Psychiatric management of mental health conditions in Intellectual disability

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Prescribing for psychiatric conditions in Intellectual disability (ID)

1. **Direct prescribing** i.e. anxiety/ low mood

2. **Indirect prescribing**: target symptoms rather than for specific conditions e.g., irritability, aggression, hyperactivity, sleep difficulty

3. **General principles for prescribing in young people with ID:**

- Start low, go slow – minimum effective dosing is often better
- Start one medication at a time
- Have clear target symptoms and behaviours
- Regular review of effectiveness and side effects
- Avoid polypharmacy where possible

Challenges in psychiatric prescribing in young people with ID

1. Evidence-base really limited; drawing from trials in children without ID or adult trials.
2. Higher rates of side-effects* and lower effect sizes compared to non-ID population.
3. Difficulty in establishing side-effects due to reporting difficulties for the young person
4. Difficulty in managing young people to accept and adhere to medication – including challenges of some medication not being available as liquids, and liquid medicine having unacceptable taste and texture profiles.
5. Consent / capacity issues.
6. Caution when there are co-occurring medical conditions such as epilepsy or cardiac conditions and / or if the young person is taking other medicine such as anti-epilepsy medicine, or bladder medicine.

* Pediatric Psychopharmacology - Fast Facts, D Connor, B Meltzer. Norton and Company 2006.

Challenges in psychiatric prescribing in young people with ID

In some genetic syndromes certain medications can lead to severe side-effects or are contraindicated e.g.

- Phelan-McDermid Syndrome: Patients often show poor tolerance to stimulants and SSRIs.
- Fragile X Syndrome (FXS): Stimulant medications for ADHD can increase agitation in some.
- Valproate is contraindicated in disorders from mutations of mitochondrial DNA polymerase, such as Alpers-Huttenlocher syndrome, as it can trigger acute, fatal liver failure. Valproate is also contraindicated in Urea Cycle Disorders as it can cause hyperammonaemia
- Photosensitivity in Cockyane syndrome impacts on medication choices for cyclical mood disorder common in this condition but care re: Lamotrigine.
- In HLA-B*1502 Genotype individuals (particularly of Asian descent) – carbamazepine poses a high risk of Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN).

Pharmacological Management of Anxiety and depression in OD:

- Selective serotonin reuptake inhibitors (SSRIs), i.e., fluoxetine and sertraline are prescribed because of their evidence for efficacy in typically developing youths.

- Alpha-agonists (clonidine, guanfacine) and beta-blockers (propranolol) are sometimes used for management of anxiety. However, there are no trials investigating the use of these medications for this indication in children with ID.

- Benzodiazepines are not generally recommended for the treatment of chronic anxiety in children with ID. They can worsen behavioural state, cause agitation and dependence. Benzodiazepines such as Lorazepam are however used in Catatonia – which sometimes develops after a period of high anxiety and / or low mood.

- Others: Buspirone and Lamotrigine.

Sertraline vs Fluoxetine

❖ **Which one to use on what occasion?**

❖ **Sertraline tablet is available as 25 mg, 50 mg and 100 mg**

- Sertraline – start at 12.5 mg per day

❖ **Fluoxetine start as an oral solution (20 mg / 5ml)**

- 0.5 ml once per day for 7 or 14 days, followed by
- 1 ml once per day for 14 days, followed by
- 1.5 ml once per day for 28 days, followed by
- 2 ml once per day for 28 days

Other medications for anxiety

- Citalopram
- Propranolol
- Buspirone
- Clonidine
- Oro-dispersible Risperidone before procedure
- Promethazine for agitation / acute distress
- Mirtazapine
- Topiramate
- N-Acetylcysteine

SSRIs in self-injury and irritability

- Self-injury is often a sign of stress / anxiety and low mood but pain and physical conditions important to rule out.
- Self-injury may be part of compulsive self stimulation.
- Swayer eat al. Psychopharmacological treatment of challenging behaviours in adults with autism and intellectual disabilities: A systematic review. Research in Autism Spectrum Disorders. 07 Jan 2014. 1750-9467 https://doi.org/10.1016/j.rasd.2014.03.02
- **Fluvoxamine and Risperidone** were found to be effective – with much more studies on Risperidone
- RICKETTS et al. **Fluoxetine Treatment of Severe Self-Injury in Young Adults with Mental Retardation**. Journal of the American Academy of Child & Adolescent Psychiatry, 32, 865-869

