

Serotonin Re-uptake Inhibitors (SRIs) and shock-like paraesthesias

Introduction

The first selective serotonin re-uptake inhibitor (SSRI) fluvoxamine (Fevarin[®]) was approved for marketing in The Netherlands in 1985. This new drug was soon to be followed by, in chronological order, fluoxetine (Prozac[®], 1989), paroxetine (Seroxat[®], 1991), sertraline (Zoloft[®], 1994), venlafaxine (Efexor[®], although strictly speaking not a selective but an unselective serotonin re-uptake inhibitor) and citalopram (Cipramil[®], 1997). The SSRIs are approved for the treatment of depressive episodes, obsessive-compulsive disorders (fluvoxamine, paroxetine), panic disorders or social or generalised anxiety (paroxetine, venlafaxine) and bulimia nervosa (fluoxetine). SSRIs inhibit the presynaptic serotonin re-uptake. The most frequent adverse effects include gastrointestinal complaints, headache, agitation, and insomnia. Despite the minimal anticholinergic properties of the drugs, anticholinergic adverse events have been reported and include dry mouth, constipation, and visual disturbances. The Netherlands Pharmacovigilance Centre Lareb received nine reports of sensations resembling an electric shock related to the use of SSRIs including venlafaxine. The SPCs of paroxetine, sertraline, citalopram, and venlafaxine mention paraesthesia as a possible adverse event. The SPC of fluoxetine specifies paraesthesia as a possible complaint at withdrawal. None of the SPCs mentions shock-like paraesthesias[1].

Reports

An overview of the reports received by the Netherlands Pharmacovigilance Centre is provided in Table 1.

Table 1. reports of electric shock-like paraesthesia associated with the use of SRIs

Sex, age	Drug Indication	Concomitant medication	Suspected ADR	Time to onset, outcome
F, 46	fluvoxamine -	Moclobemide alprazolam	'shocks in the head' paraesthesia, hyperhidrosis, paroniria, insomnia, fatigue	2 days, unknown
F, 56	fluoxetine -	None	'small electric shocks' rash, joint swelling, back pain	6 months, medication continued
F, 35	paroxetine depressive episode	None	electric shocks paraesthesia, dizziness	2 months, medication continued
F, 27	paroxetine depressive episode	None	electric shocks paraesthesia	4 days after lowering dose, recovered
F, 45	paroxetine obsessive-compulsive disorder	Levothyroxine	'small electric shocks through arms' agitation, hyperhidrosis, abdominal discomfort	2 months, not yet recovered
F, 56	paroxetine, -	None	'electric shocks in head and coccyx'	shortly after dose increase, decrease and withdrawal, recovered
F, 34	paroxetine, depressive episode	None	'small shocks in the head 6 times a day' paraesthesia legs	8 months, first aggravation after withdrawal, recovered after 4-5 weeks
F, 49	fluvoxamine, anxiety disorder	Oxazepam, estradiol/ cyproteronacetate	'small electric shocks' shivers	a few days, unknown
M, 29	venlafaxine anxiety disorder	None	'paroxysmal electric shock through whole body' dizziness	a few hours, first aggravation after withdrawal, recovered

The time to onset of the paraesthesias is rather heterogeneous and varies from shortly after administration to eight months after start. Paraesthesia was reported to occur 4 days after dose reduction (patient D), after onset and withdrawal (patient F), and to aggravate on withdrawal followed by full recovery (patients G & I). Two thirds of the patients did not use any other

medication. In four reports, other types of paraesthesias were mentioned besides the sensations of electric shocks.

Other sources of information

Literature

A search in the Medline database generated two articles on shock-like paraesthesias and one article of Lhermitte's sign associated with the use or discontinuation of SSRIs. Lhermitte's sign is a stabbing, electric-shock-like sensation running from the back of the head down the spine, brought on by flexion of the neck. The first article reports on three patients who experienced shock-like sensations after discontinuation of paroxetine / sertraline: all three patients were young men (22-28 years) who used the SSRI for obsessive-compulsive disorder, anxiety attacks and depression, respectively. They discontinued the use after periods varying from three weeks to two months. The latency period after withdrawal was two days, two days, and one day, respectively. One patient complained of "electric shocks", lasting two seconds, which ran quickly through his upper body and down to the arms and hands. The second patient reported five-second "electric waves" that ran from his forehead to his chest and abdomen. The third complained of one-second long "electric shocks" occurring primarily in the neck and chest that travelled to the fingers and toes. All men fully recovered[2].

The second article relates three cases of shock-like paraesthesias associated with the initiation of paroxetine treatment. A 25-year-old woman, who was prescribed paroxetine (indication: depression), experienced facial paraesthesias of a mild, shock-like nature, each episode lasting 5 minutes. A 29-year-old woman experienced several paroxysms of shock-like paraesthesias in the left side of her face and head on the second day after starting paroxetine treatment for dysthymia. The third woman, 22 years old, experienced a paroxysm of shock-like paraesthesias that was confined to her head a few minutes after taking paroxetine (indication: depression) lasting approximately 15 seconds and recurring daily after each dose. None of the patients used concomitant medication or had underlying neurological disorders[3].

The third article describes a 39-year-old female treated with paroxetine for depression for a year. Thirty hours after abrupt discontinuation, she experienced electrical shocks through her back and limbs that became more severe with movement. The symptoms could be provoked by flexion of the neck and were alleviated when intake of paroxetine was resumed[4].

Databases

Our pharmacovigilance centre received a total number of 2902 reports on SSRIs including venlafaxine. Since no other drugs in our database were found to be associated with electric shock-like paraesthesias, we were not able to determine the statistical significance of an association between SSRIs and shock-like sensations. On the other hand, this may also point to an exclusive association.

In the database of the WHO Monitoring Centre the MedDRA term "electric shock sensations" did not yield a match. However, of the 15 reports found using the WHO-art term "electric shock" 10 reports were associated with paroxetine use. The Reporting Odds Ratio was calculated at 236 (CI₉₅:81-690). For other SSRIs no instances of electric shocks had been reported.

Mechanism

The pathophysiology of drug-induced shock-like paraesthesias is not clear. The paraesthesia in some cases resembled Lhermitte's sign: "sudden 'electrical' pains occurring with neck flexion down the spine and into the upper extremities". Lhermitte's sign has been associated with various spinal cord disorders, and as an adverse effect of cisplatin and oxaliplatin[5,6]. Here, Lhermitte's sign is assumed to be due to hyperexcitability of the ascending neurons.

Conclusion

Nine cases in the Lareb database are indicative of a possible relationship between SSRIs and shock-like sensations. This type of paraesthesia may be due to neuronal hyperexcitability.

As regards the quality of the signal we found nine reports in the Lareb-database and ten cases in the WHO database on paroxetine, with three supporting articles published in international literature.

References

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