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RESEARCH ARTICLE

Interdisciplinary medication review to improve pharmacotherapy for patients with intellectual disabilities

Anne Gerd Granas[1] · Kjell Hermann Halvorsen[2] · Julie Wendelbo[3] · Cecilie Johannessen Landmark[4,5,6]

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Abstract

Background Patients with intellectual disabilities is an underserved patient group that have poor abilities to express their health complaints. *Objective* The aim of this study was to improve pharmacotherapy in patients with intellectual disability, by the use of medication reviews and interdisciplinary case conferences. *Setting* Patients with intellectual disabilities receiving home care services in Oslo, Norway. *Method* Patients receiving home care services were recruited by a nurse. A clinical pharmacist conducted medication reviews, and thereafter, the patients' general practitioner, nurse/social educator and clinical pharmacist discussed the pharmacotherapy at an interdisciplinary case conference. Patient demographics, prescribed drugs (strength, dose, indication) and drug-related problems (DRPs) were recorded. *Main outcome measure* Patient outcomes and actions taken to resolve DRPs 6 weeks after the case conference. *Results* Forty patients (34–77 years) with intellectual disabilities consented to medication reviews. They used on average 12 different drugs (range 5–23). The most commonly prescribed drugs were CNS-active drugs: analgesics (25 patients), antiepileptics (23 patients) and anxiolytics (21 patients). In total, 27 patients used between 3 and 7 different CNS-active drugs. The clinical pharmacist identified 178 DRPs in 39/40 patients (average 4.5 DRPs, range 0–13). DRPs for 30% of all prescribed drugs were resolved (145/481). Overall, 11% of drugs were deprescribed, 8% required therapeutic monitoring/follow-up, and either the dosage, formulation or route of administration were changed for 7% of the drugs. *Conclusions* Patients with intellectual disabilities receiving home care services were prescribed many unnecessary drugs and needed adjustment of pharmacotherapy for about one third of their prescribed drugs. The interdisciplinary case conferences improved pharmacotherapy for this vulnerable patient group.

Keywords CNS-active drugs · Deprescribing · Drug-related problems · Intellectual disabilities · Interprofessional collaboration · Norway · Medication reviews

Impacts on Practice

- Research on the complex drug therapy for patients with intellectual disabilities is scarce.
- Patients with intellectual disabilities need pharmacists, GPs or other health personnel to initiate therapeutic drug monitoring (TDM), to identify sub-optimal treatment, and to agree on a strategy for deprescribing.
- In patients with intellectual disabilities, untreated pain and adverse drug effects must receive more attention to improve their quality of live.

✉ Anne Gerd Granas
a.g.granas@farmasi.uio.no

[1] Department of Pharmacy, University of Oslo, Blindern, Box 1068, 0316 Oslo, Norway

[2] Department of Pharmacy, Faculty of Health Sciences, UiT The Arctic University of Norway, 9037 Tromsö, Norway

[3] Centre for Development of Institutional and Home Care in Oslo, Oslo, Norway

[4] Programme for Pharmacy, Department of Life Sciences and Health, Oslo Metropolitan University, Oslo, Norway

[5] The National Center for Epilepsy, Oslo University Hospital, Oslo, Norway

[6] Department of Pharmacology, Oslo University Hospital, Oslo, Norway

Introduction

People with intellectual disabilities have many comorbidities but experience inequities in access to health care [1]. A number of health conditions are more common for people with inherited intellectual disability, such as seizures, otitis media and gastrointestinal problems [2]. A few studies have investigated patterns of drug use, i.e., psychotropic drugs, CNS-active drugs, antiepileptics and antiasthmatic drugs in patients with intellectual disability [3–7]. Adults with intellectual disability also have higher rates of overweight and obesity [8]. Older patients with intellectual disabilities have a higher burden of somatic diseases than the general population, however evidence-based pharmacotherapy options are limited [9, 10].

People with intellectual disabilities are more likely than the general population to be prescribed potentially inappropriate medications (PIM) such as drugs with anticholinergic effects, benzodiazepines and antipsychotics [11]. Due to higher number of diseases and comorbidities, patients with intellectual disabilities are more prone to polypharmacy [12]. A medication review should therefore be conducted regularly to determine patient adherence and to monitor effect, adverse effects and drug interactions [13]. Community pharmacists would typically dispense the medicines but not perform a medication review, whereas a clinical pharmacists, usually employed by the municipality, would take part in interdisciplinary teams and perform in-depth medication reviews [14].