Risperidone in irritability and aggression

- Risperidone improves symptoms of irritability and aggression as well as additional problem behaviours associated with conduct disorder (CD) and oppositional defiant disorder (ODD) in children with ID. (Butelaar et al, Van Bellingham et al, Aman et al, Snyder et al)

- In studies the positive findings typically started within 2 weeks of initiation and in 2 open label studies the benefits were sustained 48-week extension studies. (Findling et al, Tugay et al)

- Buitelaar JK, Van der Gaag RJ, Cohen-Kettenis P, Melman CT. A randomized controlled trial of risperidone in the treatment of aggression in hospitalized adolescents with subaverage cognitive abilities. J Clin Psychiatry. 2001;62:239-248.
- Van Bellinghen M, De Troch C. Risperidone in the treatment of behavioral disturbances in children and adolescents with borderline intellectual functioning: a double-blind, placebo-controlled pilot trial. J Child Adolesc Psychopharmacol. 2001;11:5-13.
- Aman MG, De Smedt G, Derivan A, et al. Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviors in children with subaverage intelligence. Am J Psychiatry. 2002;159:1337-1346.
- Findling RL, Aman MG, Eerdekens M, et al. Long-term, open-label study of risperidone in children with severe disruptive behaviors and below-average IQ. Am J Psychiatry. 2004;161:677-684.
- Snyder R, Turgay A, Aman M, et al. Effects of risperidone on conduct and disruptive behavior disorders in children with subaverage IQs. J Am Acad Child Adolesc Psychiatry. 2002;41:1026-1036.
- Turgay A, Binder C, Snyder R, Fisman S. Long-term safety and efficacy of risperidone for the treatment of disruptive behavior disorders in children with subaverage IQs. Pediatrics. 2002;110:e34-e34.

Aripiprazole

1. **Owen et al**. Aripiprazole in the Treatment of Irritability in Children and Adolescents with Autistic Disorder. *Pediatrics* **2009**;124;1533

2. **Marcus RN et al.** A placebo-controlled, fixed-dose study of aripiprazole in children and adolescents with irritability associated with autistic disorder. J Am Acad Child Adolesc Psychiatry. **2009** Nov;48(11):1110-9.

3. **Marcus RN et al.** Aripiprazole in the treatment of irritability in pediatric patients (aged 6-17 years) with autistic disorder: results from a 52-week, open-label study. J Child Adolesc Psychopharmacol. **2011** Jun;21(3):229-36.

4. **Ching et al.** Aripiprazole for autism spectrum disorders (ASD). Cochrane Database Sys Rev **2012**

5. **Hirsch et al.** Aripiprazole for autism spectrum disorders (ASD). Cochrane Database Sys Rev **2016**

6. **Curran MP.** Aripiprazole in the treatment of irritability associated with autistic disorder in pediatric patients. Paediatr Drugs **2011**; 13:197-204

7. **Douglas-Hall P et al**. Aripiprazole: a review of its use in the treatment of irritability associated with autistic disorder patients aged 6-17. J Cent Nerv Syst Dis **2011**; 3:1-11

Sample dose titration for Aripiprazole and Risperidone

Aripiprazole Liquid (1mg/ml)

- *0.25 ml per day for 7 days*
- 0.5 ml per day for next 14 days
- 1 ml per day for next 14 days
- 1.5 ml per day for next 14 days
- 2 ml per day for next 14 days/ cont..

- Aripiprazole, minimum tablet dose is 5 mg and ½ tablet at 2.5 mg dose can be used

Risperidone oral solution (1mg/ml)

- 0.25 ml per day for 7 to 14 days
- 0.5 ml per day for next 14 to 28 days

- Is the same in tablet form.
- Some young people will need 1 mg per day (or 0.5 mg twice per day)
- Evening dose can help with sleep (e.g. 0.25 mg am and 0.75 mg pm)

Studies of Guanfacine in children with ID

- Guanfacine in Children with Autism and/or Intellectual Disabilities. Haden et al. Journal of Developmental & Behavioral Pediatrics 29(4):p 303-308, August 2008.

