Psychotropic Medication Use in Adolescents with Intellectual Disability Living in the Community

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Running head: Psychotropic use in Australian adolescents with ID
Word count: 2720
Statement about prior postings and presentations: This work has not been previously presented anywhere else.

Key words: adolescent, community, intellectual disability, psychotropic medication

Funding source: National Health and Medical Research Council of Australia. Project Grant No. 401647

Conflicts of interest: Uniquest (the corporate arm of The University of Queensland) owns the Comprehensive Health Assessment Program (CHAP) health review tool used in this study and receives a licensing fee from organisations that use the CHAP. One third of this licensing fee is paid to NL as the inventor of the CHAP. BT and SE are the co-authors of the Developmental Behaviour Checklist used in this study. BT and SE make no personal financial gain or profit from the sale of this checklist. The remaining authors have no conflicts of interest to disclose.

Key points:

- 20% of community-based Australian adolescents with intellectual disability in this study used psychotropic medications.
- Psychotropic medication use was strongly associated with male gender and the presence of major behaviour problems.
- Further studies examining the rationale for psychotropic prescribing in adolescents with intellectual disability are needed.

Abstract

Purpose. Information on the use of psychotropic medications in adolescents with intellectual disability is scant. Such information can guide interventions to improve psychotropic medication use in this population. We investigated the prevalence of, and factors associated with, psychotropic medication use in adolescents with intellectual disability in Australia who live in the community.

Methods. Cross-sectional data were obtained from adolescents with intellectual disability living in the community in South-East Queensland, Australia, between February 2007 and September 2010. Self-reported information on medication use was extracted from a health screening tool. Demographic and medical data were collected through parent/caregiver surveys. Medications were classified according to the Anatomical Therapeutic Chemical classification system. Psychopathology was assessed using the Developmental Behaviour Checklist Short Form. Logistic regression analysis was used to assess the association of demographic and medical characteristics with psychotropic medication use.

Results. There were 176 participants (median age=16 years, range=11-19 years; 55% male). Psychotropics were used by 20% of participants. Psychostimulants were the commonest psychotropic class, used by 9% of participants. Multipsychotropic prescribing was not common with only seven participants using more than one psychotropic agent. After adjusting for potentially confounding variables, use of psychotropic medications was significantly associated with male gender (adjusted odds ratio=3.6; 95% confidence interval=1.3-9.5) and having major behaviour problems (3.1; 1.1-8.9).

Conclusions. Adolescents with intellectual disability use a wide range of psychotropic medications. Being male and having major behaviour problems are associated with use of psychotropic medications. Research examining the rationale for psychotropic prescribing in this population is needed.

Introduction

The prevalence and patterns of prescription of medications in people with intellectual disability vary considerably; however, the consensus view is that people with intellectual disability are among the most medicated populations residing in either institutions or the community.[1-3] Most of the existing literature considering medication use in people with intellectual disability has investigated use in adults only or combined data on medication use in both adults and children. Little is known about the magnitude of, and factors associated with, medication use in adolescents with intellectual disability.

Adolescents with intellectual disability are characterised by a high prevalence of psychiatric disorders and behaviour problems compared with their typically developing peers.[4,5] Psychotropic medications have been widely used to treat psychopathological conditions in this population.[6] However, their use remains controversial due to limited empirical efficacy data and potential deleterious adverse effects such as tardive dyskinesia, akathisia, and/or extrapyramidal symptoms.[6] As such, the widespread use of psychotropic medications in adolescents with intellectual disability has become a major concern of healthcare planners worldwide.[6,7] Without an understanding of how psychotropic medications are being prescribed in this population, suggesting measures to improve the quality use of these medications is difficult. To date, there are only three medication use studies focusing on adolescents with intellectual disability.[8,9,10] These studies have discrepant results. Two studies were conducted in the Netherlands - a 2005 study of 912 individuals[8] and a 2006 study of 862 individuals[9] aged 4 to 18 years of all levels of intellectual disability who lived both in the community and institutions. Both studies reported 10% of the sample used psychotropics.[8,9] A more recent population-based study of 1419 Taiwanese adolescents (aged 12 to 17 years) living both in the community and institutions found 24% of adolescents used prescribed medications on a regular basis.[10] These studies suggested the need for additional research to

