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Structured Medication Review to Improve Pharmacotherapy in People with Intellectual Disability and Behavioural Problems

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Background Polypharmacy and chronic drug use are common in people with intellectual disability and behavioural problems, although evidence of effectiveness and safety in this population is lacking. This study examined the effects of a structured medication review and aimed to improve pharmacotherapy in inpatients with intellectual disability.

Methods In a treatment facility for people with mild to borderline intellectual disability and severe behavioural problems, a structured medication review was performed. Prevalence and type of drug-related problems (DRPs) and of the recommended and executed actions were calculated.

Results In a total of 55 patients with intellectual disability and behavioural problems, 284 medications were prescribed, in which a DRP was seen in 106 (34%). No indication/unclear indication was the most prevalent DRP (70). Almost 60% of the recommended actions were also executed.

Conclusions This high prevalence of DRPs is worrying. The structured medication review is a valuable instrument to optimize pharmacotherapy and to support psychiatrists in adequate prescribing of both psychotropic and somatic drugs.

Keywords: drug-related problems, intellectual disability, psychotropic drugs, structured medication review

Introduction

People with intellectual disability has a three- to fourfold increased risk of developing psychopathology, including behavioural problems, compared to children and adults with normal intelligence (Wallander *et al.* 2003; Handen & Gilchrist 2006). Psychotropic drugs are often used in the treatment of psychopathology and behavioural problems in this patient population. Research on the prevalence of psychotropic drug use in people with intellectual disability shows prevalences ranging from 25 to 60% depending on the setting (Aman *et al.* 1995; Stolker *et al.* 2001; Holden & Gitlesen 2004; De Kuijper *et al.* 2010; Scheifes *et al.* 2013). In people with intellectual disability, it is more difficult to establish psychiatric diagnoses, to assess the course of psychiatric illness, to monitor the effects of therapy and to discriminate between manifestations of an underlying behavioural/psychiatric disorder and medication-emergent side effects (Dosen & Kenneth 2001; Valdovinos *et al.* 2005). Medication initiation and changes are often driven by emerging symptoms, and the majority of those changes are increases in or additions to psychotropic medication regimens. Although evidence of the effectiveness and safety in this population is lacking, polypharmacy and chronic drug use are common (Stolker *et al.* 2001; Handen & Gilchrist 2006; Scheifes *et al.* 2011; Edelsohn *et al.* 2014; Hobden *et al.* 2013). All of these factors may result in suboptimal pharmacotherapy and polypharmacy (including drugs for somatic diseases) that may lead to drug–drug interactions and severe side effects (Deb *et al.* 2001;

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Ulzen & Powers 2008; Zarcone *et al.* 2008; Haider *et al.* 2014; Hassler *et al.* 2014).

The problems associated with polypharmacy or inappropriate prescribing are well known in elderly populations (Leendertse *et al.* 2008; Stafford *et al.* 2011). The structured medication review is an effective intervention used to improve pharmacotherapy in the elderly and prevent harmful effects (Zermansky *et al.* 2006; Stuijt *et al.* 2008; Vinks *et al.* 2009; Leendertse *et al.* 2013). This includes the structured review of current medication, preparation of a pharmaceutical care plan based on drug-related problems (DRPs) that were detected and actions planned, followed up and monitored. The intervention is performed jointly by the physician, the pharmacist and the patient. As polypharmacy and chronic drug use are common factors in both the elderly population and in people with intellectual disability and behavioural problems, a structured medication review could also be an effective intervention in this population. Previous initiatives to improve pharmacotherapy in people with intellectual disability mainly focused on discontinuation of medication (Wressell *et al.* 1990; Ahmed *et al.* 2000; De Kuijper *et al.* 2014). The aim of this study was to examine the effects of a structured medication review on medication use in people with intellectual disability and behavioural problems treated with psychotropic drugs admitted to a specialized inpatient treatment centre.