- A Randomized Double-Blind Placebo-Controlled Trial of Guanfacine Extended Release for Aggression and Self-Injurious Behaviour Associated With Prader-Willi Syndrome

Challenging Behaviour (Aggression, Self-Injurious Behaviour)

Drug Class	Agents	Notes
Atypical antipsychotics	Risperidone, Aripiprazole	Most evidence; use at lowest effective dose;
SSRIs	Fluoxetine, Fluvox, Sertraline	If related to anxiety/ low mood
Mood stabilizers	Lamotrigine, Valproate, Lithium	If mood dysregulation underlies the behaviour
β-blockers	Propranolol	May reduce impulsive aggression; limited pediatric ID evidence
Naltrexone	—	Some evidence for self-injurious behavior; especially in ASD+ID
Clonidine	—	Hyperarousal-driven aggression
Guanfacine		Poor impulse control

Compulsive behaviours and OCD

- Use of SSRIs for repetitive behaviours in children with ID is based on the effectiveness of SSRI in individuals with obsessive-compulsive disorder (OCD) meta-analysis of randomized controlled trials: *Soomro GM et al, SSRIs versus placebo for obsessive compulsive disorder. Cochrane Database Syst Rev 2008*.

- Sertraline and Fluoxetine commonly used in practice

- Be aware of SSRI interaction with stimulants (serotonergic syndrome)

Buspirone for RRB*

- Randomized control trial - N= 166 (ages 2-6 yrs)
- 5 mg vs 2.5 mg vs Placebo
- Primary outcome: ADOS scores
- 2.5 mg group showed statistically and clinically significant improvement in RR- behaviours.
- PET measures of tryptophan metabolism and blood serotonin levels were assessed as predictors of Buspirone efficacy.

* Chugani et al. Low dose Buspirone for restricted and repetitive behaviour in young children with ASD. Journal of Pediatrics 2016: 170:45-53

Psychotic Disorders & Schizophrenia

Drug Class	Agents	Notes
Atypical antipsychotics (1st line)	Risperidone, Aripiprazole, Quetiapine	Risperidone has most evidence in paediatric ID; monitor metabolic parameters closely
Olanzapine	—	Effective but high metabolic burden — weight gain, dyslipidaemia
Clozapine	—	Reserved for treatment-resistant cases; requires haematological monitoring (agranulocytosis risk)

Bipolar Disorder & Mood Dysregulation

Drug Class	Agents	Notes
Mood stabilizers	Lithium	Narrow therapeutic window; requires regular serum level monitoring; effective for classic bipolar
	Valproate (Sodium valproate)	Also has anti-epileptic benefit; teratogenic — caution in adolescent females *and males*.
	Lamotrigine	Better tolerated; requires slow titration (Stevens-Johnson syndrome risk)
Atypical antipsychotics	Aripiprazole, Quetiapine, Risperidone	Useful for acute mania and maintenance

Side-effects of anti-psychotics

- Increased appetite / weight gain (Aripiprazole causes least weight gain in all the anti-psychotics)

- Dyslipidemia
- ECG changes, such as prolongation of QTc

- Fatigue (esp in first few days or on higher dose)
- Increase in prolactin (not with Aripiprazole, it reduces prolactin)

- Less common: acute dystonic reactions, tardive dyskinesia, akathisia (subjective sense of restlessness, often accompanied by voluntary movements of the limbs or trunk).

Epilepsy & Psychopharmacology — Critical Interactions

Children with ID have high rates of epilepsy – keep in mind important interactions:

- **Valproate + SSRIs** → serotonin syndrome risk
- **Carbamazepine** → induces metabolism of many psychotropics (reduces efficacy)
- **Lamotrigine + Valproate** → lamotrigine toxicity (levels doubled)
- **Guanfacine + Valproate** → increased levels of valproate (can affect platelets)
- **Antipsychotics** → can lower seizure threshold (especially clozapine, chlorpromazine)
- **Quetiapine/Aripiprazole** have relatively lower epileptogenic risk

- Useful online free tool is: ***Medscape medication interaction checker***

Anti-psychotics monitoring

- NICE guidance on prescribing and monitoring anti-psychotics in children
- Pre-use blood tests – and review bloods
- Baseline ECG
- **Height/ weight**/ BP and Pulse

General guidance on monitoring

Parameter	Frequency
Weight, BMI	Baseline, then every 3 months on antipsychotics
Fasting glucose & lipids	Baseline, 3 months, then annually
ECG	Baseline for antipsychotics, TCAs, some times for stimulants
Prolactin	If high prolactin risk – but questionable?
LFTs, FBC	Valproate, carbamazepine, clozapine
Movement disorder assessment	Antipsychotics — every 6–12 months
Drug levels	Lithium, valproate, carbamazepine