provide further insight into the use of medications, especially psychotropic medications in these vulnerable populations. This study endeavours to address this need by investigating the prevalence of, and factors associated with, psychotropic medication use in community-based Australian adolescents with intellectual disability.

Methods

We investigated a sample of adolescents with intellectual disability living in the community in South-East Queensland, Australia, between February 2007 and September 2010. The data reported were derived from a large randomised controlled trial investigating the effectiveness of a health intervention package in improving the long-term health of adolescents with intellectual disability.[11] Trial participants were adolescents with intellectual disability aged 10 to 18 years who were receiving education either in a special education school (SES) or in a special education unit (SEU) on the campus of a secondary school. In Queensland, students receiving education in a SES have significant intellectual disabilities and/or multiple disabilities. They usually require specialist teaching and therapy services that facilitate an individualised education program. Students attending a SEU in a primary or secondary school may have a range of disabilities, and usually access the mainstream curriculum and receive specialist teaching and therapy services. The trial was approved by both The University of Queensland Behavioural and Social Sciences Ethical Review Committee (Clearance number: 2004000081) and the Queensland Government Department of Education and the Arts (File number: 550/27/424).

The health intervention package employed in the trial consisted of two main components: the *Ask (Advocacy Skills Kit)* Health Diary and the Comprehensive Health Assessment Program (CHAP). The *Ask* Health Diary is a personalised hand-held health record. The CHAP is a one-off health check. It is partially completed by the adolescent with intellectual disability and their parent/caregiver prior to a general practitioner (GP) consultation, and includes a self-

reported health history of the adolescent including all medications used. The CHAP is completed by the GP during the consultation. After each GP assessment, the CHAP booklet was returned to the research team. The *Ask* Health Diary,[12] the CHAP[13] and the trial[11] have been comprehensively described previously.

We used the self-reported medication data from completed and returned CHAP booklets. Medications were classified according to the Anatomical Therapeutic Chemical (ATC) classification system developed by the World Health Organization for medication utilisation research.[14] The ATC system groups medications into categories according to the organ or system on which they act and/or their chemical, pharmacological and therapeutic characteristics.[14] For medications that could be classified into several categories, determination of the ATC category was based on the purpose of the pharmacotherapy and the medical history of the adolescent. Psychotropic medications were defined as medical agents for the central nervous system, excluding analgesics and anticonvulsants.[9] They included antipsychotics, antidepressants, anxiolytics, anti-Parkinson medications, hypnotics/sedatives, alpha2-agonists (clonidine and guanfacine) and atomoxetine.[9] On two occasions where prescribing information from the CHAP booklet was unclear, medical records were accessed to confirm the information. Data on age, gender, school type, level of mobility and health status were derived from baseline surveys completed by the adolescents' parents/caregivers at the commencement of the trial. Information regarding the presence/absence of epilepsy, Down syndrome and autistic spectrum disorder was obtained from the CHAP booklets. Body Mass Index (BMI, weight/height^2) calculations were based on the heights and weights recorded by the GP in the CHAP. We used age- and gender-specific BMI cut-offs for children and adolescents reported by Cole *et al.*[15] for overweight and obesity and by Cole *et al.*[16] for underweight.

