THE USE OF RISPERIDONE IN ADULTS WITH ASPERGER SYNDROME

R. T. Alexander, D. M. Michael and S. K. Gangadharan

Introduction

Risperidone is an atypical anti-psychotic that has been used in the management of behavioural problems in those with autistic disorders. A number of open label studies and case reports have been published of children or adolescents with autistic spectrum disorders who were treated with this drug (Purdon et al., 1994; McDougle et al., 1995; Demb, 1996; Fisman et al., 1996; Fisman and Steele, 1996; Hardan et al., 1996; Frischauf, 1997; Horrigan and Barnhill, 1997; Perry et al., 1997; Findling et al., 1997; McDougle et al., 1997; Nicolson, 1998). It is reportedly superior to placebo in reducing repetitive behaviour, aggression, anxiety, nervousness, depression, irritability, and overall behavioural symptoms of autism. In adults with an autistic spectrum disorder, Risperidone appears to be equally effective. Indeed, a double blind, placebo controlled study (McDougle et al., 1998) on 31 adults treated with the disorder found that Risperidone was superior to placebo.

Asperger syndrome is a condition within the autistic spectrum where language development is relatively normal. Although people with this diagnosis may function at a higher level than those with core autism, there will be clear deficits in communication and social functioning. Motor dysfunction manifesting as general clumsiness or repetitive movements may also present more often than in people with autism. The diagnostic criteria for this disorder which include severe impairment in reciprocal social interaction, an all absorbing narrow interest, imposition of routines on others, speech and language problems and non-verbal communication problems have been well elucidated (Gillberg, 1995).

There is very little published information on the use of Risperidone in adults...
with Asperger syndrome. Although some of the earlier studies on the use of Risperidone in autistic disorders have included children with this syndrome (Fisman and Steele, 1996) to date there has been only one case report on the use of the drug in an adult with Asperger syndrome (Raheja et al., 2002).

In this paper, we describe three adults with Asperger syndrome who were treated with Risperidone for their behavioural problems. All three had dramatic improvements, not only in the area of behaviour but also mood, interest in activities and skills.

Method and Results

Case Report 1

AB is a 34 year old man with a borderline to mild level of intellectual disability who lives in a residential home run by social services.

He was born of a full term, induced labour. A delay in development was first noted when he was around 18 months. He started walking only at the age of 4 years and went on to have a stilted, unusual gait. Although there was a delay in his speech development, he soon caught up and developed a wide vocabulary, albeit with a characteristic monotonous tone and an odd prosody. He tended to repeat questions and found it difficult to take cues from others during a conversation. He was quite clumsy and this would become worse when he was distressed.

As a young child, he seemed unaware of the presence of others. He used to play on his own and was unable to use toys imaginatively. He never made good eye contact during conversations. As he grew up, he was described more as a loner. He could be very polite to others, but generally never initiated a conversation. AB has had a particular interest in diaries and calendars. He shows an exceptional ability to identify the correct day of the week of any date given to him.

He was quite rigid and routine bound from an early age. He has had many obsessive/compulsive behaviours. At one point, he was ‘fascinated’ by hair and would try to pull his and others’ hair. He also had compulsions to switch lights on and off continuously. Any change to his routine, either at home or at the day centre, would make him extremely upset. As a child, he developed episodes of shrieking associated with a tendency to spin around and head bang. Since then, he has resorted to similar or other disruptive behaviour (spitting, burping loudly, becoming agitated, being verbally and physically aggressive to others, smashing up furniture etc.) when he feels unsettled. AB was diagnosed as having an Asperger syndrome according to Gillberg’s criteria (Gillberg, 1995). He did not show evidence of any mental illness.

The behavioural problems were addressed initially by non-pharmacological means; but the intensity of the outbursts meant that psychotropic medication had to be considered. Although he was tried on anti-psychotics (Haloperidol and Thioridazine), Anxiolytics (Lorazepam) and mood stabilisers (Carbamazepine), no sustained improvements were evident. Following serious concerns about his behaviours such as head banging, throwing furniture and aggression to people, he was started on Risperidone initially at a dose of 1 mg per day. Due to an inadequate response, the dose was gradually increased to 4 mg per day over a period of 6 months. On this dose, not only did his severe aggressive behaviour settle down, he also
showed significant improvement in the level of alertness, concentration and interest in activities at the day centre.

He has now been on Risperidone for 3 years. The outcome was audited using the global improvement and efficacy index scores of the Clinical Global Impression (CGI) Scale (Guy, 1976). On global improvement, he was in the ‘very much improved’ category and he had an efficacy index of 02 (i.e. ‘marked therapeutic effect’ with ‘side effects that do not interfere significantly with patient’s functioning’). Using the CGI in this way for outcome audits of drug treatments in the psychiatry of learning disability has been described before (Thalayasingam et al., in press) and the same methodology was adopted here.