A few studies have identified PIMs in patients with intellectual disabilities [15–17]. Evidence from systematic reviews and meta-analyses support the provision of pharmacy services to a range of patient groups [18], however, clinical pharmacists are rarely involved in the care for patients with intellectual disabilities [19].

In Norway, the local municipalities run social welfare and health care for all its inhabitants, including people with intellectual disabilities. Smaller living facilities or individual apartments have at large replaced live-in institutions. Most people with intellectual disability are dependent on home care nurses to accommodate daily living activities, and general practitioners (GPs) provide medical care. When needed, the GPs refer patients to medical specialists or other types of secondary health care services.

Aim of the study

The aim of the present study was to describe how interdisciplinary medication reviews may improve pharmacotherapy in patients with intellectual disability, by the use of medication reviews and interdisciplinary case conferences. This should contribute to more rational pharmacotherapy and improved patient safety and medical care in this vulnerable patent group.

Ethics approval

The study was reported to the Norwegian Data Inspectorate. Ethical approval was not needed, as usual care was provided by the nurses, social educators and clinical pharmacist employed at The Centre for Development of Institutional and Home Care, and by the individual patient's GP. A written informed consent was obtained from either the patient or their legal guardian. All data were anonymised for study purposes.

Methods

Setting and inclusion criteria

Patients > 18 years with intellectual disabilities prescribed at least four drugs, receiving home care services from the Oslo Municipality in 2016, were eligible for inclusion. The nurse or the social educator (authorized health care professional) recruited patients in collaboration with the GP based on the following concerns: more than one prescribing doctor, behavioural challenges, weight reductions, pain or agitation.

Training and study design

In accordance to Pharmaceutical Care Network Europe, a drug-related problem (DRP) is defined as; *"an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes"* [20]. DRPs are normally identified by performing medication reviews at an individual or a population level. The way the medication reviews and the way DRPs are recorded, relies on several factors including health personnel's knowledge, skills and attitudes.

In our study, we used an established method developed by the Norwegian Patient Safety Program for health personnel conducting medication reviews. The method is described in a previous study [14]. The Centre for Development of Institutional and Home Care provided training in how to perform medication reviews, using an Integrated Medicines Management (IMM-model) in accordance with a national guideline for medication reviews. The IMM-model consists of four main steps. (1) The nurses recruit and fill in a checklist with information about the physical and psychological health of the patient. The nurse would also construct a medication list based on the available information, and ask the GP to order

relevant blood tests. (2) The nurses pass this information to the clinical pharmacist who perform a systematic medication review (i.e., identifies potential drug-related problems and assess if the prescribing is according to national guidelines). (3) Findings from the medication reviews are discussed at a joint case conference between the physician, nurse and clinical pharmacist; the actions and intervention to resolve identified problems are discussed. Finally (4) the nurse updates information about the interventions agreed upon and takes responsibility to observing how the patient responds to changes and also gives feedback on the patients reactions to the GP when needed [14].

The DRPs were categorized into six main classes designed to capture the range of concerns identified in systematic medication reviews. These categories were: *drug choice* (i.e., additional, unnecessary or inappropriate drug), *dosing* (i.e., too high or low dose, suboptimal dosing scheme or formulations), *adverse effects, interactions, adherence issues* (i.e., drugs administered by the patient) and *other problems* [21]. All DRPs were initially categorized by the clinical pharmacists (JW), and reliability confirmed or corrected by two of the co-authors. All drugs were coded using the Anatomical Therapeutic Chemical (ATC) classification system (https://www.whocc.no). The frequency and types of DRPs, and the interventions agreed and acted upon at the case conferences, were followed up after 6 weeks.

Results

Forty patients with intellectual disabilities, aged 34–77 years (mean 55 years, 50% women), consented to have an interdisciplinary medication review. They used on average 12 drugs (range 4–23). The most commonly prescribed drugs treatments were CNS-active drugs, indigestion/constipation, dietary supplements and respiratory drugs (Table 1).

