



**UNIVERSITY OF
ALBERTA**
FACULTY OF MEDICINE & DENTISTRY

A Reduction in Polypharmacology has Positive Outcomes in the Developmental Disability Population

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- **Potential for conflict(s) of interest:**

Dr. Pierre Chue has received funding from organizations whose product(s) may/are being discussed in this presentation:

Sunovion, AstraZeneca, Bristol Myers Squibb, Otsuka, Eli Lilly, Glaxo Smith Kline, Janssen, Mylan, Lundbeck, HLS, Pfizer, Allergan, Alkermes

- **Mitigating potential bias:**

Clinical trial data, peer reviewed publications, approved communications from FDA including US Package Inserts (USPI), Health Canada including Product Monographs (PM), and European Medicines Agency (EMA) summary of product characteristics (SmPC)

Objectives

- **Be introduced to the disease burden in intellectual disability (ID) and effect on morbidity and mortality**
- **Be aware as to the prevalence and risks of potentially inappropriate medications (PIM) in the treatment of persons with ID**
- **Discuss studies that examine the withdrawal/discontinuation of psychotropic medications and potential benefits**
- **Be informed as to the latest recommendations for prescribing in ID**

Pre-test questions

- **The mortality rate in intellectual disability (ID) is lower than in the general population:**
 - True or false
- **The rate of psychotropic medication use in ID is reported to be up to:**
 - 13% ; 55%; 74%; 82%
- **Polypharmacy increases the risk of adverse events (AEs):**
 - True or false
- **Patients with ID usually receive more pain medications than those without ID:**
 - True or false

Disease burden in ID

- **People with intellectual disability (ID) have a higher disease burden than the general population**
- **Although life expectancy has risen mortality rate is still higher compared to the general population**
- **People with ID, are reported to have up to 2.5 x as many health problems as among those without ID and to receive 4x as many repeat prescriptions**
- **Higher CV risk and health declines at an earlier age in ID than the general population**

Disease burden in ID

- **Medical conditions include ocular, neurological (epilepsy), musculoskeletal (osteoporosis) , nutritional and gastrointestinal problems (GERD, H-pylori, dysphagia, constipation)**
- **Psychiatric conditions include ADHD, schizophrenia, mood, anxiety (including OCD), cognitive (dementia), sleep and stress-related disorders**
- **Psychiatric conditions identified in 45% of ID**

- **Medications are used to treat psychiatric symptoms and problem behaviors for which they are not approved**
 - **No indication in 70% (n=55; 284 medications)**
- **No evidence to support the effectiveness of psychotropic medications to manage problem behaviors**
- **Excessive use of medications (especially antipsychotics) including polypharmacy and higher than recommended**
- **Long-term use without audits/reviews**

- **Off-label use of psychotropic medications especially antipsychotics**
- **Use of medication without explicit patient consent**
- **Lack of monitoring**
- **Development of AEs which are difficult to assess**
- **Difficulty in carrying out necessary investigations such as blood tests for AEs**
- **Inappropriate use of drugs to treat AEs**

- **Differences in metabolism create different pharmacokinetics and pharmacodynamics**
- **Greater vulnerability to developing more adverse effects (AEs)**
- **Communication issues may make detection of AEs challenging**
- **Polypharmacy is common:**
 - **70% prescribed ≥ 1 psychotropic and 22% received 3+; correlated with female, residential care and >1 psychiatric diagnosis**
- **Polypharmacy increases risk of AEs**

Multimorbidity & polypharmacy in ID

- **Patients with multimorbidity or polypharmacy at baseline (n=1050) were 2.60 (95% CI = 1.86-3.66) and 2.32 (95% CI =1.70-3.16) times more likely to decease, respectively independent of age, sex, level of ID**
- **Hospitalization associated with polypharmacy (and aggression) but not schizophrenia or severity of ID (n=234)**

- **Rate of use of psychotropic medication in ID ranges from 32 – 85%**
- **Use of psychotropic medication does not typically decrease after discharge**
- **Little evidence available to guide clinicians on the safety and tolerability of psychotropic medications in ID**
- **Most studies are on antipsychotic medications as they are the most widely used psychotropic medications in ID**

- **92% taking at least 1 medication (n=735):**
 - **32.2% polypharmacy (5 – 9 meds)**
 - **21.5% excessive polypharmacy (10 + meds)**
 - **Antipsychotics were the most commonly prescribed:**
 - **64.6 % in XS polypharmacy and 54.9% in polypharmacy**
 - **1/3 using laxatives (75% in XS polypharmacy)**
- **Most frequently reported chronic conditions:**
 - **Eye (51.3%), psychiatric (47.7%), neurological (36.3%) and gastrointestinal (26.7%)**
- **Psychiatric/neurological illness, age, ID severity and residential care correlated with polypharmacy**

Potentially inappropriate medication (PIM) prescribing in ID

- **More PIM overall in elderly, women and ID**
 - **Greater sensitivity to AEs in ID and elderly patients**
- **In ID (n= 6976; older patients) compared with general population:**
 - **More prescriptions of psychotropic medications with anticholinergic effects, benzodiazepines, and antipsychotics (and also at higher dose and for longer)**
 - **Fewer prescriptions for pain medications including NSAIDs and tramadol (also lower dose and for shorter)**
- **More PIMs and less pain medication in ID**