Methods

Setting

The study was carried out from October to December 2011 in a specialized inpatient treatment facility for adults with mild to borderline intellectual disability and severe behavioural problems located in the Netherlands. The treatment facility had 100 beds and was part of Altrecht Institute for Mental Health Care. All medication for these patients was supplied by the pharmacy department. The standard pharmacy service included, besides dispensing, monitoring of medication profiles, including identifying drug–drug interactions using an electronic system (Zamicon®, HI-systems, Oosterhout, the Netherlands). The structured medication review was performed as part of good clinical practice to improve the quality of pharmacotherapy. Therefore, a review procedure by a medical ethics committee was not necessary, because our analysis was based on secondary use of data.

Study population

All admitted patients using at least one psychotropic drug were included in the study population. For the selection, an accurate list of the current medication both regular and as needed was provided by the pharmacist of this institution, to be able to select the patients with at least one psychotropic drug. Of the selected patient information of gender, age and diagnosis was collected as well.

Intervention

The intervention consisted of a structured medication review of the medication with the intention to improve the pharmacotherapy of the patient. The structured medication review consisted of several steps (Figure 1). The steps involved awareness of the current medication situation including identification of potential DRPs by a pharmacist and a pharmaceutical anamnesis by a nurse and the patient, defining actual DRPs by the pharmacist and psychiatrist in the treatment analysis, the formulation and execution of a pharmaceutical care plan by the pharmacist and the psychiatrist and, finally, monitoring

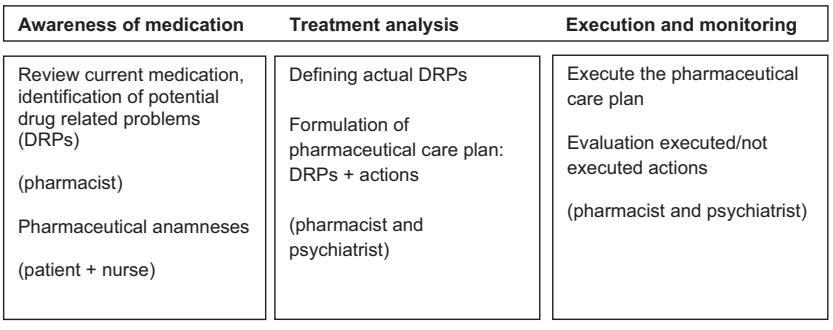

Figure 1 Structured medication review.

and follow-up evaluation of the pharmaceutical care plan and changes in pharmacotherapy. To coordinate and monitor the review for reporting purposes, a researcher A. S. was involved in all the steps. The different steps of the structured medication review will be described in more detail in the next section.

Awareness of medication

The pharmacist reviewed the current medication and identified potential DRPs as a preparation for the treatment analysis. A potential drug-related problem is a situation which involves or is suspected to involve pharmacotherapy with a possible undesired effect or risk thereof, now or in the future, experienced by an individual patient. The pharmacist had data on current prescribed medication, medication history and laboratory parameters. The pharmacist identified potential DRPs by combining pharmacological and (patho)physiological knowledge of the patient using Table 1 as a guide.

The pharmaceutical anamnesis to gather information from the patient about his or her drug therapy is also part of the awareness of medication. A form was designed with a few questions adapted to the level of intellectual functioning of the patients in this population. The patients of the wards filled in the form supported by the nurses. The questions addressed the patient's medication use and experiences including beliefs, understandings, attitudes and concerns about the pharmacotherapy as well as concomitant use of OTC (Over the Counter) drugs or other health products (Table 2).

Treatment analysis

The goal of the treatment analysis is to define actual DRPs and formulate actions on these problems. The pharmacist and the psychiatrist involved with the patient discussed the medication prescribed supported by a list with the current prescribed medication, information on the medication history, laboratory parameters, the medical file of the patient, the identification of potential DRPs in advance by the pharmacist and, where available, the information of the pharmaceutical anamnesis performed by the nurse. All drug-related problems were defined according to a list with DRPs (Table 1), and actions to improve the pharmacotherapy (Table 1) were formulated. These interventions were documented in the pharmaceutical care plan including information on who is responsible for a certain action (psychiatrist or pharmacist) and when the action was to be evaluated.