Psychopathology was assessed using the Developmental Behaviour Checklist Short Form (DBC-P24)[17] developed from the 96-item Developmental Behaviour Checklist (DBC-P).[18] The DBC-P24 consists of 24 items concerning emotional and behaviour disturbance frequently observed in children and adolescents aged 4 to 18 years with intellectual disability.[17] Parents/caregivers reported the presence of each of the 24 items in their child for the past six months on a three-point scale: "very true or often true" (score of 2), "somewhat or sometimes true" (score of 1), or "not true" (score of 0).[17] Mean behaviour problem scores were calculated as the sum of responses to the 24 items divided by the total number of items each parent/caregiver answered.[17] Participants with a mean score of 0.48 or higher were considered to have evidence of behaviour problems.[17] This cut-off point was determined by assessing the checklist's ability to classify individuals with and without behaviour problems over a range of behaviour problem scores, which was quantified by using the Receiver Operating Characteristics curve.[18] The curve was a plot of the true positive rate against the false positive rate of the checklist at each threshold setting.[18] The optimal cut-off point was where the true positive rate was highest and false positive rate was lowest.[18] This corresponded to the cut-off point of 0.48 for the DBC-P24.[17] The higher the score, the more severe behaviour problems the participants had.[17,18] The DBC-P and DBC-P24 have been demonstrated to have very good sensitivity and specificity in classifying cases with and without behaviour problems.[17,18] Einfeld and Tonge[18] and Taffe *et al*.[17] described in detail how the DBC-P and DBC-P24 were developed and how the cut-off point was determined. To more usefully categorise participants we calculated the median of mean behaviour problem scores for all participants with behaviour problems (i.e. mean behaviour problem scores $\geq$ 0.48), which allowed us to examine the effect of behaviour problems in more detail. The value of this median was 0.75. In doing so, the data set was divided approximately into thirds. The lowest third included non-behaviour problem cases (i.e. mean behaviour problem scores

< 0.48); the middle third included minor behaviour problem cases (i.e. mean behaviour problem scores ≥ 0.48 but < 0.75); and the highest third included major behaviour problem cases (i.e. mean behaviour problem scores ≥ 0.75). Participants in the third tertile had behaviour-associated problems that were more obvious and happened more frequently than those in the second tertile.

We computed the prevalence of medication use, and investigated the associations between variables of interest and the use of psychotropic medications by computing unadjusted odds ratios as well as adjusting for potentially confounding variables using logistic regression analysis. Variables examined were: gender, school type, weight classification, self-reported health status, self-reported level of mobility, and the presence/absence of behaviour problems, epilepsy, Down syndrome and autistic spectrum disorder. Analyses were conducted using Stata statistical software version 11 (StataCorp, College Station, TX, USA).

Results

One hundred and one schools were approached, of which 85 agreed to participate in the trial. At baseline there were 728 participants, 425 of whom were randomised to receive the health intervention package; of these, 176 completed and returned the CHAP booklets. Adolescents who completed and returned the CHAP booklets were similar to those who did not in terms of gender (55% male versus 53%); age (median(range)=16(11-19 years) versus 16(12-22 years)); school type (55% SES versus 56%); and mean behaviour problem score (median(interquartile range)=0.63(0.39-0.88) versus 0.70(0.42-0.88)). All participants included in the present study lived with their parents or caregivers. Characteristics of participants are presented in Table 1; 96 (55%) attended a SES, 150 (85%) reported their level of mobility as being completely independent and 33 (19%) reported they had epilepsy. The median value of the mean behaviour problem scores for adolescents with behaviour problems, which was used to separate minor and major behaviour problems, was 0.75. There were 62

(35%) adolescents who did not have behaviour problems; 58 (33%) who had minor behaviour problems and 55 (31%) who had major behaviour problems.

