

LETTER TO THE EDITOR

Desogestrel and panic attacks – a new suspected adverse drug reaction reported by patients and health care professionals on spontaneous reports

Correspondence Sarah Watson, MSc Pharm, Uppsala Monitoring Centre, Box 1051, SE-751 40 Uppsala, Sweden. Tel.: +46 1865 6060; Fax: +46 1865 6088; E-mail: sarah.watson@who-umc.org

Received 23 November 2017; **Revised** 28 March 2018; **Accepted** 12 April 2018

Sarah Watson¹  and Linda Härmak²

¹Uppsala Monitoring Centre, Uppsala, Sweden and ²The Netherlands Pharmacovigilance Centre Lareb, 's-Hertogenbosch, The Netherlands

Desogestrel is known to be commonly associated with mood changes, depressed mood and decreased libido [1]. Anxiety and panic attacks have however not yet been described with desogestrel use.

In this letter, we highlight the potential relationship between desogestrel and panic attacks, which has been described by mainly patients and some health care professionals in spontaneous reports [individual case safety reports (ICSRs)] from VigiBase, the WHO global database of ICSRs [2, 3].

Contraceptive drugs are commonly used worldwide. Desogestrel is a hormonal progestin used as monotherapy or in combination with ethinylestradiol. The contraceptive effect is, in contrast to traditional progestogen-only pills, achieved primarily by inhibition of ovulation [1].

A panic attack is defined as a discrete period of intense fear or discomfort, often accompanied by physical symptoms such as palpitations and trembling. Experiencing repeated, consistent panic attacks that get in the way of everyday functioning is considered a defining symptom of panic disorder [4].

In VigiBase, there are a total of 25 reports for *panic attacks and disorders* [MedDRA high level term (HLT)] for desogestrel used as monotherapy reported between 2003 and October 2017. These reports were identified in a signal detection screening activity focusing on reports received primarily from patients. In the case series, 19 out of 22 reports, which had mentioned the qualification of the reporter, originated from consumers or nonhealth professionals. A disproportionality measure was used to highlight potential signals, and for this particular drug and ADR (MedDRA preferred term panic attacks), 1 case of panic attacks was expected but as many as 17 were reported [5]. A subsequent search in

VigiBase revealed eight additional reports for the MedDRA HLT *panic attacks and disorders*. In all reports, the causality was individually assessed. The well-described reports are all from Europe and concern women between 18 to 48 years (median age 30). In 17 cases, desogestrel is the only drug reported to have been used. Of the eight other reports that had additional drugs reported, only three reports suspected another drug in addition to desogestrel for the reaction. Ethinylestradiol/levonorgestrel was co-suspected and possibly contributing to the panic attack in two cases while in the third case, the co-suspected drug, lymecycline, was unlikely contributing to the reported event. Only one patient had a documented medical history of panic attacks but she had not had a panic attack for five years. Fifteen days after starting desogestrel, she experienced a panic attack. In 11 reports, it was documented that the panic attacks occurred within 2 months of starting the contraceptive drug. The median time from start of drug intake to occurrence of the panic reactions, in the reports where such information was available, was 15 days. Commonly co-reported terms were anxiety (15 reports) and depression (7 reports). In 17 cases, the patients were reported to be recovering/have recovered (one with sequelae) after withdrawal of the drug and in one case psychiatric problems (not further specified) reoccurred when the drug was started again. In five cases, it was reported that the patients had not recovered from the panic attacks at the time of reporting. Eighteen reports were classified as serious among the 22 reports that had added information about the seriousness of the case.

Often, the panic attacks were not recognized as adverse drug reactions (ADRs) due to desogestrel, as illustrated by these quotes from the patients:

Severe depression, anxiety and panic attacks. Sought additional treatment for depression/anxiety from general practitioner but symptoms abated once stopped taking Cerazette®.

Episodes of anxiety, panic and panic attacks in pressured situations. I connected this to my current life situation before I stopped Cerazette® At the same time the panic attacks I anticipated in certain situations did not occur. I did never suspect Cerazette® to have any role in my anxiety or panic attacks before I stopped the drug and realized that my problems went away.

The link with the drug as a cause for the panic attacks were often only identified after the patient had stopped taking desogestrel. This association has not to our knowledge been highlighted as a suspected ADR in the scientific literature previously. However, a structurally similar progestin, levonorgestrel, has been described to cause panic disorder in two cases. In both cases, the panic disorder occurred within 1–2 months after inserting levonorgestrel as a contraceptive device [6].

It is important to communicate the potential risks of anxiety and panic attacks while using desogestrel, which can have major impact on the daily functioning of a person. As the consumers of contraceptive drugs are mainly otherwise healthy women, the acceptance of undesirable adverse reactions is low. With this letter, we would like to ask prescribers and consumers of desogestrel to consider the possibility that desogestrel could be a possible cause for any anxiety or panic attacks experienced while using the drug.

Competing Interests

There are no competing interests to declare.

The authors are indebted to the national centres who make up the WHO Programme for International Drug Monitoring and contribute reports to VigiBase. However, the opinions and conclusions of this study are not necessarily those of the various centres nor of the WHO.

References

- 1 Electronic medicines compendium: summary of product characteristics for desogestrel (Cerazette®). Available at <https://www.medicines.org.uk/emc/medicine/10098> (last accessed 10 November 2017).
- 2 Lindquist M. VigiBase, the WHO global ICSR database system: basic facts. *Drug Inf J* 2008; 42: 409–19.
- 3 Caveat document; accompanying statement to data released from VigiBase, the WHO international database of suspected adverse drug reactions. Available at https://www.who-umc.org/media/1417/umc_caveat_201605.pdf (last accessed 10 November 2017).
- 4 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). American Psychiatric Association May 18, 2013. ISBN:978-0-89042-554-1.
- 5 Norén GN, Hopstadius J, Bate A. Shrinkage observed-to-expected ratios for robust and transparent large-scale pattern discovery. *Drug Saf* 2013; 22: 57–69.
- 6 Wagner KD, Berenson AB. J Norplant-associated major depression and panic disorder. *Clin Psychiatry* 1994; 55: 478–80.