Off-label use of antipsychotic medication in people with intellectual disabilities

Ramerman, Lotte

CHAPTER 8

Summary

The aim of this thesis was to add to the evidence-based use of antipsychotic drugs in people with intellectual disabilities, by studying the prescription practice, the long-term effectiveness of risperidone for reducing challenging behaviours and the effects of long-term used antipsychotic drugs on quality of life.

Antipsychotic drugs are frequently used long-term for the management of challenging behaviours, despite mixed results from scientific studies. Risperidone is one of the few antipsychotic drugs that is licenced for the short-term use for the management of challenging behaviours, in people with intellectual disabilities. Some studies found evidence for its short-term effectiveness in reducing challenging behaviours, mainly aggression, while others disputed the effectiveness. Although the evidence for the effectiveness of antipsychotic drugs is conflicting, findings about side-effects are consistent. Side-effects may occur in many clients, including metabolic, neurological, and endocrine symptoms. Side-effects are known to affect health-related quality of life. Furthermore, challenging behaviours may also negatively influence health-related quality of life, which may still exist despite the use of antipsychotics.

Chapter 1 provides an overview of the current literature on antipsychotics drugs, side-effects, guidelines and quality of life. Furthermore, the aims of the thesis and an outline are provided.

Chapter 2 describes the adherence of clinicians to guideline recommendations on prescribing antipsychotic drugs in people with intellectual disabilities. A checklist was developed, based on the Dutch guideline on psychotropic drugs for people with intellectual disabilities and (inter-) national guideline recommendations on antipsychotic drugs in general, and specifically for people with intellectual disabilities. This checklist was used to screen 299 medical records from clients of three service providers of intellectual disability care and two organisations for mental health care.

In all organisations, similar reasons for the prescription of antipsychotic drugs were found: 75% used antipsychotic drugs primarily for challenging behaviours in the presence of a non-psychotic psychiatric disorder, including autism spectrum disorder; 7.4% used antipsychotic drugs primarily for challenging behaviours without a psychiatric diagnosis; 5.4% for a diagnosis of a psychotic disorder or schizophrenia; and for 11.4% the reason of prescription was unknown. In 56% of the medical records, more than one specific reason for prescription was found, with aggressive and destructive behaviour as the most frequent reasons. In the service providers, only 30% of the clients received a psychosocial intervention, before or during their treatment with antipsychotic drugs, compared to 53% in mental health care. The majority of the clients used antipsychotic drugs for longer than one year, including 61% of the clients in service providers, who used the

medication for longer than 10 years. Of all clients, 50% had a dosage reduction or an attempt to discontinue in the last five years. The presence of side-effects was the main reason for a dosage reduction. Side-effects were annually monitored in 85.8% of the clients in the service providers, compared to 59.7% in the mental health care organisations. Overall, weight was monitored most frequently (54.5%), neurological side-effects less frequently (14.7-23.7%). In mental health care, laboratory testing was barely done (1.1-4.3%), while service providers performed laboratory testing more often (up to 38.1% for fasting glucose).

To conclude, there is insufficient adherence to guideline recommendations on prescribing antipsychotic drugs in people with intellectual disabilities, especially with regard to providing additional psychosocial interventions, the evaluation of treatment effects and the monitoring of side-effects.

As the use of guideline recommendations on prescribing antipsychotic drugs to people with intellectual disabilities remains insufficient, the question arises why this is so difficult? Therefore, **Chapter 3** presents the results of a qualitative interview study with clinicians, on the barriers and facilitators they experience in using guideline recommendations on antipsychotic drugs.

Two organisations had more integration of the guideline recommendations on antipsychotic drugs than the other organisations. Both had actively translated guideline recommendations into organisation specific policies, by involving the relevant clinicians. This improved the collaboration between physicians and behavioural scientists or psychologists. Furthermore, the presence of a nursing team was a facilitating factor. Such a team was able to assist in the monitoring of treatment effects and side-effects, and was more approachable for behavioural scientists or psychologists for consultation, compared to physicians. In general, the electronic patient records were a barrier. The electronic patient records had the opportunity to support monitoring. However, the systems often did not work accordingly, therefore they were perceived as a barrier.

The psychiatrists and ID physicians agreed in general with the content of the guideline recommendations, as did behavioural scientists or psychologists. However, the latter were often unaware of the existence and content of the recommendations, as these were initially aimed at physicians. Moreover, the guideline recommendations are less in line with the needs of support staff. They perceive antipsychotic drugs as a tool to maintain “peace” in the living facilities. Clients themselves are a facilitator, as they are often motivated to use as little medication as possible. However, when a discontinuation attempt fails, this can have a negative effect on the client’s confidence. The network of the client can both be a barrier and a facilitator when prescribing antipsychotic drugs, but also specifically when considering discontinuation. There is often fear

of the return of previous challenging behaviours when medication is withdrawn, which may lead to resistance against discontinuation.

To conclude, to promote the use of guideline recommendations, organisations should actively translate the recommendations into organization specific treatment policies, involving all relevant clinicians. Furthermore, the use of guideline recommendation in clinical practice should be supported by nursing teams and a functional electronic patient system for monitoring effects and side-effects.