Thirty-eight of the 40 patents received CNS-active drugs such as analgesic (25 patients), antiepileptic (23 patients) and anxiolytic drugs (21 patients) (Table 1). For complaints in the alimentary tract, 30 patients were prescribed drugs for constipation (n = 15) or ulcus/gastroesophageal reflux disease drugs (n = 11). A total of 28 patients received one or more dietary supplements, and 24 patients were prescribed drugs for the respiratory system such as antihistamines (n = 12), cough medicine (n = 11) and asthma or chronic obstructive pulmonary disease (COPD) (n = 10).

Polypharmacy was common: 16 patients used 4–10 drugs, 14 used 11–15 drugs and 10 used 16–23 drugs. Concomitant use of CNS-active drugs was in particular common, both within and between different therapeutic classes (ATC-groups). Figure 1 illustrates that patients used between 0 and 3 drugs from the same therapeutic classes, ranging from zero to 9 different CNS-active drugs. More specifically: 40 patients used between 0 and 7 different CNS-active drugs. Eleven patients concomitantly used CNS-active drugs from 1 to 2 therapeutic classes, 15 patients from three therapeutic classes, 8 patients from four therapeutic classes, and 4 patients used 5–7 therapeutic classes. Ten patients used antiepileptic drugs concomitantly with two other therapeutic classes, and 11 patients used antiepileptic drugs from three or more therapeutic classes of CNS-active drugs.

Drug-related problems

The clinical pharmacists identified 178 DRPs in 40 patients before the case conferences, based on the medical records provided by the nurses (Table 2). On average 4.5 DRPs were identified per patient (range 0–13). Only one patient had no DRPs. The most frequent DRPs identified were Unnecessary drug (n = 46) and Too low/high dose (n = 27), Monitoring required (N = 17), Unclear documentation of medication record/prescription (N = 17) and Adverse drug reactions (N = 17).

Six weeks after the interdisciplinary case conferences, 81.5% of the DRPs identified by the clinical pharmacists had been resolved, i.e., the GP and the nurse had agreed and actioned these. The most common action was to discontinue a drug (n = 53), follow-up (monitor) and assess the impact of change (n = 40) and to change dosage, formulation or route of administration (n = 35) (Table 2).

CNS-active drugs was the overall most commonly prescribed therapeutic class (n = 168) and also had the most DRPs (n = 75) (Table 1). The most commonly deprescribed CNS-active drugs were anxiolytics (n = 9), antipsychotics (n = 3) and antidepressants (n = 8). In addition, 11 CNS-active drugs had adverse adverse drug reactions or needed dose adjustments (n = 15) (data not shown in table).

Patient case: medication review and interdisciplinary case conference

To illustrate the thoroughness and the complexity of discussions taking place at the interdisciplinary case conferences, we have summarized the complex treatment, DRPs and conversation between the GP, clinical pharmacist (CP) and nurse for one of patients, “Sarah”, 65 years old (Table 3). She was prescribed 19 drugs/supplements: eight for the respiratory system, five CNS active drugs, three for constipation, one diuretic drug, one hormonal drug and one nutritional supplement.

During the systematic medication review, the clinical pharmacist identified 11 potential DRPs for “Sarah”. After the interdisciplinary case conference, six drugs were discontinued and one added, one dose was increased, and one formulation changed from regular to slow release, one dosage was changed from *prn* to *regular*, two drugs lacked

Table 1 The number of patients taking drugs from different therapeutic classes, including DRPs identified, actioned, or deprescribed