**Case Report 2**

CD is a 22 year old lady with a borderline to mild level of intellectual disability who lives with her parents. She attended a mainstream school and is able to read and write reasonably well. Her motor movements were reportedly clumsy from an early age and her co-ordination was poor.

Social situations made her extremely anxious and she had great difficulty in following the rulers for such social interactions. Although she was quite keen to initiate conversations, she had difficulty in taking turns and tended to talk on the topic that interested her at that moment for a long time. Her speech, though superficially perfect, was often repetitive and she used certain phrases or sentences repeatedly during conversation. She often struggled to understand the meaning of what people said or did and often repeatedly asked for clarification. This repeated questioning often had an obsessive-compulsive quality. She seemed to have particular difficulty not only in understanding other people’s emotions, but also in controlling her own. Her mood was often described as labile-changing from angry, shouting and screaming to being happy and laughing. There was however, no evidence of any sustained mood changes suggestive of a major affective disorder.

She was totally preoccupied with the subject of make up and would collect a lot of trivial information about it, which she was keen to let others know. She usually spent a couple of hours in the morning and evening doing make up. She was also preoccupied with gathering information about music stereo systems.

When distressed, angry or frustrated, she would exhibit behavioural problems, which included severe verbal and physical aggression towards staff or other vulnerable clients at the day centre. There were similar problems at home too. She would often have self-referential thinking and accuse others of talking about her. This did not amount to delusional intensity and there was no evidence to suggest a psychotic disturbance.

The clinical diagnosis of Asperger syndrome was confirmed using Gillberg’s criteria (Gillberg, 1995). There were no major affective or psychotic illnesses.

By the age of 20, her social anxiety, the obsessional questioning, the preoccupation with issues like make-up, stereos etc. had got markedly worse and this was leading to very severe behavioural disruption. Treatment with psychotropic medication had to be considered because of inadequate response to behavioural measures alone.

Because of the prominent anxiety symptoms, Propranolol was introduced at a dose of 30 mg per day gradually
increased to 120 mg per day. The response was not adequate. Respiridone at a dose of 0.5 mg twice daily was added to the Propranolol. The response was quite dramatic. Within 4 weeks, her behaviour had settled down and she became less anxious, more polite and approachable. Her overall mood also improved considerably with her being more cheerful and relaxed. This dramatic improvement, gratefully acknowledged both by staff at the college which CD attended as well as by her parents, was sustained for over a year. Subsequently, there was some reappearance of her anxiety and obsessional behaviour, although not to the same intensity as before. The dose of Risperidone was increased to 1 mg twice daily with good effect. She was on Risperidone for 3 years and the outcome audit using the CGI showed her to be in the ‘very much improved’ category with an efficacy index of 0.2 (i.e. ‘marked therapeutic effect’ with ‘side effects that do not interfere significantly with patients’ functioning’). Subsequently, anxiety and obsessional behaviour re-emerged and the Risperidone was gradually increased up to 5 mg per day. At this dose, she started having side effects such as muscle stiffness, tics and galactorrhoea and the drug had to be discontinued.

Case Report 3

EF is a 57 year old lady with mild learning disability living in a residential home. She was born of a full term normal delivery. Details regarding her early development are not available. She attended infant school until she was 7 years old. Thereafter she spent 4 years at home before starting in a special school at the age of 11 years. Earlier notes suggest that she never initiated conversation and that she could be ‘quite abrupt’ in her responses. She also would not make good eye contact during conversation. Her speech was quite relevant and coherent, but had an odd tone and prosody. She was described as ‘phobic of new situations’, ‘requiring lots of reassurance and gentle persuasion’. She has always had a particular interest and fascination with cars and developed elaborate rituals about counting them in a particular manner.

In her late 30s, following the death of her mother, she was admitted to a long stay hospital. The main reason for the admission was her behaviour. She was described as a rigidly routine bound person who had a number of elaborate rituals that she had to adhere to. She would become extremely disruptive if any of these were interfered with. She would often refuse to go to bed until the early hours of the morning, refuse to go out of the house and refuse to change clothes or wash. When she was distressed, she would scream, kick out and be verbally and physically aggressive. Usually these behaviours would begin abruptly in response to any stressful situations or in response to her routines being thwarted. During her time in hospital, she was treated with various psychotropic drugs including Chlorpromazine, Haloperidol and Diazepam. She stayed in the hospital till her early 50s and was then discharged to a residential home.