Execution and monitoring

The psychiatrist and the pharmacist had 2 months to execute their actions. The psychiatrist together with the researcher verified after 2 months whether the planned interventions, described in the pharmaceutical care plan,

Table 1 Classification of drug-related problems and actions

Classification of drug-related problems (DRPs)	*Classification of actions according to the pharmaceutical care plan*
Drug selection:	**1.** Clarify indication
1. Duplication	**2.** Consultation general practitioner/specialist
2. Outdated medication	**3.** Cessation of drug (Stop)
3. Lack of indication or unclear indication	**4.** Addition of drug (Start)
4. Contra-indication	**5.** Dose frequency/schedule change
5. Drug–drug interaction	**6.** Advise monitoring
Dosage/formulation:	**7.** Advising patient
6. Dosage too high	**8.** Further evaluation medication history
7. Dosage too low	**9.** Switch
8. Inappropriate dose frequency/schedule	**10.** Change in formulation
9. Inappropriate formulation	**11.** Other
10. Undertreatment	**12.** No intervention
11. Adverse event/side effect	
12. Insufficient monitoring	
13. Non-adherence	
14. Unclear utilization information	
15. Other	

Table 2 Pharmaceutical anamnesis: questions for the patient

1	Do you know why you receive this medication?
2	Do you think this medication will help you to feel better, and if yes how?
3	Do you experience any adverse events?
4	Do you agree with taking this medication?
5	Do you actually take this medication?
6	How do you take your medication, is the use easy or difficult?
7	Do you use any medication that is not prescribed by your doctor?
8	Finally, is there anything you would like to say about your medication use?

were executed and recorded the reasons if this was not the case.

Outcomes

The primary outcomes of the study were the frequency and type of DRPs as documented in the pharmaceutical care plans. Secondary outcomes were (i) the frequency and type of planned actions as documented in the pharmaceutical care plans and (ii) the outcomes of the monitoring and evaluations of the actions after 2 months defined as executed actions, not executed actions with a reason and not executed actions without a reason. If patients were discharged before the 2 months' time period, their medication at the date of discharge was used to evaluate the plan.

Descriptive variables

Medication was coded according to the World Health Organization Anatomic Therapeutic Chemical (ATC) classification system (WHOCC – ATC/DDD Index). The following groups were distinguished for the psychiatric indication: antipsychotics, benzodiazepines, antidepressants, psychostimulants, mood stabilizers, drugs used in addictive disorders, biperiden, propranolol and promethazine. For the somatic indication: alimentary tract and metabolism, cardiovascular, dermatologicals, analgesics, respiratory system, other and no ATC-code. Other includes the following: systemic hormonal preparations, anti-infectives for systemic use and drugs for sensory organs.

Demographic characteristics of the patients were collected from the medical files including age, gender and data on psychiatric DSM-IV disorders. In addition, the prevalence of major diagnoses was reviewed and combined into categories according to clinical similarities to reduce the number of reported groupings. The following groups of psychiatric disorders were defined: psychotic disorder, mood disorder, anxiety disorder, substance dependence/abuse, pervasive disorder, ADHD and disruptive disorder, personality disorder and other. Intellectual disability was divided into the following: borderline intellectual disability, mild/moderate intellectual disability and intellectual disability not specified.

Data analysis

Data were analysed using IBM SPSS STATISTICS for Windows, version 19.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics were used to determine the prevalence and type of DRPs and of the recommended actions.

Results

Population

Of the 96 patients with intellectual disability and behavioural problems admitted to the specialized inpatient treatment centre, 65 had a prescription of at least one psychotropic drug, and 31 had no known use of psychotropic drugs. Of the 65 selected patients, 10 were discharged or did not use psychotropic drugs anymore at the day of the structured medication review. Finally, 55 patients were included in the study population. The baseline characteristics of the study sample are presented in Table 3. Of the included patients, the average age was 28.8 years (range 18–53). Of the 55 patients, 37 were male. The most prevalent diagnoses were psychotic disorder (26/55) and substance dependence/abuse (19/55). The 55 patients had a total of 284 drug prescriptions with a mean of 5.2 prescriptions per patient. Antipsychotics and benzodiazepines were the most prevalent psychotropic drugs, respectively, 37/55 and 36/55 patients. Of the somatic drugs, there were 21/55 patients with dermatological prescriptions and 20/55 patients with prescriptions of analgesics.

