

Possible association between norethisterone and paraesthesia: data from the VigiBase

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Background

Paraesthesia, abnormal perception defined as altered sensitivity characterized by tingling, burning, pins punctures and painful numbness in hands, feet, mouth, upper and lower limbs, is caused by insults to the sensory nerve transmission, due to various disorders or drugs (e.g. ritonavir, cyclosporine and statins). Paraesthesia is not reported in the current Summaries of Product Characteristics (SPCs) of medicines containing oral progestogens. No reports of paraesthesia or other related reactions such as tingling, peripheral neuropathy or abnormal sensitivity have been reported in literature [1-2]. Recently, as Regional Centres of Pharmacovigilance, we analyzed our national database (Rete Nazionale di Farmacovigilanza) and detected a potential signal concerning progestogens and paraesthesia.

Aim

To investigate a potential signal concerning progestogens and paraesthesia, analyzing the WHO Global Individual Case Safety Reports (ICSR) database (VigiBase).

Methods

Data were obtained from the VigiBase, which is maintained by the Uppsala Monitoring Centre. We collected all the suspected reports of paraesthesia associated with oral progestogens (i.e., excluded combinations with estrogens) and classified in VigiBase according to WHO-Adverse Reaction Terminology (WHO-ART) critical term 'paraesthesia'. A disproportionality analysis was conducted using the Information Component (IC) and the standard deviation (IC025) as a measure of disproportionality between observed reporting and expected reporting of a specific drug-ADR pair.

Results

Out of 7,332,991 reports collected in VigiBase between January 1972 and 1 June 2012, paraesthesia was associated with progestogen therapy in 920 reports. Nine-hundred and six out of 920 reports involved females with an average age of 36.6 years. The Anatomical Therapeutic Chemical (ATC) code G03AC ('Progestogens') had the highest number of suspected reports of paraesthesia associated with progestogen therapy (n= 864), followed by the other ATC groups considered (G03DA, n= 254; G03DC, n= 48 and G03DB, n= 21).

Among all suspected drugs involved in the analysis, only norethisterone (with its 46 reports) was associated with paraesthesia. Results showed for norethisterone a positive IC (0.47) and IC025 (0.02). The time to the onset of paraesthesia was determinable for 22 out of 46 reports: in 10 reports the neurological ADR appeared within 7 days after the first administration of norethisterone, in 9 reports between 8 and 30 days, and in 3 reports after more than two months.

Conclusion

Results suggest the hypothesis of a positive association between norethisterone and paraesthesia, whereas other progestogens do not appear to be involved in this association. In the light of the few reports collected and the large time span covered by our analysis, norethisterone-associated paraesthesia appears to be a rare outcome. However, the widespread use of progestogens in medical practice suggests that it is a complaint that can impair the women's quality of life. Since paraesthesia can be caused by several drugs, clinicians should consider that it may be also caused by norethisterone when facing with this ADR in a patient under polytherapy.

References

- 1) Farmadati. Compendio farmaceutico telematico. 2012;
- 2) DRUGDEX_ System. Thomson Reuters (Healthcare), Inc.2012. Available from: <http://www.thomsonhc.com> [Cited 6 July 2012]