BMJ Case Reports

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TITLE OF CASE ***Do not include "a case report"***

Administration of a long acting antipsychotic injection to a child whilst managing contra-indicated poly-pharmacy interactions and transition between services.

SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

Second generation antipsychotics (SGAs) are used to treat a variety of psychiatric symptoms and illnesses as well as the behavioural aspects of various neurodevelopmental disorders. However, there is reluctance in using second generation long acting injectable antipsychotics (SG-LAIAs) in child psychiatry services. We present a case of a 12yr old child whose presentation and medication regime warranted the use of aripiprazole Long Acting (LA) injection against a backdrop of potential CYP P450 enzyme interactions as a consequence of poly pharmacy. The case also describes the difficulties encountered working across different health sectors and agencies and highlights the ongoing need for skills based Continuous Professional Development for CAMHS based nursing staff.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Second generation antipsychotics (SGAs) are increasingly used in children and adolescents to treat a variety of psychiatric illnesses and the behavioural aspects e.g aggression, impulsivity associated with various neurodevelopment disorders.[1,2] Whilst the oral use of SGAs is becoming more routine within child & adolescent mental health services (CAMHS), prescribers can still be wary and reluctant to prescribe the depot or long-acting injectable form of the same antipsychotic.[3] Unfortunately, long acting (depot) formulations of medicines or any type of intramuscular administration is often negatively perceived by patients, their families and even healthcare staff. Intramuscular administration of antipsychotics can be a sign that the patient is so unwell that they require 'fast acting' if not, more potent medication, often within the guise of safety or risk containment. The actual physical act of intramuscular administration is often negatively portrayed in the media and if not handled sensitively, can also become a source of distress for the patient. The inherent issues associated with drug toxicity, side effects and the logistics of administration can make it difficult to encourage greater uptake of long acting/depot formulations, and so they tend to be largely prescribed when oral compliance to treatment is compromised, either intentionally or unintentionally. The benefits of depot/long acting formulations, such as freedom from daily administration of medication, lesser reliance on co-ordination of ordering repeat prescriptions are however, rarely mentioned. The additional governance and patient safety issues associated with using unlicensed medication, further complicates their routine use. This case report aims to show that second generation long-acting injectable antipsychotics (SG-LAIAs) can be safely used in children but this requires exceptional communication across different sectors and staff who feel competent in its administration.

CASE PRESENTATION ***Presenting features, medical/social/family history***

The patient had epilepsy, secondary to Tuberous Sclerosis (TS), diagnosed at age 6yrs and a mild Learning Disability. The patient was admitted age 10½ yrs to a children's psychiatric ward with a history of behavioural and perceptual disturbance over several months. The patient was clearly responding to visual and auditory hallucinations, but could not provide an accurate history as she would also become mute on occasions whilst still appearing perplexed and distracted in the throes of a psychotic episode. Sleep disturbance and major distress also suggested psychosis. The patient was admitted using Mental Health Act legislation and discharged on a Community Treatment Order.

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INVESTIGATIONS ***If relevant***

An MRI brain scan was performed but did not show any changes from a previous MRI brain scan and did not add any clarification