Most commonly prescribed drugs from various therapeutic classes	Number of patients n = 40	Number of prescribed drugs n = 481	DRP identified n = 178	DRP actioned n = 145 (%)	Drugs deprescribed n = 53
Alimentary tract	30	83	25	22 (88)	5
Dietary supplements	28	54	11	10 (91)	4
Respiratory drugs	24	57	27	24 (89)	8
Musculo-skeletal drugs	19	26	11	9 (82)	1
Cardiovascular drugs	18	43	14	8 (57)	2
Blood and blood forming organs	8	11	4	4 (100)	1
Dermatologicals	8	16	2	2 (100)	1
Genito urinary system and sex hormones	6	7	5	4 (80)	3
Systemic hormonal preparations, excl. sex hormones and insulins	4	4	0	–	–
Sensory organs	4	4	2	2 (100)	2
No code	3	3	0	–	–
Antiinfectives for systemic use	3	4	2	1 (50)	0
Antineoplastic and immunomodulating agents	1	1	0	–	–
CNS-active drugs (2 or more users)	38	168	75	59 (79)	26
Analgesics and pyretics	25	29	7	7 (100)	1
Paracetamol (29)					
Antiepileptics	23	38	13	7 (54)	0
Valproic acid (11), carbamazepine (9), oxcarbazepine (5), clonazepam (4), levetiracetam (4), lamotrigine (2)					
Anxiolytics	21	34	14	13 (93)	9
Diazepam (21), oxazepam (11)					
Antipsychotics	18	27	18	14 (78)	3
Risperidone (6), olanzapine (4), Levomepromazine (3), quetiapine (3), haloperidol (2), zuclopenthixol (2), lithium (2)					
Antidepressants	16	22	14	11 (79)	8
Amitriptyline (2), fluoxetine, citalopram (6), escitalopram (4), mianserin (4), mirtazapine (3), venlafaxine (2)					
Hypnotics and sedatives	6	7	5	3 (60)	3
Midazolam (2), zopiclone (2), melatonin (2)					
Opioids	4				
Codeine (2)		5	3	3 (100)	2
Anticholinergic agents	2	2	0	–	–
Biperiden (2)					
Anesthetics, local	1	1	0	–	–
Antimigraine preparations	1	1	0	–	–
Dopaminergic agents	1	2	1	1 (100)	0

monitoring of effect/toxicity and therefore 6-monthly measurement of serum concentration was initiated by the GP.

Discussion

Most of the patients in this study had, despite polypharmacy and a heavy CNS-drug load, not had their overall pharmacotherapy adjusted or reviewed in a long time and had been taking PIMs. As a result of the interdisciplinary medication reviews, 11% of drugs were stopped, 8% required further follow up and assessment of changes made, and 7% of drugs changed dosage, formulation or route of administration (Table 3). People with intellectual disability typically depend on either their GP, nurse, social educators or legal guardians to initiate a review of pharmacotherapy. Below we discuss concerns and challenges regarding pharmacotherapy.

Pharmacotherapy concerns

The total drug burden of CNS-active drugs is illustrated in Fig. 1, and concomitantly use affects most patients. Many