Frequency/prevalence of drug-related problems

Of the 55 patients, 11 patients had no DRP at all, 18 had 1 DRP, and 26 had ≥2 DRPs, resulting in a mean of 1.9 DRPs per patient. With 106 (34%) of the 284

Table 3 Baseline sociodemographic and drug-related characteristics of the included patients

Characteristics	*n* = 55
Male	37
Female	18
Age, mean year (range)	28.8 (18–53)
Psychiatric diagnosis at admission[1]	
Psychotic disorder	26
Substance dependence/abuse	19
Personality disorder	13
Pervasive disorder	9
ADHD and disruptive disorder	9
Anxiety disorder	7
Mood disorder	2
Other	8
Intellectual Disability	55
Mild/moderate intellectual disability[2]	20
Borderline intellectual functioning	28
Intellectual Disability not specified	7
Number of prescription drugs per patient, mean (range)	5.2 (1–15)
Prescribed drug groups[3]	
Psychiatric Indication	
Antipsychotics	37
Benzodiazepines	36
Antidepressants	11
Psychostimulants	9
Mood stabilizers	8
Drugs used in addictive disorders	8
Biperiden	6
Propranolol	4
Promethazine	4
Somatic indication	
Dermatologicals	21
Analgesics	20
Alimentary tract and metabolism	15
Respiratory system	11
Contraception/urological	11
Cardiovascular	6
Other[4]	5
No ATC-code	7

[1]Adds up to >100% because of multiple diagnoses used.
[2]Of the 20 patients: two moderate intellectual disability and 18 mild intellectual disability.
[3]Adds up to >100% because of multiple drug groups used.
[4]Other is systemic hormonal preparations, anti-infectives for systemic use and drugs for sensory organs.

prescriptions (156 psychiatric indication and 128 somatic indication), a DRP was formulated. Of those 106, there were 55 drugs for a psychiatric indication and 51 for a somatic indication. Table 4 shows the type and subtype of the DRPs. The most prevalent DRP is lack of indication or unclear indication, 70/106 which is equally distributed in psychiatric indication DRPs 33/55, and somatic indication DRPs 37/51. Insufficient monitoring is especially seen in the psychiatric indication group, 9/55. The DRP adverse event/side effects were not mentioned at all in the pharmaceutical care plans.

Recommended actions and executed actions

In Table 5, the number and type of the recommended actions are presented, also specified in executed action, not executed actions with reason and not executed actions without reason. In total, 102 actions were formulated of which 58 (56.9%) were executed, 26 (25.5%) were not executed with reason, and 18 (17.6%) were not executed at all. With four DRPs, there were no actions formulated because the psychiatrist was aware of them and did not find an intervention necessary. The action to clarify the indication was documented 35 of

Table 4 Drug-related problems (DRPs)

	Total DRP, n = 106	*Psychiatric indication, n* = 55	*Somatic indication, n* = 51
DRP type and subtype			
Drug selection	78		
Duplication	4	3	1
Outdated medication	3		3
Lack of indication or unclear indication	70	33	37
Contra-indication	1		1
Drug–drug interaction	0		
Dosage/formulation	12		
Dosage too high	1	1	
Dosage too low	5	3	2
Inappropriate dose frequency/schedule	6	5	1
Inappropriate formulation	0		
Undertreatment	2		2
Adverse events/side effects	0		
Insufficient monitoring	9	9	
Non-adherence	2		2
Unclear utilization information	3	1	2
Other	0		

Table 5 Type of action recommended and executed

Action	*Recommended action, n*	*Executed action, n*	*Not executed action with reason, n*	*Not executed action without reason, n*
Clarify indication	35	23	6	6
Consultation General Practioner/Specialist	21	11	8	2
Cessation of drug (Stop)	18	7	7	4
Addition of drug (Start)	1	1	0	0
Dose frequency/schedule change	9	4	3	2
Advise monitoring	10	5	2	3
Advising patient	5	5	0	0
Further evaluation medication history	1	1	0	0
Switch	0	0	0	0
Change in formulation	0	0	0	0
Other	2	1	0	1
Total	102	58	26	18
No intervention[1]	4	na	na	na

[1]With 4 DRPs, there was no recommended action, no intervention.
na, not applicable.

