CASE REPORT

Combined use of amisulpride and clozapine for patients with treatment-resistant schizophrenia

Brian Cook and Gerry Hoogenboom

Objective: *To report on a trial of adding amisulpride to clozapine.*

Methods: *Description of six cases.*

Results: *Six patients who had been on clozapine were commenced on amisulpride. All patients had had unwanted effects with clozapine, particularly sedation, hypersalivation, or weight gain. Five patients reported a high level of satisfaction with the regimen, having a reduction in the level of sedation and improvement in levels of motivation and energy, without recurrence of positive symptoms.*

Conclusion: *The combined use of amisulpride and clozapine would appear to be an appropriate and beneficial treatment.*

Key words: *amisulpride, clozapine, polypharmacy, treatment-resistant schizophrenia.*

In prescribing psychotropic medication, there are several guiding principles. These include (i) aim to eradicate or reduce the severity of the symptoms of mental illness; (ii) avoid polypharmacy; and (iii) manage side-effects of medication when they occur. We support these principles however, as noted by Stahl (1999),[1] the practice of prescribing two or more antipsychotic agents is relatively common.

Unwanted effects of clozapine reported by patients attending the Bundaberg Clozapine Clinic, Queensland, include sedation, weight gain, hypersalivation and the need to have monthly blood tests and monitoring. However, most patients also report a willingness to accept these, understanding that they also benefit from the wanted effects of the drug. When a number of patients approached the clinic requesting a review of their clozapine medication, the treating psychiatrist and clozapine coordinator counselled them about their current medication and mental health status and provided details regarding an alternative, amisulpride (which became available in Australia in September 2002). This paper describes our experience with these patients.

Three patients, A, B, and C, expressed a desire to cease clozapine and start amisulpride (Table 1). A transition programme was set up to slowly reduce clozapine while introducing amisulpride, including weekly reviews to monitor the effects. The initial aim was to cease clozapine and switch to amisulpride. During the transition, it became evident that amisulpride alone did not adequately treat the symptoms and all experienced a recurrence of delusional thoughts and auditory hallucinations. Two of the patients (A and C) requested to be placed back on clozapine in week 3 of transition. Patient B persisted with the trial but after 6 weeks it became evident that she was deteriorating (she experienced side-effects of amisulpride and recurrence of acute psychosis) and was recommenced on clozapine. Because these patients were now on amisulpride, clozapine was retitrated to a dose approximately equivalent to half their pre-trial dose. Weekly monitoring continued and the patients reported reduction in

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acute symptoms. They returned to their state of health when on clozapine alone and in some ways were improved due to a lack of sedation and hypersalivation and an increase in motivation.

As a result of the experience with the first three patients, three other patients (D, E and F), who had concerns regarding side-effects of clozapine but had not asked for a change of medication, were counselled and given the option of adding amisulpride to their medication and reducing clozapine. Amisulpride was gradually introduced and clozapine reduced slowly. Patients D and E reported satisfaction with the combination treatment. Patient F requested to

Table 1: Information about patients on both clozapine and amisulpride

Patient	*Gender*	*Age (years)*	*Diagnosis*	*Pre-trial dose*	*Years on clozapine*	*Current dosages*
Phase 1						
A	Male	46	PS	C: 500 mg/day	9.4	C: 300 mg nocte A: 200 mg a.m.
B	Female	30	PS	C: 600 mg/day S: 200 mg/day	1.4	C: 200 mg nocte A: 200 mg a.m.; 200 mg noon S: 100 mg a.m.
C	Male	32	S	C: 400 mg/day	6.7	C: 200 mg nocte A: 200 mg a.m.
Phase 2						
D	Male	54	SD	C: 700 mg/day	7.5	C: 400 mg nocte A: 200 mg a.m.
E	Male	26	PS	C: 450 mg/day S: 100 mg, a.m.	4.0	C: 250 mg a.m. A: 200 mg a.m. S: 100 mg a.m.
F	Male	35	S	C: 400 mg/day	8.1	C: 200 mg nocte A: 200 mg a.m.

PS, paranoid schizophrenia; S, schizophrenia; SD, schizoaffective disorder; C, clozapine; A, amisulpride; S, sertraline hydrochloride.

Table 2: Patient feedback about combined clozapine–amisulpride therapy

Patient	*Feedback*
A	'The Solian [amisulpride] treatment alone did not work and I experienced symptoms with paranoid thoughts returning. However, combined treatment has given me back my life, that's the way I feel about it. I never really knew how much the clozapine was sedating me, I had to sleep during the day and now I have enough energy to do the things I need to do. You would be surprised at how much I have achieved recently.'
B	'After the first 12 months on clozapine I felt really well, but then I started to deteriorate. I don't know why really. When I was on Solian [amisulpride] alone, I had side-effects. I felt OK but my symptoms returned. On combined therapy, I have noticed less sedation, but I am still not as well as I was after the first 12 months on clozapine.'
C	'I think I feel better, I feel more comfortable going into society, not as panicky in some social situations and a definite reduction in the level of sedation.'
D	'Thank you, I am very pleased with the new drug, Solian [amisulpride]. I feel so much better, I don't feel sedated, I am walking more, don't have to sleep during the day and the silly ideas have not come back. Thank you.'
E	'I am very happy with the new medication, I don't feel anywhere near as tired as I did on the Clozaril [clozapine] alone.'
F	'I don't like the effects of the Solian [amisulpride]. I don't know how to explain it but I feel strange. I am less tired but I would still rather be on Clozaril [clozapine] alone.'

cease amisulpride after 2 weeks, stating that although he had more energy and was less sedated, he did not like its effects overall.

Patient feedback regarding the combination therapy is given in Table 2.

DISCUSSION

While we generally advocate monotherapy, the experience gained and feedback provided by the patients appears to be positive regarding the combination of clozapine and amisulpride. During the trial, clinical staff maintained close contact with patients through clinic visits and phone contact to ensure that any untoward effects could be dealt with. All patients were encouraged to discuss the medication trial with their families, and clinical staff also discussed the issues with the primary caregiver.

In conclusion, the combination of clozapine and amisulpride appears to be beneficial. Meltzer and Kostakoglu raise the issue of efficacy in combining antipsychotics,[2] the decision to publicize our experience is made in the hope that doing so will lead to more research and debate on polypharmacy generally and, more particularly, on the potential benefits and/or dangers of combining antipsychotic medication.

REFERENCES

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