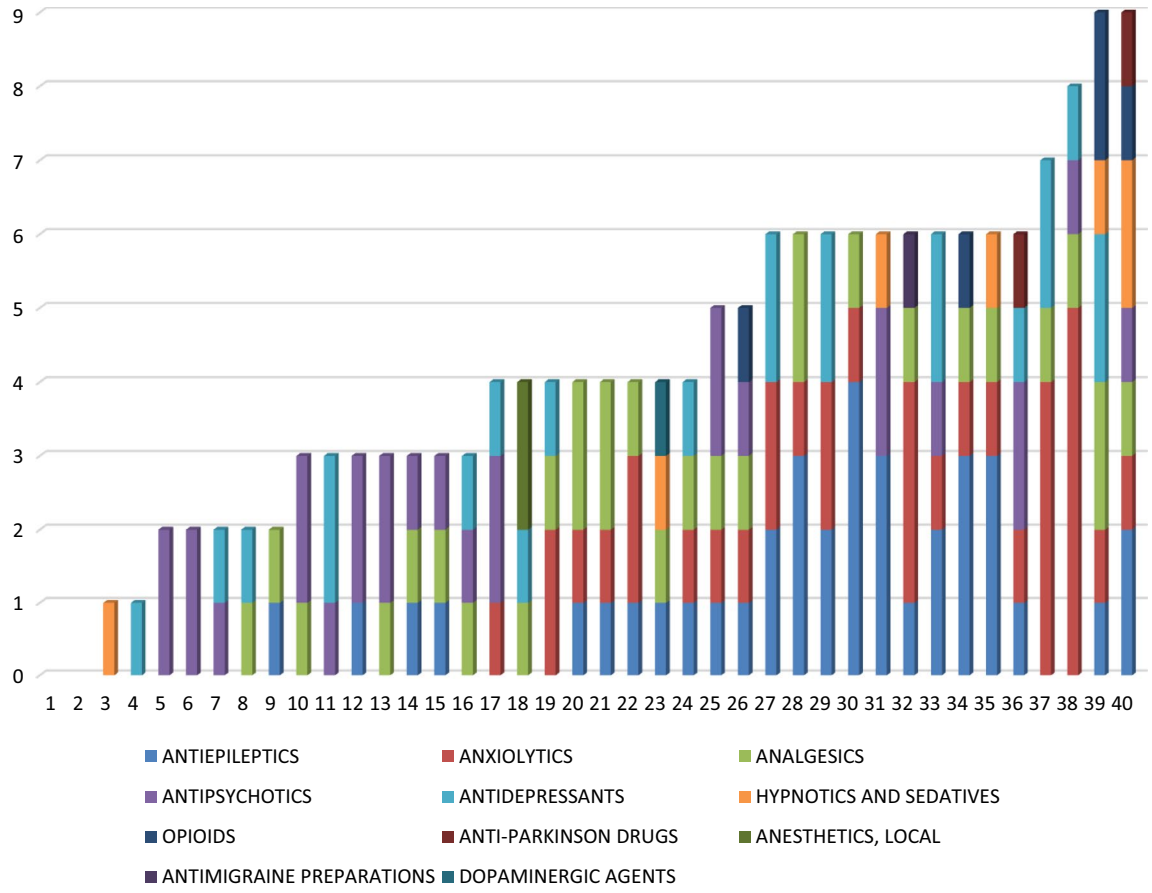

Fig. 1 Concomitant use of one or more CNS active drugs for 40 patients with intellectual disability. Patients used CNS-active drugs from 0 to 7 different therapeutic classes and 0–3 drugs from the same therapeutic class

CNS-active drugs were considered unnecessary or inappropriate, dosages were too high or too low, or that the patient experienced adverse effects. In line with others, we found that pain management was under-recognized and undertreated [11, 22]. One third of drugs were intervened on, in line with other publications supporting comprehensive and individualized review to optimalize pharmacotherapy [23, 24]. According to Matson et al. the effectiveness of psychotropic medications in managing challenging behaviors is very poor, and there is a need for larger controlled trials [25]. Extensive use of antidepressants to patients with intellectual disability was confirmed in our study and were stopped or the dose adjusted in many cases. In another study, it was shown that up to one third of the patients lack a clinical diagnosis for depression [24].

Of 40 patients, 23 were prescribed antiepileptic drugs. The clinical indications include epilepsy, but also increasingly neuropathic pain and psychiatry (including off-label use) [26]. This increases the risk of pharmacodynamic and pharmacokinetic interactions [27]. Antiepileptic drugs are associated with long-term or lifelong treatment, a fine-tuned balance between efficacy and tolerability, extensive pharmacological variability, serious adverse effects and many pharmacokinetic interactions [28, 29]. The majority of patients used antiepileptic drugs with a high potential to cause pharmacokinetic interactions, as the enzyme inhibitor valproate, and enzyme inducers as carbamazepine and oxcarbamazepine. The DRPs mostly addressed the lack of therapeutic drug monitoring (TDM) or adverse effects. It has been demonstrated that medication reviews lead to a decrease in adverse effects of antiepileptic drugs and benzodiazepines and maintenance of seizure control [6, 30]. Implementation of therapeutic drug monitoring for assessment of drug concentrations and markers of toxicity is a pivotal tool in this regard, and the reference ranges of all antiepileptic drug were recently updated and harmonized to improve the quality control of the interpretation of the use of monitoring [28, 29, 31, 32].