Chapter 4 describes the association between health-related quality of life and side-effects of antipsychotic drugs and challenging behaviours. When antipsychotic drugs are used long-term for the management of challenging behaviours, the remaining challenging behaviours may still influence health-related quality of life. Furthermore, side-effects associated with antipsychotic drugs can influence health-related quality of life. Baseline data of two discontinuation studies were combined. These included outcomes on challenging behaviours (measured with the Aberrant Behavior Checklist; ABC), side-effects (parkinsonism, dyskinesia, akathisia, autonomic symptoms) and health-related quality of life (measured with the RAND-36 and the emotional- and physical well-being subscales of the Personal Outcome Scale). The RAND-36 is an outcome measure with domains on physical well-being, limitations in role functioning caused by physical and emotional problems, social functioning, mental well-being, vitality, pain, general health and changes in health.

The results indicated that parkinsonism, urinary problems, dysphagia, dizziness and temperature dysregulation negatively influence the physical domains of quality of life. The mental health domains of health-related quality of life were negatively associated with symptoms of irritability, lethargy and stereotypy. Overall, mental well-being was significantly lower in people with intellectual disabilities, who use antipsychotic drugs long-term for the management of challenging behaviours, compared to the scores of the general population of the Netherlands.

The results of this study show a clear negative association of symptoms of side-effects and challenging behaviours with health-related quality of life, in people with intellectual disabilities who were prescribed long-term antipsychotic drugs.

Chapter 5 discusses changes in health-related quality of life, which occurred during the discontinuation of antipsychotic drugs, which were used long-term for challenging behaviours. The data on health-related quality of life (RAND-36) from two discontinuation studies were combined. Health-related quality of life was compared between participants who fully

discontinued antipsychotic drugs at 16 and 40 weeks and participants who did not achieve this. Furthermore, the changes in the domains of the RAND-36 between baseline, 16 weeks and 40 weeks were analysed on their association with changes in parkinsonism, autonomic symptoms, irritability, lethargy and stereotypy.

The results showed an improvement in physical well-being when complete discontinuation was achieved. Changes in physical well-being were negatively associated with parkinsonism. Social functioning temporarily deteriorated during discontinuation in the participants with incomplete discontinuation. Mental well-being ratings were consistently lower in the group that was unable to fully discontinue from antipsychotic drugs. However, both participants with complete and incomplete discontinuation temporarily deteriorated in mental well-being during withdrawal, regardless of the ability to completely discontinue antipsychotic drugs. Changes in both social functioning and mental well-being were negatively associated with irritability, lethargy and stereotypy.

To summarize, changes in health-related quality of life during the discontinuation of antipsychotic drugs are associated with changes in parkinsonism, irritability, lethargy and stereotypy. Furthermore, complete discontinuation may result in an increased physical well-being, while negative effects of incomplete discontinuation on quality of life, are likely to subside after withdrawal is suspended. Last, initial decreases in mental well-being may be expected, unrelated to the ability to completely discontinue from antipsychotic drugs.

Chapter 6 presents the results of a placebo-controlled, double-blind, randomised discontinuation study of risperidone, used long-term for reducing challenging behaviours. A discontinuation group, which gradually withdrew from risperidone to a placebo, was compared with a control group, which continued the use of the baseline dosage of risperidone. The study started with 14 weeks of discontinuation. After 24 weeks, the blind was broken.

In the discontinuation group, 82% could successfully complete the blinded phase of the study and discontinue risperidone, compared to 79% in the control group. The primary outcome of this trial, the irritability subscale of the ABC, did not differ between the discontinuation group and control group over time. Also, lethargy, hyperactivity and inadequate speech did not differ between groups over time. However, stereotypical behaviour showed a less favourable course in the discontinuation group. There were no differences between the discontinuation group and the control group on extrapyramidal symptoms, even though two participants had severe withdrawal dyskinesia. Furthermore, weight, body mass index and waist circumference showed a more favourable course in the discontinuation group, compared to the control group.

Last, prolactin levels and testosterone levels also followed a more favourable course in the discontinuation group, compared to the control group.

The findings of the trial suggest that the discontinuation of risperidone is possible without significant deterioration in challenging behaviours, except for stereotypical behaviours, and with an improvement in health outcomes.

The final chapter, **Chapter 7** contains a general discussion and conclusion of this thesis. Clinical implications from the studies were clear: (1) The effects of discontinuation on health parameters, challenging behaviours and health-related quality of life underline the need to make the withdrawal from antipsychotic drugs a priority. Moreover, withdrawal is possible, without lasting negative effects on health-related quality of life. (2) More effort is desired to translate guideline recommendations into organisation specific treatment policies and more support/facilitation is desired to support the application of the recommendations in practice.

To conclude, although the long-term effectiveness of risperidone remains unclear, discontinuation is often possible, with an improvement in health outcomes. The effects of discontinuing antipsychotic drugs on health-related quality of life confirm this. Furthermore, health-related quality of life will not permanently deteriorate when complete discontinuation is not achieved. These results underline the need to improve current practice of insufficiently evaluating the treatment effects and monitor the side-effects of antipsychotic drugs regularly.

8