102 times. The action 'consultation with general practioner/specialist' was documented in 21 of 102 times and 'cessation of drug' 18 of 102 times. The actions 'switch of medication' and 'change in formulation' were not mentioned in the pharmaceutical care plans at all. Reasons not to execute an action mentioned were, for example, as follows: there still is an indication for the medication, change of psychiatrist, attention for treatment relationship and early discharge of the patient.

Discussion

In patients with intellectual disability and behavioural problems using at least one psychotropic drug, a DRP was found in one of three prescribed drugs. The majority (44/55) of patients had at least one DRP. No indication or an unclear indication was the most prevalent DRP, seen in two-thirds of the DRPs. The DRPs were equally distributed between drugs with a psychiatric indication or a somatic indication. Almost 60% of the subsequent actions that were recommended were also executed. In 25% of the cases, there was a clear reason why the action was not executed. The remaining planned actions were not followed up. Psychiatrists reported a positive influence of the structured medication review on their awareness of the prescribed medication. An extraordinary finding was the lack of adverse events/side effects reported by the psychiatrist and the pharmacist as DRPs in this study, although patients did mention them in the pharmaceutical anamnesis.

There have been several initiatives to improve appropriate pharmacotherapy in people with intellectual disability. Two small studies investigating the effect of medication reviews by multidisciplinary teams performed before 1995 showed a positive effect on the number of psychotropic drugs, the dosage and the costs (Findholt 1990; Lepler 1993). More recent studies to improve pharmacotherapy focus on discontinuation of medication, especially antipsychotic drugs (Wressell *et al.* 1990; Ahmed *et al.* 2000; De Kuijper *et al.* 2014), as far as the present authors know there are no recent studies in people with intellectual disability comparable with the structured medication review performed in this study.

However, there has been ample experience with structured medication reviews in non-intellectual disability elderly populations. The medication-related problems including polypharmacy, chronic drug use, off label use and lack of evidence-based treatment in elderly are comparable to those seen in patients with intellectual disability. In older individuals with intellectual disability, the prevalence of relevant prescription errors was 27% (Zaal *et al.* 2013), and risk factors for drug-related problems included higher age, less severe intellectual disability, polypharmacy and use of medicines acting on the central nervous system. In comparison, the prevalence of prescription errors in older individuals in the general population ranged from

20% in outpatients (Zaveri 2010) to 40% in care institutions (Stafford *et al.* 2011). In a high-risk elderly population, 91% of the patients had a DRP (Leendertse *et al.* 2013). Our population could be described as a high-risk population as well, with a comparable 80% rate of DRPs. In the elderly population, a structured medication review is more and more part of good clinical practice (Stafford *et al.* 2011; Blenkinsopp *et al.* 2012). Structured medication reviews can lead to a substantial number of medication changes, as seen in geriatric inpatients in a Dutch study (Van Dijk *et al.* 2009). However, a decrease in the number of DRPs does not automatically lead to a similar decrease in number of drugs (Vinks *et al.* 2009). According to our results, only a few drugs are really stopped although the majority of the formulated actions are executed. The high prevalence in our study of DRPs because of no indication or an unclear indication was similar in studies in the elderly population with polypharmacy (Finkers *et al.* 2007; Vinks *et al.* 2009). A high percentage of more than 65% of implemented actions was found by Leendertse *et al.* (2013) and Van Dijk *et al.* (2009). On the other hand, in the SMOG trial of Vinks *et al.* (2009), a lower percentage of 28% was found. This could be explained by the positive effect of an integrated care setting in which the pharmacist works together with the physician and the participation of the patient. In our study with an integrated care setting, the percentage of executed actions was high as well (almost 60%), taken in to account the short time for evaluation and actions which were extended because of several reasons.