Thirty of our patients were prescribed a total of 83 antacids or laxatives, and 22 DPRs were actioned for these drugs. It is common for people with inherited intellectual disability to have increased prevalence of gastrointestinal problems, and the side effects from psychoactive drugs add to these problems [2, 33]. The adverse effects from psychoactive

Table 2 Drug-related problems identified during the medication reviews and outcomes taken at the interdisciplinary case conferences

(Row) Actions taken to resolve drug-related problems (Column) Drug related problems	Tapered and/or depre-scribed	Follow-up and assess impact of change	Dosage, formu-lation or route changed	No changes made	Update of medical record	New medicine prescribed	To be dis-cussed with physician	Medi-cine changed	To be dis-cussed with patient	Action taken	No action taken	Total
I. Drug choice problem												
Need for addi-tional drug	2	2	2	2		7	1			12	4	16
Unnecessary drug	40	2	2	2						43	3	46
Inappropriate drug choice	2	4		1	1			4	1	8	5	13
II. Dosing problem												
Too high dose			8							8		8
Too low dose		4	11	3			1			15	4	19
Sub-optimal dosing scheme		1	1							2		2
Sub-optimal formulation	4		2							6		6
III. Adverse drug reactions	1	7	3	5				1		9	8	17
IV. Drug-drug interactions	2	2		4						4	4	8
V. Inappropriate drug use												
Administered by health personnel		1			1		1			2	1	3
Administered by patient									1	1		1
VI: Other												
Monitoring required		16					1			15	2	17
Unclear docu-mentation of medication record/pre-scription	2		5		10					17		17

Table 2 (continued)

(Row) Actions taken to resolve drug-related problems (Column) Drug related problems	Tapered and/or deprescribed	Follow-up and assess impact of change	Dosage, formulation or route changed	No changes made	Update of medical record	New medicine prescribed	To be discussed with physician	Medicine changed	To be discussed with patient	Action taken	No action taken	Total
Not classified /complex problem		1	1	1			1		1	3	2	5
Total	53	40	35	18	12	7	5	5	3	145	33	178

drugs is often treated with laxatives and gastroesophageal reflux drugs [34].

Also, 24 of our patients were prescribed 57 different drugs for the respiratory system. The medication review resolved 24 DRPs, mainly because they were no longer taken or because the indication could not be found in medical records. It is recognized that patients with intellectual disabilities often have physical and cognitive deficits which prevent them from using their inhaler correctly and that this potentially represents a therapeutic problem [35].

Four inhalers were stopped for "Sarah" because the nurse reported that they were no longer in use, and her asthma treatment is now easier to manage, with twice-yearly measurement of the serum concentration of potassium. In addition, two more drugs were deprescribed and several other DRPs were resolved (Table 3). A pivotal question is of course if all the changes makes any difference to "Sarah" and her health and wellbeing? It certainly reduces the number of drugs to manage, reducing the chance of medication errors. The reduction of medical burden will most probably result in improved quality of life and improved cognition in many patients that may have been heavily sedated by polypharmacy and excessive adverse effects over years [36].

Polypharmacy and deprescribing

Polypharmacy is challenging to manage for all partners involved. Our patients used on average 12 different drugs including 4 different CNS drugs. All but one of the patients were prescribed five or more drugs, keeping in mind that the inclusion criterial were 4 or more drugs. The concomitant use of drugs were both intraclass and interclass polypharmacy, as illustrated for CNS-active drugs in Fig. 1 [37].

In total, DRPs for 30% of all prescribed drugs were resolved, and 81% of DRPs were acted upon within 6 weeks, in line with another comparable study on patient with intellectual disability [38]. The implementation rate is comparatively high compared other studies [15, 38]. The high acceptance rate implies that the DRPs in our study were relevant and important. It is worth dwelling on that a high proportion of the drugs were found either unnecessary or inappropriate, that dosages needed adjustments, that monitoring was required and that the documentation in medication records were insufficient. There was a lack of system for monitoring of effect or serum concentrations when required, and medical records and prescription data was often unclear or lacking.

It is also of concern that many of the patients with intellectual disability seem to have insufficient follow-up from their GP with regards to medication reviews. The need for regular medication review of people with intellectual disabilities has been emphasized by others [24, 39]. Daaleman argues that adults with intellectual and developmental

Table 3 Interprofessional medication review of a 65-year old patient with intellectual disabilities: Medication therapy, drug-related problems (DRPs), comments and actions taken