DIFFERENTIAL DIAGNOSIS ***If relevant***

NA

TREATMENT ***If relevant***

The patient was initially commenced on oral risperidone, at a dose of 500mcg bd which was gradually increased over a period of 5 months until it reached a total daily dose of 4mg. [carbamazepine 500mg bd, which is a known inhibitor of the P450 CYP 2D6 enzyme, was also being prescribed as an anti-epileptic drug (AED) which was why aripiprazole (a substrate for this enzyme) was initially considered, but rejected even though its side effect profile is more favourable compared to risperidone]. The patient's response to risperidone was variable and given its propensity to increase prolactin levels and the patients age and impending puberty, doses were not maximised and another antipsychotic was tried instead. Given the adverse metabolic side effect profile of some SGAs,[4] aripiprazole was deemed as the best option in this situation but its co-use with carbamazepine is strongly discouraged due to the effect on plasma levels.[5] Nevertheless, the highly specialist nature of the ward alongside an experienced clinical team (including a specialist psychiatric pharmacist) meant that a decision to persevere with the treatment plan of initiating oral aripiprazole (5mg) alongside carbamazepine (500mg bd) and continue with low dose lorazepam (0.5-1mg) (to address catatonia) was taken. This combination had a positive effect and the dose of aripiprazole was gradually increased over 8 months to a maximum oral dose of 15mg daily. Whilst the psychotic symptoms appeared to diminish, there were reports of a greater instance of absence type seizures (a possible effect of the reduction in seizure threshold caused by the aripiprazole). The overall improvement in presentation and social engagement meant there was reluctance (predominately by the parents) to stop the aripiprazole. Instead, a decision was made in consultation with the patient's neurologist to change the AED to oxcarbazepine given its lower propensity for enzyme induction. Compliance with oral medication was inconsistent on the ward and on passes home. Social stories were used to aid understanding of the need for medication. Specialist CAMHS Speech and Language Therapist and consultant psychiatrist worked with the patient to gain insight into the patient's delusions. Poor compliance was related to delusions that the medication was poisoning the patient. It was decided that if the psychosis could be treated with sustained (peak) levels of antipsychotic it would bring a resolution of the delusions and improve overall oral compliance. Interestingly, the social story regarding compliance with medication to control menstruation (which was also causing huge distress) was successful, demonstrating that the wider social story approach was effective in improving compliance, albeit not for those medicines affected by the delusions, i.e the antipsychotics and AEDs.

To avoid deterioration in mental state and after careful consideration, it was decided that the patient would benefit from a monthly intramuscular injection of the long acting form of aripiprazole. This would provide consistent plasma levels of antipsychotic and would also give the health care team more frequent contact with the patient and potentially identify much quicker if and when the patient's health started to deteriorate.

The merits of the long acting form were recognised and largely accepted but there was reluctance and anxiety at using a 'depot' in someone so young. The detained status of the patient meant that a 2nd opinion was required before the treatment could be initiated. This was forthcoming and also helped to provide the necessary safeguards for the clinical team as well as the patient. The problem of managing the interaction and subsequent enzyme induction was

still outstanding. Baseline plasma levels of (oral) aripiprazole and its metabolite, dehydroaripiprazole, were determined. The plasma levels in our patient were found to be much lower (42 and 19mcg/ml) than the adult reference range of 150-300mcg/ml. The dose range for aripiprazole LA injection is 200-400mg monthly in adults. Given the relatively low plasma levels (against a background of oral oxcarbazepine administration) in our patient, it was decided that an initial dose of 300mg IM would be appropriate. It was reinforced to staff and parents that the patient **must continue** to take the oxcarbazepine as directed- if it was stopped, the enzyme inducing effect upon aripiprazole would cease and aripiprazole plasma levels could rise. Sudden Unexplained Death from Epilepsy (SUDEP) was acknowledged to be a risk but there was little that could be done given the lack of compliance with the AED. It was felt that the risk was justified and accordingly, there was close collaboration between consultant psychiatrist and the consultant paediatric neurologist. Additionally, the patient was nursed on 1:1, including throughout the night, during the medication transition period as well as deploying camera observation to detect seizure activity. Plasma levels were monitored where possible. Oral aripiprazole was given for an additional 14 days to allow the LA injection to reach steady state plasma levels. No deterioration in functioning was evident doing the transition period and the patient was discharged shortly thereafter.

