the medicine cabinet:

Fluoxetine and Autism

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Fluoxetine belongs to a class of medications known as the Selective Serotonin Reuptake Inhibitors (SSRIs) which increase the levels of serotonin in the body. There have been several clinical trials for use of fluoxetine in major depression, premenstrual dysmorphic disorder, panic disorder, bulimia and obsessive compulsive disorder (OCD) in adults and then paediatric clinical trials for major depression and OCD . These have led to the licensing or approval for use of fluoxetine for these conditions in children and adolescents by the FDA (USA Food and Drug Administration, the federal medication licensing organisation). Unfortunately, probably due to low patient numbers in Australia the same government support for treatment has not yet happened here with the TGA (Therapeutic Goods Administration of Commonwealth Department of Health the Australian medication licensing body). Nonetheless in 2005 ADRAC (Adverse Drug Reaction Advisory Committee) of the TGA recommended that fluoxetine to be the SSRI of choice for adolescent major depression. Over the last decade, the use of Fluoxetine amongst other SSRIs in children with autism has become increasingly common, both in Australian and overseas.

SSRIs increase the amount of the neurotransmitter serotonin in certain parts of the brain particularly the higher centres of the frontal lobes. In the mid-1980s clomipramine, an early non-selective serotonin reuptake inhibitor belonging to the tricyclic group of antidepressants was found effective in reducing OCD symptoms. Cerebrospinal fluid studies of levels of serotonin metabolite are shown to rise during clomipramine treatment. This effect in OCD was specific to those the antidepressants with inhibitory effects on serotonin reuptake (SSRIs).

Fluoxetine is the oldest of the SSRIs on the market and the original trade name was Prozac. Randomised control studies have show that SSRIs (eg fluoxetine) with clinical case management are beneficial for adolescent depression and are as effective as SSRI treatment in conjunction with cognitive behaviour therapy and cheaper (eg Dubicka et al, 2010). However CBT remains the first line of treatment recommended for mild and moderate depression.
Although SSRIs are used for children and adolescents with autism with comorbid depression and OCD, there is a specific clinical research hypothesis that SSRIs may have role in reducing repetitive behaviours, one of the core features of Autism. The clinically observed benefits of SSRIs in Autism has suggested that there may be similarities between the mental processes of OCD and stereotypic behaviour. Children and adolescents may display many forms of repetitive or stereotypic behaviours. It is postulated that these may be caused by low levels of the neurotransmitter, serotonin in the brain, which are also found in many cases of Autism. These repetitive behaviours include the following;
Stereotypy – purposeless movement, such as hand flapping or body rocking.
Compulsive behaviours – following certain rules that must be applied rigidly, such as arranging objects in a certain way.
Sameness or resistance to change – for example, insisting that furniture not be moved, wearing the same clothes or shoes, eating the same food, or refusing to change activity.
Rituals and routines – performance of daily activities in the same way each time, such as routines around mealtime or bedtime.
Restricted behaviour – limited range of interests, such as preoccupation with a particular television program or character.
Self-injury – actions that injure oneself, such as biting and head-banging.
These behaviours can cause problems at home, at school, and interfere with the child's ability to learn and interact socially.

As with all medications introducing them into the body can cause adverse effects, these can be minimized by starting at a low dose and this could be a quarter of the tablet and then slowing increasing the dose. As the tablets are dispersible in water a solution can also be made and a dose taken from the solution to give the correct dose. When introducing medication in this fashion the body can adjust to some of the minor adverse effects and thus minimise inconvenience.

Most tables of adverse effects come from the clinical trials conducted in adults when fluoxetine is compared to inactive placebo medication. Those adverse reactions when compared to placebo are ranked:
Common, ie. an incidence of 1% or more: nausea, agitation, insomnia, drowsiness, tremor, dry mouth, diarrhoea, dizziness, headache, sweating, weakness, anxiety, weight gain or loss, sexual dysfunction, rhinitis, muscle pain and rash.

Infrequent, an incidence of between 0.1-1%: sedation, confusion, palpitations, tachycardia, hypotension, electrolyte and blood problems eg bruising or bleeding, and extrapyramidal (neurological) reactions.

Rare, an incidence less than 0.1%: elevated liver enzymes and other potentially serious effects on the liver, blood, and central nervous system.

Allergic reactions such as rashes, itching and hives have been reported and if these happen should lead to medical review. Amongst other adverse effects that should have medical review are an increase in suicidal thoughts or actions and changes in mood that reflect increased agitation, activity, excitability or irritability. There has been particular publicity concerning this small risk of "behavioural activation" with increased impulsive behaviour that includes self harming behaviour. This side effect does seem to be more frequent in children and adolescents than adults. There is no evidence of increased actual suicide, which overall has fallen dramatically as these medications have become more available.

Fluoxetine can also interact with numerous medications and complementary medicines such that it can affect the blood levels of the other medication. So always let the clinicians treating other conditions know when fluoxetine is being taken.

When fluoxetine is given to be effective it has to reach a therapeutic dose as well as blockade of the receptors that it is targeting in the brain. This can take up to 4 -6 weeks depending on how long the therapeutic dose takes to achieve ie these medications are not quick fixes. Then the length of time to be on fluoxetine will depend on how the medication is being used.

Currently a group of clinicians at the Children's Hospital at Westmead, Sydney Children's Hospital Network, are part of a national, multisite randomised research trial to test the value of fluoxetine on the repetitive behaviours of children and adolescents with Autism. If anyone is interested in further information please contact Simone Cohen, study coordinator mobile phone number : 0402522249