Therapeutic area	Medication therapy	Drug related problem identified by Clinical Pharmacist (CP)	DRP actioned
Asthma Chronic obstructive lung disease? Tight chest	Salbutamol 0.1 inhaler prn	Sub-optimal formulation	Drug is stopped Is no longer in use
	Salmeterol and fluticasone inhaler, 2 puffs × 3	Sub-optimal formulation	Drug is stopped Is no longer in use
	Beclometasone inhaler prn	Sub-optimal formulation	Drug is stopped Is no longer in use
	Budesonide inhalation fluid prn	Sub-optimal formulation	Drug is stopped Is no longer in use
	Theophylline depot tablets	Need for/lack of monitoring of effect and toxicity	Serum concentration of potassium is initiated to be measured every 6 months
	Acetyl cysteine 200 mg dissolvable tablets, 1 + 1 + 1 prn	Lack of or unclear documentation of the drug chart/prescription	Changed drug from prn to regular dosage
	Salbutamol 0.5 mg/ml inhalation fluid		
	Montelukast 10 mg tablet, 1 + 0 + 0		
Epilepsy/psychiatry	Valproic acid depot. 300 mg 2 + 0 + 2		
	Olanzapine	Need for/lack of monitoring of effect and toxicity	Serum concentration is to be measured every 6 months
	Diazepam rectal		
Constipation	Tramadol 50 mg 1 + 1 + 1	Too low dose	The dose is increased, and the formulation changed to slow release
	Paracetamol 1000 mg 1 + 1 + 1		
Pain	Movicol prn Macrogol	Unnecessary drug	Drug is stopped
	Toilax enema Bisacodyl	Drugs administered by health personnel	Drug was added to medication list
	Lactulose prn		
Edema	Furosemide 20 mg 1 + 0 + 0	Unnecessary drug	Drug is stopped. No indication found for use
Hypothyroidism	Levothyroxine sodium 0.5 mg		
Supplements lipids	Omega 3		

disabilities needs a primary care service which an interdisciplinary approach and that medication review should be conducted at regular intervals to check for polypharmacy [22].

A limitation of patients with intellectual disabilities include that many have a reduced ability to express adverse effects, which make close monitoring even more important. Evidence-based guidelines and studies for improved comprehensive care of this patient group are therefore needed [10]. In retrospect, there seems to be a need for more individualized treatment and monitoring of these patients, which would include regular use of therapeutic drug monitoring of the CNS-acting drugs such as antidepressant, antipsychotic and antiepileptic drugs. This could contribute to more adjustments of the doses to control for pharmacokinetic interactions and poor adherence, increase efficacy and decrease adverse effects [29].

Methodological considerations

In our study, the patients' GP was responsible for any changes in treatment and the nurse was responsible of obtaining patient consent. All patients or a legal guardian were offered to take part in the case conference, and one legal guardian accepted [40]. The sample of patients is not random, and not generalisable.

According to Norwegian legislation, GPs should, when necessary, perform medication reviews if patients are prescribed four or more drugs. This review can, but must not, include other health professionals. Interdisciplinary medication reviews including clinical pharmacist are not established in home care services in Norway.

A strength is that a comprehensive medication review was performed including the patients' the GP, nurse or social educator, and a clinical pharmacist. Involving only

one clinical pharmacist on the sample of 40 patients was a strength because it provided continuity of using the methods for medication reviews in different case conferences. It is a weakness because other clinical pharmacists may have identified other DRPs. Other limitations of this study is that only 40 participants were included. There is a risk of selection bias in the sampling as the neediest patients may not have been identified or able to consent. Another limitation is that the selection was not randomized, but based on care needs assessed by the nurse or social educator. A systematic screening for adverse drug reactions was not performed, and considering polypharmacy and the high CNS drug burden, this might have been beneficial.

The method used in the interdisciplinary case conferences to identify DRPs has been used in similar settings in primary and secondary care in Norway and elsewhere [14, 15, 38, 41]. The development of specific tools aimed at patients with intellectual disabilities seems plausible, but this was however presently not available in Norwegian [15].

Conclusions

Medication reviews and interdisciplinary case conferences improved pharmacotherapy for the patients with intellectual disabilities. Drug-related problems were resolved for one-third of all drugs prescribed for 39 of the 40 patients. Polypharmacy and concomitant use of CNS-active drugs is problematic due to pharmacodynamics and pharmacokinetic interactions. It is necessary to follow-up the pharmacotherapy and heavy drug load with serum concentrations measurements to limit adverse effects and to improve patient safety for this vulnerable patient group.

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Conflicts of interest The authors declare that they have no conflicts of interest.

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