The Medicine Cabinet:
Anxiety treatment when SSRI's fail

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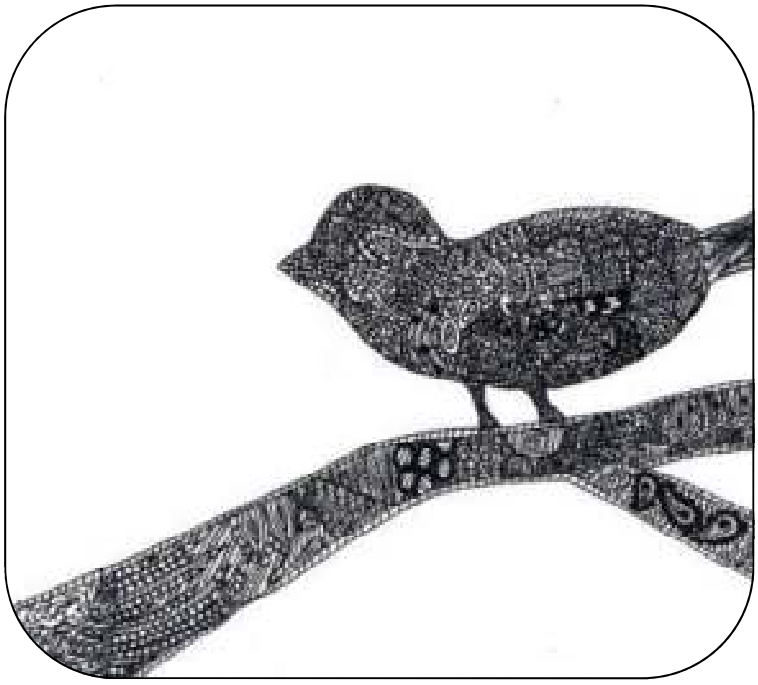
In the latest National Youth mental health Survey – Young Minds Matter recently released the incidence of anxiety amongst the 4-17 year olds was for males 7% and females 6.8% with the majority experiencing mild symptoms of one of the anxiety disorders. This represents half of all people aged 4-17 years with a mental health diagnosis. The most common form of anxiety was separation anxiety representing 4.3% of the study participants. Overall 18.7% of children and adolescents with an anxiety disorder had a severe disorder whilst 25.9% had a moderate severity.

Whilst some of the SSRIs (e.g. sertraline and fluvoxamine) have a license for obsessive compulsive disorder in Australia there is evidence for their use in both OCD and other anxiety disorders in children and adolescents. This article will concentrate on what other medications can be used when SSRIs are not effective (MHCAIDD, V2, Iss 2).

There are no published clinical trials for use of any medications for treatment of severe anxiety symptoms in ASD. There have been some psychological trials with moderate anxiety in high functioning autism, although the numbers are small. Anxiety in the ASD population can present in many different ways such as impulsivity. Thus looking at the impulsivity literature the following medications have potential for use. These are also second or third line pharmacotherapies for ADHD. These have been discussed in previous articles so refer to those on amitriptyline and clonidine (MHCAIDD, V4, Iss 3&4).



Other medications for anxiety include the use of propranolol (MHCAIDD, Vol 6, Iss 2) which has also been discussed earlier. Sometimes there is use of small doses of antipsychotics, typically either olanzapine or quetiapine (MHCAIDD, Vol 4, Iss 2) especially when the anxiety has a strong component of sleeplessness. As discussed, it is important to remember that these medications even at low doses can still contribute to significant weight increases so this should be monitored carefully as the long term implications can include diabetes and other metabolic conditions.

Naltrexone, a mu receptor antagonist used primarily to block the effect of opioid medications has been prescribed for alcohol dependence in the adult population. Naltrexone is used in autism for patients who experience significant self-injurious behaviour. The rationale behind this is to block the endogenous opioids generated by the self-injurious behaviour. There is some literature to suggest that the self-injurious behaviour is generated due to anxiety especially in the autistic population who have poor communication. Common adverse effects include nausea and vomiting as well as decreased appetite. Some experience sedation and worsening of the anxiety. As naltrexone blocks the opioid receptor, if having any planned surgery or needing strong pain relief with opioids, then the prescriber needs to be aware of the naltrexone, as the pain relief will be rendered ineffective.

Most paediatric studies in treatment of anxiety associated with obsessive compulsive disorder (OCD) have been with the SSRIs (fluoxetine, fluvoxamine, paroxetine, sertraline and citalopram). Trials for anxiety treatments for anxiety not associated with OCD are very limited and these include imipramine and venlafaxine XR. There is one small study (n=63, age 12-18 yrs) for use of imipramine with cognitive behavioural therapy for school refusal over an 8 week period but the results were poor and this is in a population who would be able to access the use of CBT.

Venlafaxine is a serotonin noradrenaline reuptake inhibitor but these effects are dose dependent thus at higher doses it is both a serotonin and a noradrenalin reuptake inhibitor. The venlafaxine XR trial had mixed results for a larger study (n=320, 6-17yrs) for generalised anxiety disorder. A short

term study showed positive results but this was unable to be replicated.

When venlafaxine is used there can be a withdrawal reaction due to the short half-life, this can be helped by the XR preparation but some patients will also need to be weaned slowly. It is important to note that overdose is dangerous. Most of the adverse effects are due to the lower dose serotonin blockade causing nausea, vomiting, headache, nervousness and insomnia. At higher doses the noradrenergic effects of blood pressure increase will occur due to inhibition of the noradrenergic receptors.

Compton and colleagues (2007) point out that one should weigh up if the condition in the child is sufficiently serious to warrant pharmacological intervention. Although much has been learned, many questions regarding the treatment of these paediatric anxiety disorders remain. Preferably, psychosocial interventions are usually combined with medication as these can augment each other, this provides the impetus to overcome anticipatory anxiety through initiating medication and then using the psychosocial interventions to consolidate any benefit from the medication. These studies were done in neurotypical patients which could apply to the autistic population, however more studies are needed.

There is a protocol to examine the evidence for other medications in the Cochrane library has only just been submitted (Livingstone et al, 2015). This protocol will look at other medications for irritability, self-injury and aggression in ASD besides the ones that have already been reported. These include risperidone for which there is some evidence for its effectiveness in irritability as well as aripiprazole.

In conclusion there is a paucity of any studies for medications other than fluoxetine for use in ASD population. More trials and studies of combination treatments of both psychological and pharmacotherapies are needed for one to say that one medication might be effective over another. Ongoing single trials for each individual patient will continue.

References

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