OUTCOME AND FOLLOW-UP

Ward nursing experience of administering intramuscular injections in someone so young was limited so assistance was sought from the local adolescent unit. Similarly, when the patient was discharged into local authority care to a residential school, issues around the supply of the injection also proved challenging. For example, who would prescribe it and where would it be administered? Several iterations involving an ad hoc supply from the (original) children's ward resulted in a plan whereby the medication was prescribed on a GP10 prescription that was dispensed at a local community pharmacy. School staff would collect it from there and together with the patient, attend a local CAMHS outpatient clinic for administration by a suitably trained nurse. Additional complexities including the patient's level of distress at receiving the injection, and availability of suitable nursing staff, resulted in the arrangement being untenable. Plans were put in place for the injection to be given at the local adolescent inpatient unit instead. Other logistical issues manifested themselves almost on a monthly basis. Nevertheless, detailed planning to allow the community pharmacy to keep the item as 'stock' and appropriate record keeping (injection administered on a 28 day cycle and NOT monthly) and 'named person ownership' by the outpatient team did allow the successful transition and treatment of an otherwise very disturbed young person.

An additional complexity in this particular case was the patient's refusal to engage in antipsychotic (physical health) monitoring due to the level of distress this caused. This led to the need for a detailed risk vs benefit analysis which decided to proceed with the ongoing antipsychotic prescription without the required monitoring. This required engagement with the child's family to provide parental consent and ongoing efforts from community staff to seek these investigations at every opportunity. Whilst it has not been possible to obtain blood or cardiac investigations, it has been possible with graded exposure to obtain physical observations.

This patient's perspective and understanding of the use of an injectable antipsychotic was impacted upon because of their learning disability. The patient lacked capacity to fully engage in the decision making process, however was able to clearly communicate distress on attending for administration. Subsequently a transition from injectable to oral antipsychotic was carried out which has been successful in managing psychotic symptoms. This required close observation of

the patient's mental state and consideration of the other co-morbidities.

DISCUSSION ***Include a very brief review of similar published cases***

This case demonstrates the importance of ensuring medication compliance in a complex and risky situation, especially when there is contra-indicated poly-pharmacy. The community team faced many challenges in successfully administering a long acting/depot antipsychotic due to the limited number of staff who felt competent to do so. It was interesting to note the response of colleagues when the patient's age was taken into consideration and the aversion of some professionals as well as the family when considering this type of treatment for this complex and seriously unwell person. The practicalities around administering the injection also required careful consideration and multi-agency working to ensure that each injection followed a carefully curated care plan with appropriate monitoring around it within the confines of a patient with reduced capacity.

The situation also highlighted training issues associated with the administration of injections for mental health nurses specialising in CAMHS. This is perhaps unsurprising given the general lack of such procedures in this population compared to nurses specialising in adult mental health services. Service providers should be cognisant of this fact as it could have an impact on nurse competencies and their ability to practice safely.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Second generation long-acting injectable antipsychotics (SG-LAIAs) can be safely used in children.
- Contra-indicated therapies due to Cytochrome P450 enzyme interactions should not automatically rule out a particular therapy.
- Staff working in CAMHS run a risk of becoming deskilled in the administration of injectable medication and so should prioritise training in this area.

REFERENCES ***Vancouver style (Was the patient involved in a clinical trial? Please reference related articles)***

1. Otasowie J, Duffy R, Freeman J, Hollis C. Antipsychotic prescribing practice among child psychiatrists and community paediatricians. *Psychiatrist*. 2010;34:126–9.
2. McDougle CJ et al. Atypical antipsychotics in children and adolescents s with autism and other pervasive developmental disorders. *J Clin Psychiatry*. 2008; 69 Suppl4:15-20
3. Cahling L, Berntsson A, Broms G & Ohrmalm L. Perceptions and knowledge of antipsychotics among mental health professionals and patients. *BJPsych Bulletin*. 2017;41:254-259
4. Maayan L et al. weight gain and metabolic risks associated with antipsychotic medications in children and adolescents. *J Child Adolesc Psychopharmacology*. 2011; 21:517-535.
5. Otsuka Pharmaceuticals, Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection (Aripiprazole Summary of Product Characteristics). Electronic Medicines compendium. https://www.medicines.org.uk/emc/product/7965/smpc

FIGURE/VIDEO CAPTIONS ***figures should NOT be embedded in this document***

NA

PATIENT'S PERSPECTIVE ***Optional but strongly encouraged – this has to be written by the patient or next of kin***

NA

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