of treatment and is more prominent at night.(1)There are limited numbers of previous studies of amisulpiride add-on for the treatment of clozapine-induced hypersalivation (CIH) To our knowledge here we present the first long-term study such 60 days in literature (1–3).

Methods: Nine patients with schizophrenia, receiving clozapine, had CIH. Amisulpiride (100–400 mg/day) was administered in addition to ongoing clozapine treatment (clozapine:100 mg/d to 400 mg/d). Nocturnal hypersalivation was recorded using the 5-point Nocturnal Hypersalivation Rating Scale (NHRS)(4). The NHRS was administered six times over a 60 day period; at baseline, after 7, 14, 28, 42 and 60 days. Statistical comparison of baseline, 7–14–28–42–60 day follow-up values was done using analysis of variants with repeated measures (one-way-ANOVA). Results were reported in mean values with standard deviations.

Results: At the end of the trial, following 60 days of sulpiride treatment a linear reduction in the level of CIH was reported as measured by NHRS scores. Mean (±S.D.) baseline scores were 3.22 (0.66). Mean (±S.D.) scores following 7 days of treatment were 1.77 (1.09). The difference was not significant at first week (p: 0.051) but at the following weeks a significant amelioration was shown ($p < 0.05$). Mean (±S.D.) scores following 60 days of treatment were 0.4 (0.5) [$F(8,526)$, $p < 0.05$]. None of the patients reported specific side effects except one patient who complained of sedation and dropped out at the 28. days of study. Other measures included the Scale for the Assessment of Positive Symptoms, the Scale for the Assessment of Negative Symptoms, Clinical Global Impression Scale and Simpson-Angus Scale, weight, prolactin level. With amisulpride add-on treatment, there was a significant increase in the prolactin level as an indicator of compliance but the results of other scales were not significant.

Conclusion: CIH is a common and socially stigmatizing side effect, which results in poor treatment compliance. Our findings suggest that amisulpiride addition to clozapine therapy may ameliorate CIH. In this preliminary study we examined the effect of amisulpiride addition on CIH in a small sample size. A larger sample sized study is presently being performed to further investigate the clinical results of combined therapy both on hypersalivation and on other parameters.

P-02.21 Aripiprazole augmentation of clozapine in treatment-resistant schizophrenia: An open clinical observation

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Objective: Therapeutic options for patients with treatment-resistant schizophrenia are limited. In such cases combined application of atypical antipsychotic drugs is an often used strategy. We tested the hypothesis that the combination of aripiprazole and clozapine would lead to an improvement in these patient group.

Methods: 11 patients with treatment-resistant schizophrenia participated in this clinical observation and recieved a combination of aripiprazole and clozapine. Patients had to have remained on a stable dose of clozapine for at least 6 months in order to ensure a reasonable opportunity to respond to clozapine monotherapy. Clinical status was evaluated at baseline, 3 months and 6 months follow-up using the Brief Psychiatric Rating Scale (BPRS).

Results: All patients completed 6 months combination treatment. There was a significant reduction in the mean BPRS score of 8 patients over the 6 months of combination treatment. The mean improvement of the BPRS over the 6 months was 28.6%. The augmentation of aripiprazole in clozapine treated patients did not result in a corresponding increase in side effects. There was a significant decrease in weight and body mass index comparing baseline to study endpoint.

Conclusion: The combined application of clozapine and aripiprazole follows a neurobiological rationale and appears to be safe and well tolerated without increasing the risk of side effects.

P-02.22 Assessment of cognition in nonaffected full biological siblings of patients with schizophrenia

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Objective: To assess neurocognitive functions in nonaffected full biological siblings of patients with schizophrenia and to compare these neurocognitive functions with normal healthy controls.