[Insert Table 1 here]

Thirty six (20%) participants were using psychotropic medications (Table 2). Multipsychotropic regimens were administered to seven (4%) participants. The commonest combination of psychotropics was an atypical antipsychotic (risperidone) and a selective serotonin reuptake inhibitor (SSRI) antidepressant (citalopram or sertraline). Participants who received this combination had major behaviour problems, abnormal weight, autistic spectrum disorder, were male and received education in a SES. Psychostimulants were the commonest psychotropic class (used by 9% of the total sample), followed by antidepressants (6%) and antipsychotics (5%). Other psychotropic classes (alpha2-agonists, anti-Parkinson medications, hypnotics/sedatives) were used infrequently. The association between characteristics of interest and psychotropic medication use is displayed in Table 1. Gender and behaviour problems were significantly associated with the use of psychotropic medications. Male participants were 3.6 times more likely to take psychotropic medications than female participants (adjusted odds ratio [AOR]=3.6; 95% confidence interval [95% CI]=1.3-9.5). Participants with major behaviour problems were 3.1 times more likely to use psychotropic medications than those without major behaviour problems (AOR=3.1; 95% CI=1.1-8.9).

[Insert Table 2 here]

Anticonvulsants were taken by 27 (15%) participants; 26 (96%) of whom were reported by their parent/caregiver to have epilepsy. Of those taking anticonvulsants, 59% were receiving one anticonvulsant agent, 30% two and 11% three. Among anticonvulsants, valproate was the most frequently prescribed agent (used by 55% of participants taking anticonvulsants), followed by lamotrigine (37%), carbamazepam (22%), topiramate (15%), levetriacetam (7%), clonazepam and vigabatrin (4% each).

Discussion

A range of medications was administered to this sample of adolescents with intellectual disability. Psychotropics and anticonvulsants were prescribed for 20% and 15% of participants respectively. Psychotropic medications were used more by males than females. This may be in part explained by a higher prevalence of psychiatric disorders observed in male participants compared with their female counterparts (25% males versus 6% females had autistic spectrum disorder, 63% versus 49% had behaviour problems). In addition, males may experience more severe symptoms of a psychiatric disorder than females with the same diagnosis.[19] Studies examining the association between gender and psychotropic medication use in people with intellectual disability are limited; however, this gender disparity in psychotropic medication use is consistent with findings from existing publications relating to typically developing children and adolescents.[20,21] Participants with major behaviour problems used more psychotropic medications than those without behaviour problems, consistent with previous studies.[9,22] This suggests psychotropics were prescribed for this population either to control or treat behaviour problems. The associations between psychotropic medication use and autistic spectrum disorder and epilepsy became insignificant after adjustment for confounding factors. The insignificant association between psychotropic medication use and autistic spectrum disorder may be explained by the fact that the condition usually manifests as behaviour problems.[23,24] Although epilepsy is prevalent in this patient population, it is treated by using anticonvulsants, rather than psychotropic medications.[3]

In their review of pharmacoepidemiology of intellectual disability using data from studies undertaken from 1986 to 1995, Singh *et al.*[25] reported 19-29% of children and adults with intellectual disability living in the community used psychotropic medications. We observed 20% of participants used these medications, within the range reported by Singh *et al.*[25] However, this prevalence is higher than the 10% reported by Tobi *et al.*[8] and de Bildt *et al.*[9] in

children and adolescents aged 4 to 18 years with intellectual disability in the Netherlands. The 20% prevalence of psychotropic medication use observed in our study is lower than the figures reported in adults with intellectual disability who live in the community in Australia (35%)[26] or internationally (34-37%).[2,27] These differences in the prevalence of psychotropic medication use highlight the effect that different sample frames can have on estimates of prevalence of medication use. The present study supplements the limited population-level knowledge that exists and suggests that, overall, Australian adolescents with intellectual disability are twice as likely to be prescribed psychotropic medications as their Dutch peers. However, most of the prescribing occurs in individuals with major behaviour problems.

