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Risperidone and Megacolon

D K Lim, R Mahendran

ABSTRACT

Risperidone is an atypical anti-psychotic medication with both 5HT2 receptor and D2 dopamine receptor antagonism. Its use has been reported to be generally safe with very few gastro-intestinal (GI) adverse or side effects. In this paper, we describe a case of megacolon associated with the use of risperidone. A 44-year-old man suffering from schizophrenia was treated with risperidone and developed gross abdominal distension after twenty-five days. Abdominal X-ray and colonoscopy showed megacolon. He improved following a surgical decompression and a reduction of risperidone dosage. We discuss the neuro-electro-physiological mechanisms of gastro-intestinal motility and conclude that the risperidone-associated megacolon may be dose-related and that there should be a heightened awareness of such possible GI complication when using risperidone.

Keywords: Risperidone, megacolon, dose-related, constipation, schizophrenia

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Department of General Psychiatry Institute of Mental Health/ Woodbridge Hospital Singapore 539747

D K Lim, MBBS, MMed (Psy), FAMS
Consultant Psychiatrist

R Mahendran, MBBS, MMed (Psy), FAMS
Senior Consultant Psychiatrist

Correspondence to:
Dr D K Lim
National Centre for Treatment & Development
Christchurch School of Medicine
University of Otago
P.O.Box 4345
Christchurch,
New Zealand
Tel: (64) 3-3640480
Fax: (64) 3-3641225
Email: dominic.lim@chmeds.ac.nz

INTRODUCTION

Risperidone, an atypical anti-psychotic medication, has predominant central serotonin 5HT-2 receptor antagonism, together with dopamine D-2 receptor blockade, histamine H-1 and adrenergic alpha-1 and alpha-2 receptor actions[1,2]. In short-term controlled studies of patients with schizophrenia, risperidone has been shown to be effective in treating both the positive and negative symptoms with a low incidence of extrapyramidal side-effects compared to classical neuroleptics[3,4]. Thus far, no known major gastro-intestinal (GI) adverse effects or complications have been reported with the use of risperidone. In a study involving 338 schizophrenic subjects treated with risperidone ranging from 2 to 16 mg, the rate of constipation was found to be zero[3]. In another multi-national, multi-centre, double blind efficacy trial involving 1,362 chronic schizophrenic patients on risperidone ranging from 1 mg to 16 mg in dosage, the rates of constipation reported were similarly low, ranging from 13.7% to 15.4%[4].

Table I. Etiology of megacolon.

Congenital
• Aganglionic megacolon (Hirschprung's disease)
• Chronic idiopathic megacolon
Acquired
• Trypanosoma Cruzi infection (Chagas' disease)
• Severe neurologic disorders – *Cerebral atrophy* – *Spinal cord injury* – *Parkinson's disease*
• Myxoedema
• Infiltrative disease – *Amyloidosis*
• Scleroderma
• Narcotic drugs – *Morphine* – *Codeine*
• Chronic constipation

Megacolon, or giant colon is characterised by massive distension of the colon usually accompanied by severe constipation. This condition can be either congenital or acquired and is seen in all age groups (Table I)[5]. We report an unexpected case of megacolon associated with the use of risperidone.

CASE REPORT

Mr A, a 44-year-old Chinese man was diagnosed with schizophrenia following his index admission to our hospital. He presented with a two-year history of auditory hallucinations, delusions of reference and charm against his wife who had since left him, along with socio-occupational deterioration. He had no past history or family history of any psychiatric treatment, gastro-intestinal disease or surgical problems. Physical examination did not reveal any abnormality and routine blood investigations were all normal.

With his consent, he was enrolled in an open clinical trial of risperidone, starting with 0.5 mg twice daily. The dosage was steadily increased at 1 mg per week to 3.5 mg per day as part of the research protocol,

which also included routine screening of side effects. He began to improve mentally and the positive schizophrenic symptoms resolved after a week. While in the ward, he was eating and sleeping well. No complaints of constipation or abdominal discomfort were elicited until 25 days after starting risperidone when he was noted to have abdominal distension with overflow diarrhoea. In addition, the patient did not present with any history of vomiting, melaena, bleeding per rectum, systemic symptoms or other physical discomfort. The patient's usual bowel habit was once every three to five days. Immediately upon admission and before he consented to the trial of risperidone, he received an intra-muscular injection of Haloperidol of 5 mg, a total of 10 mg of Trifluoperazine and 4 mg of Benzhexol for mental state stabilisation.

Abdominal examination revealed non tender left iliac fossa fullness while abdominal X-ray showed faecal shadowing of the entire large intestines with gross proximal colon dilation with classical fluids level resembling megacolon. No evidence of small bowel dilatation was found. Despite two courses of fleet enema and the reduction of risperidone to 2 mg per day over the next one week, the distension and megacolon did not subside. The patient was referred for a surgical assessment and the colonoscopy showed a dilated megacolon filled with liquid faeces, necessitating acute surgical decompression and short term lactulose use. He was rechallenged with risperidone which was maintained at 1 mg per day with good remission of his schizophrenic symptoms and he experienced no further GI problems.

DISCUSSION

Gastro-intestinal motility may be affected by numerous complex neuro-electro-physiological mechanisms of varying significance, which were interactive and integrative in terms of morphology and function. Dysfunction and abnormal regulation of these contributory factors on GI motility mechanisms may result in constipation. Animal studies indicate that central D-I and D-2 dopamine blockade[6], cholinergic and muscarinic receptors affecting motility of proximal colon[7] can effect GI mobility. Other factors include: an alteration of excitatory and inhibitory neurotransmission[8], electro-physiological mechanisms affecting the coordination for continence and defaecation[9,10], neuro-humoral control[11], exercise[12] (which affects small bowel transit and possibly colonic motility), intramural load[13], local paracrinal neuro-modulator actions[14], degenerative neuropathy of myenteric plexus[15] and myxoedema[16].

Conventional neuroleptics and anticholinergic medications have been known to cause constipation and GI motility problems, presumably via the stimulation of parasympathetic nervous system innervating the gastro-intestinal tract. However, risperidone has no known anticholinergic action[4].

While accepting the need for urgent intervention, it would have been better if more elaborate physiological work-ups were done to delineate the other possible causes of the megacolon. While direct attribution might be debatable, risperidone appeared to be the most likely contributing factor in the development of megacolon in this patient given that there was no underlying GI problem such as idiopathic chronic constipation. If indeed it was causal, this would be the first reported case of megacolon associated with risperidone and the effect appeared to be dose-related.

As a precaution, heightened awareness should be directed to persons who have pre-existing chronic constipation or colonic mobility problem even while prescribing an atypical antipsychotic medication such as risperidone, the reasons being that acute toxic megacolon and further complications may potentially result from non-recognition and delayed intervention.

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