Strengths and limitations

This is the first study which describes a structured medication review in this specific clinical population. A strength of this study is that it is grounded in daily clinical practice. Accurate pharmacy data, information from medical files and laboratory parameters were available. Assessment of potential DRPs was performed by pharmacists and physicians jointly, which may offer better insight in DRPs as the assessment errors can differ between pharmacists and physicians (Doormaal *et al.* 2008). Patients participated in the study by giving their opinion about the medication in the pharmaceutical anamnesis, which information was used in the analysis.

At the same time, the participation of patients in the medication review process is problematic. Although the questions were adapted to the specific population, the present authors do not know whether this adaption was sufficient, taking into account the different levels of intellectual disability included. People with intellectual disabilities are prone to give answers that are socially desirable.

This study did not look at whether changes in medication led to improvement in health or well-being of patients. It was a technical measurement of frequencies without information on clinical outcomes, or the beliefs of the patients afterwards. Despite lack of robust research, evidence consistently demonstrating cost or clinical effectiveness compared with traditional care, the value of medication reviews is now generally accepted based on evidence of reductions in polypharmacy and increased appropriateness of prescribing (Blenkinsopp *et al.* 2012).

The medication reviews were partly based on information from the medical files. These are not always complete. For instance, all patients were supposed to have an intellectual disability, but this was not always registered in the files. Information on indications and reasons for prescribing medication were often missing, which led to the majority of DRPs.

Surprisingly, there were no side effects reported as drug-related problems in this study. This is likely to be because of underreporting by the pharmacist and psychiatrist. However, the present authors did not include pre-specified lists with possible side effects associated with each medication in the medication review, a way to decrease underreporting (Corso *et al.* 1992). The present authors did, however, specifically ask for side effects. To improve the detection of relevant side effects, adding a side effect rating scale, for example the Matson Evaluation of Drug Side Effects Scale (MEDS), could be useful. The MEDS is a 90-item scale developed to provide a comprehensive assessment of possible medication side effects using a simple, clear rating format (Matson *et al.* 1998; Matson & Mahan 2010). A reason for underreporting could, for example, be wrong interpretation of side effects. Many side effects cause discomfort, which in turn may cause irritability and agitation that appears similar to the psychiatric or behavioural symptoms the offending drugs are aimed at treating (Valdovinos *et al.* 2005; Charlot *et al.* 2011). The acceptance of side effects by the psychiatrist as less severe than the psychiatric or behavioural problem could be another reason for underreporting. More attention to side effects in the pharmaceutical analysis is necessary, because of their negative effect on quality of life and adherence with medication in long-term use.

Feasibility

The time needed per patient in this structured medication review was approximately 60 min, divided into 15 min for the pharmaceutical anamnesis by the patient and nurse, 15 min preparation by the pharmacist, 15 min per patient by the pharmacist and psychiatrist each for the analysis and evaluation. The execution of the formulated action is seen as common clinical practice. The review is the most time-consuming for the pharmacist. Note that the time needed for preparation and analysis also depends on the selection of patients. In this study, the selection was wide, which made the range of, for example, the analysis phases differ from 1 to 20 min per patient. More complicated patients need more time.

Patient participation in the medication review process is essential. The challenges in this specific population are the psychiatric problems, behavioural problems and intellectual disability for which the questionnaire should be sufficiently adapted.

Conclusion

With a third of the prescribed drugs in patients with intellectual disability and behavioural problems a DRP was found, this high prevalence of DRPs is worrying. This structured medication review created awareness with the psychiatrists about the prescribed medication and all the indications. Pharmacotherapy was improved by clarifying indications, cessation of unnecessary drugs, adjusting dosage schedules or other changes. It is a simple intervention to improve pharmacotherapy in a vulnerable group of patients with intellectual disability and behavioural problems. A structured format helped to be consequent and as complete as possible to find all DRPs. A structured medication review should become a standard procedure in the care of people with an intellectual disability and behavioural problems.

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Conflict of interest

The authors have no conflict of interest.

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