

SSRI's and Discontinuation Events

Depression has been described as, "a disease state characterized by complex alterations in several CNS neurotransmitters and receptor systems" (Leonard, 1992). Part of the treatment involves antidepressant drugs that are known to cause adaptive changes in several CNS receptor systems, how they effect the changes and the intricacies of their action remain unknown. Thus, the action of Selective Serotonin Reuptake Inhibitors (SSRIs) cannot be simply explained as the inhibition of serotonin (5-HT) reuptake.

Natural serotonin dysfunction has been suggested as a cause for depression, migraines and selected anxiety disorders (Gardner & Lynd, 1998).

Serotonin is a monoamine neurotransmitter produced by several central cell bodies within the brain. It is a vasoconstrictor, and inhibitory neurotransmitter especially for dopamine (Caley, 1997).

The effect of serotonin on platelet activity has been indicated in studies of depression (Doogan & Caillard, 1988; Muck-Seler et al. 1991; Price, 1990). These studies have shown that serotonin affect platelet density and reduces serotonin re-uptake. The antidepressant activity of SSRIs is not only due to their inhibition of serotonin reuptake, term administration of these drugs to patients with depression have shown that platelet serotonin uptake increases (Leonard, 1992).

Recently, a growing number of discontinuation reactions have been described relating to SSRIs. Discontinuation reactions have been reported for all the SSRIs in clinical use today (Haddad, 1997). They are: Fluoxetine (Prozac); Fluvoxamine (Luvox); Paroxetine (Paxil); and Sertraline (Zoloft). Although no double-blind studies comparing discontinuation from different SSRIs have been published, data on relative incidence of discontinuation symptoms have been gleaned from several venues (Haddad, 1997).

The symptoms have been misdiagnosed or diagnosed as a side effect of another disease, syndrome or medication. There are several terms used to categorize these symptoms such as, SSRI Discontinuation Syndrome (Haddad, 1997), or Serotonergic Withdrawal Syndrome (Dominguez & Goodnick, 1995). Remember, that a syndrome is a group of symptoms. The four most common symptoms in one study included dizziness, nausea, lethargy, and headache (Haddad, 1997). Other symptoms include anxiety, parasthesia, confusion, tremor, sweating, insomnia, irritability, memory problems, and anorexia.

Dilsaver and colleagues (1987), divided symptoms of tricyclic antidepressant

discontinuation into five main groups:

- 1. GI and general somatic distress symptoms (lethargy, nausea, headache)
often associated with anxiety or agitation.**
- 2. Sleep disturbance (insomnia, excessive dreaming).**
- 3. Movement disorders (akathisia, parkinsonism).**
- 4. Behavioral activation on a continuum to mania.**
- 5. Miscellaneous symptoms (cardiac arrhythmias).**

Except for cardiac arrhythmias these symptoms have been seen with SSRI discontinuation (Haddad, 1997).

Several novel symptoms or symptom clusters, which fall outside the Dilsaver et al. (1987) group are discussed in the literature, which suggests that the symptoms of SSRI discontinuation may be more varied than those seen with tricyclic antidepressants. These include:

- 1. Problems with balance (dizziness, ataxia, vertigo).**
- 2. Sensory abnormalities including shock-like sensations (paresthesia, numbness).**
- 3. Aggressive and impulsive behavior.**

In summary, the data on SSRI discontinuation reactions are derived from data bases, published reports and adverse drug event forms that have reported to national monitoring bureaus. The incidence varies significantly from one SSRI to another, the consensus is that the majority of discontinuation symptoms occur with paroxetine (Paxil) and lowest with fluoxetine (Prozac), and varied with the others. Many symptoms overlap making the diagnosis difficult. In particular, psychiatric discontinuation symptoms (depressed mood, agitation, or irritability) may be mistaken for a relapse of depressive symptoms (Haddad, 1997). There is a need for more methodologically based studies to more clearly define the syndrome, determine causality and interventions.

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