She was referred to psychiatric services again at the age of 56 for an apparent escalation of her behavioural problems. The General Practitioner had tried her on Paroxetine, Thioridazine and Haloperidol without any clear benefit. Psychiatric assessment did not show any evidence of psychosis or a major mood disorder. There was a past history of childhood epilepsy treated with phenobarbitone, but she had
been fit free for over 40 years and not on any anti-epileptic medication. The clinical diagnosis was one of an autistic spectrum disorder - Asperger syndrome, diagnosable using Gillberg's criteria (Gillberg, 1995).

Because of the escalation of her behaviour problems, she was started on Risperidone 0.5 mg twice daily after stopping Haloperidol and Paroxetine. There was a dramatic improvement in her behaviour with the verbal and physical aggression disappearing totally. She became more co-operative and interested in various activities at the day centre. The staff reported her as being happier and her mood swings had completely disappeared. She has now been on Risperidone for 2 years. The outcome audit using the CGI showed her to be in the ‘very much improved’ category with an efficacy index of 02 (i.e. ‘marked therapeutic effect’ with ‘side effects that do not interfere significantly with patient’s functioning’).

Discussion

Autistic spectrum disorders are chronic and impairing conditions and the behavioural problems that they cause often necessitate the use of psychotropic drugs along with psychosocial interventions. Although no specific drug has been found to be specific for managing these behavioural disturbances, drugs targeting the dopaminergic and serotonergic systems have been widely used; both systems of neurotransmission being shown to be dysfunctional in many individuals with autism (McDougle et al., 2000).

Treatment with typical anti-psychotics and dopamine antagonists like Haloperidol, though effective, cause significant side effects and may have a relatively small therapeutic effect (Campbell et al., 1996; Locascio et al., 1991). An atypical anti-psychotic like Risperidone is a powerful antagonist of both dopamine D2 and serotonin 5HT2A receptors. With this mechanism of action, the drug has been effective in the treatment of negative symptoms of schizophrenia. similarities between the negative symptoms of schizophrenia and the primary symptoms of pervasive developmental disorders (autistic spectrum disorders) and the lower risk of extra-pyramidal side effects have formed part of the rationale for using atypical anti-psychotics in the treatment of behavioural problems in those with autistic disorders (Purdon, 1994; McDougle et al., 1995).

Using clinical case reports, this paper examines the use of Risperidone, prescribed for behavioural problems in three adults with the autistic spectrum disorder - Asperger’s syndrome. All three patients required only smaller doses than that used in the treatment of schizophrenia. There was a positive clinical response from the starting dose of 1 mg itself, although further increases were needed for two of the patients. The Raheja et al. (2002) paper has also reported significant clinical improvements on a low 1 mg per day dose. Significant clinical improvements on small doses of Risperidone have been reported in earlier studies involving children with autistic disorders too (Fisman and Steele, 1996). The clinical improvement, thus obtained, was not limited to the behaviour problems alone. There was an overall general improvement involving areas such as cognition, skills, mood and motivation.

All three tolerated the drug quite well at the initial lower doses and showed significant clinical improvement. At 3, 3 and 2 years respectively, the length of follow-up described in this case series is longer.
than the only other case report in literature (Raheja et al., 2002). After 3 years, Risperidone had to be discontinued for one patient, because of the reappearance of the original symptoms and her lack of tolerability of a higher dose.

In discussions with colleagues, the authors have often heard points about the clinical improvement with Risperidone ‘waning off’ after sometime or side effects affecting treatment. In the ‘evidence based’ scheme of clinical practice, these discussions have perhaps been nothing more than clinical anecdotes. However, by reporting follow-up periods of up to 3 years in this small case series, we have found that the ‘waning off’ of therapeutic benefits and the emergence of side effects late in the treatment can both be potential problems. Needless to say, the importance of carefully monitoring the drug treatment cannot be overemphasised.

There is a real need for well designed, prospective, randomised controlled trials to establish the usefulness or otherwise of Risperidone in adults with Asperger syndrome and behavioural disorders.

Summary

Risperidone is an atypical anti-psychotic that had been used in the management of behavioural problems in those with autistic disorders. There have been studies about its efficacy in treating behavioural problems in children and adults with an autistic spectrum disorder. However, to date, there has been only one case report on the use of the drug in an adult with Asperger syndrome. This paper describes three adults with the syndrome and behavioural problems who were treated with the drug. The doses used were significantly lower than the usual anti-psychotic dose of Risperidone. All three patients showed significant clinical improvements, which were sustained for up to 3 years. After 3 years of treatment, anxiety and obsessional behaviours reappeared in one patient and when the dose of Risperidone was increased there were side effects like galactorrhoea, muscle stiffness and tics which led to the drug being discontinued. This would suggest that the ‘waning off’ of therapeutic benefits and the emergence of side effects late in treatment could both be potential problems. There is a need for well designed, prospective, randomised controlled trials to establish the usefulness or otherwise of Risperidone in adults with Asperger syndrome and behavioural disorders.

References


