Psychiatria Danubina, 2015; Vol. 27, No. 3, pp 283-284 © Medicinska naklada - Zagreb, Croatia Case report

CLOZAPINE-INDUCED PARALYTIC ILEUS

Helena Sarac¹, Neven Henigsberg² & Lucija Bagaric-Krakan³

 ¹Department of Neurology, University Hospital Center Zagreb, Zagreb, Croatia
²Medical School University of Zagreb, Croatian Institute for Brain Research, Department of Psychiatry, Zagreb, Croatia
³Department of Psychiatry, University Hospital Center Zagreb, Zagreb, Croatia

received: 4.3.2015;

revised: 17.6.2015;

accepted: 4.7.2015

* * * * *

INTRODUCTION

Clozapine is an atypical antipsychotic drug with minimal extrapyramidal toxicity, used in the management of patients who are unresponsive or intolerant to at least two different antipsychotics (McEvoy et al. 2006). Ileus is a rare but life-threatening side-effect of clozapine treatment (Palmer et al. 2008). The largest study investigating risk factors of ileus in psychotic patients showed that increasing age and treatment with higher dosage of clozapine were associated with an increased risk of fatal ileus (Nielsen & Meyer 2012). The treatment of clozapine-induced ileus comprises of discontinuation with potential rechallenge of the drug (Palmer et al. 2008). We describe here a patient with treatmentresistant depressive psychosis and extrapyramidal symptoms, who developed paralytic ileus shortly after the initiation of clozapine.

CASE REPORT

A 60-year-old woman presented with extrapyramidal symptoms and psychotic-like symptoms. She has a 12year history of depression with several psychotic episodes. The patient had been treated previously with different psychotropic drugs (paroxetine, duloxetine, agomelatine, maprotilin and olanzapine) in a various psychiatric structures. Recently, the patient was prescribed 80 mg/day of ziprasidone. During the initial period of ziprasidone use, she did not develop any sideeffect. After three months, the patient presented to neurology clinic due to distressing tremor, rigiditiy, agitations and delusions. At baseline visit, her Modified Simpson-Angus Scale (MSAS) (Simpson & Angus 1970) score was 11 and her Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham 1988) score was 87. The treatment with clozapine was initiated and gradually increased dose to 150 mg/day, while ziprasidone was gradually tapered and eventually discontinued. With clozapine, her psychosis improved significantly after two weeks. At day 10, she became febrile (38.5°C), tachycardic (120 beats/min) and hypotensive. She complained abdominal fullness and nausea. Her white blood cell counted 10.2 and C-reactive protein level became elevated. A chest X-ray showed pleural

effusion. Colonocsopy did not provide evidence of pathological obstruction. Abdominal CT scan led to a diagnosis of paralytic ileus, most likely related to clozapine treatment. Clozapine was discontinued, and conservative management with prostigmin injection, colonic lavement and fluid intake, was performed with a good clinical response within 24 h. She was then put on quetiapine 50 mg/day and then was increased in increments of 50 mg/day up to 300 mg/day. After three weeks, her parkinsonian syndrome and psychosis improved significantly. She remained free of her symptoms at the 3-month follow-up visit.

DISCUSSION AND CONCLUSION

Clozapine is unique in its lack of producing extrapyramidal symptoms, even at high doses, compared to other antipsychotics. Clozapine's highest anticholinergic property is though to be the main cause of paralityc ileus. Mean time from initiation of clozapine to onset of ileus is four years (Palmer et al. 2008). Clozapine-related adynamic ileus was reported to be dose-dependant and may occured several days after initiation of treatment (Fayad & Bruijnzeel 2012). Compared with these cases, the clinical findings in our patient are unique: (1) onset of ileus shortly after initiation of low dose of clozapine and absence of other anticholinergics which could contribute to combined effects to ileus, at the time of decompensation and (2) slow titration and low dose of clozapine. Patients receiving clozapine and/or other psychotropics associated with significant muscarinic properties should undergo careful monitoring of bowel function and timely use of laxatives, and early refferal of constipated patients, because early recognition can prevent life-treathening pathologic process and fatal outcomes and enable appropriate management.

A limitation of the current study was in that we have not provided plasma levels of clozapine. Although clozapine concentrations in plasma correlated with dose in most cases, plasma levels of clozapine varies substantially and there is considerable variability in the response achieved at any given clozapine concentration. A clozapine concentration of 370 ng/ml was reported the optimal cutoff for distinguishing responders from nonresponders (Spina et al. 2000). Because many patients respond well at plasma clozapine concentrations in a low range, higher plasma clozapine concentrations require in some patients use of high dosages and imply an excessive risk of side effects including ileus. The incidence of side effects was twice as high at clozapine concentrations above 350 ng/ml compared with lower concentrations. Increasing dosage to achieve plasma levels above 400 ng/ml may be especially indicated in patients without adverse effects who failed to respond at lower or standard dosages (Spina et al. 2000).

Acknowledgements: None.

Conflict of interest: None to declare.

References

1. Fayad SM & Bruijnzeel DM: A fatal case of adynamic ileus following initiation of clozapine. Am J Psychiatry 2012; 169:538-9.

- 2. McEvoy JP, Lieberman JA, Stroup TS, Davis SM, Meltzer HY, Rosenheck RA et al.: Effectiveness of clozapine versus olanzapine, quetiapine, and risperidone in patients with chronic schizophrenia who did not respond to prior atypical antipsychotic treatment. Am J Psychiatry 2006; 163:600-10.
- 3. Nielsen J & Meyer JM: Risk factors for ileus in patients with schizophrenia. Schizophr Bull 2012; 38:592-8.
- 4. Overall JE & Gorham DR: The Brief Psychiatric Rating Scale (BPRS): recent developments in ascertainment and scaling. Psychopharmacol Bull 1988; 24:97-9.
- Palmer SE, McLean RM, Ellis PM & Harrison-Woolrych M: Life-threatening clozapine-induced gastrointestinal hypomotility: an analysis of 102 cases. J Clin Psychiatry 2008; 69:759-68.
- 6. Simpson GM & Angus JWS. A rating scale for extrapyramidal side effects. Acta Psychiatr Scand 1970; 212(Suppl 44):11-9.
- Spina E, Avenoso A, Facciolà G, Scordo MG, Ancione M, Madia AG et al.: Relationship between plasma concentrations of clozapine and norclozapine and therapeutic response in patients with schizophrenia resistant to conventional neuroleptics. Psychopharmacology 2000; 148:83-9.

Correspondence: Helena Sarac, MD, PhD Department of Neurology, University Hospital Zagreb Kispaticeva 12, 10000 Zagreb, Croatia E-mail: helenasarac57@gmail.com