Our study is the first to investigate medication use in adolescents with intellectual disability in Australia. The 176 participants shared similar demographic and behaviour characteristics with participants who were randomised to receive the CHAP, but did not return their CHAP booklets to the research team. This suggests participants are likely to be a representative sample of Australian adolescents with intellectual disability, and that these results are generalisable to other Australian adolescents with intellectual disability. The study does have some limitations; most notably was self-reported medication usage information, potentially resulting in recall and information biases. However, previous studies have shown a high concordance between self-reported medication data and official prescription database.[28,29] Another limitation stemmed from the ATC classification system. The system classifies medications based on their main therapeutic use.[14] However, medications can have more than one indication, and it is sometimes difficult to know the indication for which a medication was prescribed. Nevertheless, the system has been demonstrated to be suitable for medication use research.[30] We were unable to investigate the association between the severity of intellectual disability and psychotropic medication use due to the lack of data. Some studies found the use of psychotropic mediations increases with level of intellectual disability in both

adolescents[8,10] and adults[31] with intellectual disability; whereas others reported no association.[9,27]

Data on psychotropic medication use from the general Australian population are limited. It is estimated that 5% of Australian adolescents aged 15 to 19 years and 11% of the general Australian population aged 15 years and older use psychotropic medications.[32] In the present study, 20% of participants used these medications. Given that psychopathological disorders are more prevalent in adolescents with intellectual disability compared with the general population,[4,5] it is unsurprising that the former reported more psychotropic medications than the latter.

Antidepressant use in the treatment of depression and anxiety disorders in children and adolescents has changed dramatically over the past decade.[6] The most notable change is the replacement of tricyclic antidepressants with SSRIs, which have fewer side effects.[6,33] We found the most commonly used antidepressants were SSRIs, reflecting this trend. Tricyclic antidepressants were prescribed for four participants. Although there is no evidence supporting the use of tricyclic antidepressants in treating depression in children and adolescents,[34] they remain an evidence-based treatment for obsessive-compulsive disorder and a second-line treatment for attention deficit hyperactivity disorder in these populations.[35] Australian therapeutic guidelines recommend 'the choice of SSRI for adolescents should be made taking into account the recent evaluations of clinical trial data and product information' (page 777); and current Australian product information for SSRIs recommends against their use in children and adolescents.[36] Given that psychiatric and behaviour problems are overrepresented in children and adolescents with intellectual disability,[4,5] antidepressants may be still useful for these populations. In addition, it is possible that antidepressants are seen by prescribers as efficacious in treating emotional lability and obsessionality in children and adolescents with severe intellectual disability.[37]

Co-prescribing was a common practice, with 44% of participants using more than one medication. People with intellectual disability usually have a wide range of health problems,[38,39] therefore polypharmacy may be appropriate. However, careful monitoring of potentially harmful drug interactions must be exercised when combination therapy is employed, especially within the cytochrome P450 isoenzyme system where many medications and most psychotropic medications are metabolised.[6] Given there have been cases of potentially fatal serotonin syndrome caused by serotonergic medication combinations in children,[40] prescribers must be aware of the pharmacological effects of medications. The use of psychotropic medications to treat psychiatric and behaviour problems in children and adolescents with intellectual disability is based on extrapolation of adult data.[6] Such extrapolation is problematic because psychopathology and pharmacology of medications may be expressed differently in children and adolescents with intellectual disability compared with their adult counterparts and the general population.[3,6]

In summary, a range of psychotropic medications was administered to adolescents with intellectual disability. Evidence to support psychotropic use in this population is currently insufficient. Well-designed clinical trials of safety and efficacy of psychotropic medications in adolescents with intellectual disability are needed. Research examining the rationale for prescribing in this population is desirable.