Antipsychotics in ID

- **AP use is common and ranges from 21 – 43%**
- **Study found prevalence of AP polypharmacy (APP) (n=577) was 28.4% and associated with:**
 - **Age > 29, male sex, schizophrenia, substance use, greater number of hospital admissions, and high-dose prescribing.**
- **First-generation antipsychotics and long-acting injectables were prominent in APP combinations**
- **Co-prescription of anticholinergics and sodium valproate were significantly associated**

Use of gastrointestinal medications in ID

- **Previous studies have shown high prevalence of proton pump inhibitors (PPI) in ID**
- **Study (n=189):**
 - **28% PPI use ; > 50% female**
 - **Only 44% had an indication**
 - **67% on max dose**
 - **13% also on anti-platelet agent**
- **PPI use greatest in:**
 - **Older patients**
 - **Residential care**
 - **Severe ID (25% greater use)**

When are medications appropriate

- **Failure of non-medication based interventions**
- **Risk/evidence of harm to self or others**
- **High frequency and severity of problem behaviors,**
- **Treatment of an underlying psychiatric disorder or anxiety**
- **To help with the implementation of non-medication based interventions**

When are medications appropriate

- **Risk of breakdown of community placement**
- **Lack of adequate or available non-medication based interventions**
- **Good response to medication in the past**
- **Patient/caregiver choice**

Medication withdrawal

- **Absence of robust evidence on the most effective way to reduce or stop psychotropic medications**
- **Withdrawing medication requires:**
 - **Planned process**
 - **Multidisciplinary approach**
 - **Careful consideration of psychiatric and physical factors**
 - **Involvement of patients/carers**
- **Problem behaviors and AEs may worsen (initially) after medication withdrawal**

- **Medication reviews lead to a reduction in polypharmacy:**
 - **Systematic Tool to Reduce Inappropriate Prescribing (STRIP)**
 - **Screening Tool to Alert doctors to Right Treatment (START)**
- **Withdrawing medication requires:**
 - **Planned process**
 - **Multidisciplinary approach**
 - **Careful consideration of psychiatric and physical factors**
 - **Involvement of patients/carers**
- **Problem behaviors and AEs may worsen (initially) after medication withdrawal**

Discontinuing antipsychotics

- **Improvement in metabolic parameters (decreased weight, BMI, waist circumference, BP) after discontinuation/dose reduction of antipsychotics**
- **Discontinuing antipsychotics did not result in a worsening of behaviors in the majority of patients**
- **Recommendation that patients should be regularly reviewed as to the appropriateness of current antipsychotic regimen**

- **In other studies:**
 - **50% of cases long-term antipsychotics were completely discontinued or the dosage reduced**
 - **66.3% of individuals remained antipsychotic-free ≈10 years after discontinuation**

Recommendations (1)

- **Ensure that an assessment using a biopsychosocial approach has been conducted and recorded prior to initiating treatment**
- **Ensure that an appropriate formulation/diagnosis is completed and a treatment plan developed, prior to instigating any intervention**
- **Ensure that appropriate physical examinations and investigations have been carried out**
- **Assess the patient's capacity to consent to treatment**

Recommendations (2)

- **Discuss the treatment plan with the patient and/or carers**
- **Allow the patient and/or carers to be part of the decision-making process**
- **Clarify if the medication is prescribed outside of its approved indication, and inform on the type and quality of evidence to demonstrate its effectiveness**
- **Where possible, and when necessary, discuss the formulation and treatment plan with other relevant professionals**

Recommendations (3)

- **The treatment plan should be a holistic, person-centred approach**
- **The treatment plan must comply with the Mental Health and Capacity Acts**
- **Share the formulation and treatment plan with all the relevant parties, including GPs**
- **Identify a key person who will ensure that medication is administered appropriately and communicate all changes to the relevant parties**

Recommendations (4)

- **Consultation should take into account the communication needs of the patient**
- **Provide the patient and/or carers with a written treatment plan at the time of prescribing**
- **Method and timing of the assessment of treatment outcome should be set at the beginning of the treatment**
- **Use an objective assessment of outcomes (behavior/emerging AEs)**
 - **Use of standardized scales is recommended**

Recommendations (5)

- **Ensure follow-up assessments**
- **Prescribe one medication at a time where possible**
- **Start with a low dose and increase gradually**
- **Use medication within the recommended dose range.**
- **Ongoing consideration for withdrawing medication and exploring non-medication management options**
- **Medication may be used concurrently with non-medication based management**

Recommendations (6)

- **Document all appropriate information and share with appropriate individuals**
- **Inform about the common and serious AEs and provide accessible information in writing**
- **Advise what action to take if a serious AE occurs**
- **For “PRN” or as required medications provide as much information as possible about why and when the medication may be used and monitor regularly**

Approach to care

“A patient-centred approach to care, focusing on recovery, demands a reconsideration of how choices are made about treatment”

Post-test questions

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