Table 1. Association of psychotropic use with demographic and medical variables (*N*=176)

Variable	*N*	*n* (%)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	*p*-value**
Gender					
Female	79	8 (10)	1.0	1.0	
Male	97	28 (29)	3.6 (1.5-8.5)	3.6 (1.3-9.5)	0.011
School type					
Special education unit	80	14 (18)	1.0	1.0	
Special education school	96	22 (23)	1.4 (0.7-3.0)	1.0 (0.4-2.6)	0.944
Weight classification***					
Normal	75	15 (20)	1.0	1.0	
Underweight	25	6 (24)	1.3 (0.4-3.7)	1.0 (0.3-3.4)	0.974
Overweight	33	7 (21)	1.1 (0.4-3.0)	1.0 (0.3-3.4)	0.939
Obese	35	7 (20)	1.0 (0.4-2.7)	1.3 (0.4-4.2)	0.669
Self-reported health status					
Excellent/very good	111	18 (16)	1.0	1.0	
Good/fair/poor	65	18 (28)	2.0 (0.9-4.2)	1.8 (0.7-4.4)	0.220
Self-reported level of mobility					
Completely independent	150	29 (19)	1.0	1.0	
Other†	26	7 (27)	1.5 (0.6-4.0)	1.4 (0.4-4.4)	0.618
Behaviour problems‡					
No behaviour problems	62	9 (15)	1.0	1.0	
Minor behaviour problems	58	6 (10)	0.7 (0.2-2.0)	0.7 (0.2-2.5)	0.605
Major behaviour problems	55	21 (38)	3.6 (1.5-8.9)	3.1 (1.1-8.9)	0.035
Epilepsy					
No	143	24 (17)	1.0	1.0	
Yes	33	12 (36)	2.8 (1.2-6.5)	1.5 (0.5-4.1)	0.461
Down syndrome§					
No	148	34 (23)	1.0	1.0	
Yes	26	2 (8)	0.3 (0.1-1.2)	0.4 (0.1-2.4)	0.332
Autistic spectrum disorder					
No	143	23 (16)	1.0	1.0	
Yes	33	13 (39)	3.0 (1.3-7.1)	1.6 (0.6-4.4)	0.340

Abbreviations: OR, odds ratio; CI – confidence interval.

*Associations were adjusted for gender, school type, weight classification, self-reported health status, self-reported level of mobility, the presence/absence of behaviour problems, epilepsy, Down syndrome and autistic spectrum disorder.

**p-value for adjusted odds ratios

***Missing data for 8 participants.

†Independent but may use aids, walks with help, uses wheelchair independently, uses wheelchair with assistance, immobile.

‡Missing data for 1 participant. A cut-off point of mean behaviour problems scores of 0.48 was used to separate participants with and without behaviour problems. A cut-off point of mean behaviour problems scores of 0.75 was used to separate participants with minor and major behaviour problems.

§Missing data for 2 participants.

Table 2. Prevalence of medication use (*N*=176)

Medication category	ATC code	*n*	%
All categories of medications		120	68
Psychotropics		36	20
Psychostimulants	N06B	16	9
Antidepressants	N06A	11	6
Selective serotonin reuptake inhibitor		7	
Tricyclic		4	
Antipsychotics	N05A	9	5
Typical		1	
Atypical		8	
Anxiolytics	N05B	4	2
Alpha2-agonists (clonidine)	N02CX02	3	2
Anti-Parkinson medications	N04	1	1
Hypnotics/sedatives	N05C	1	1
Anticonvulsants	N03A	27	15
Analgesics and anti-inflammatory medications	N02/M01A	44	25
Anti-asthmatics*	R03	23	13
Sex hormones and modulators of the genital system	G03	14	8
Corticosteroids (dermatological preparations)	D07	11	6
Anti-histamines for systemic use	R06	9	5
Cough and cold preparations	R05	8	5
Laxatives	A06	7	4
Antimicrobials for systemic use	J01/J02	6	3
Beta-blockers and angiotensin converting enzyme inhibitors	C07/C09	3	2
Other**, not elsewhere classified		42	24

Abbreviations: ATC, Anatomical Therapeutic Chemical.

*Used as *pro re nata.*

**Medications for acid-related disorders (A02), antineoplastics (L01), muscle relaxants (M03), urinary antispasmodics (G04BD) and thyroid hormones (H03).

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