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Brief Communication

Side effects reported by European consumers for medications for erectile dysfunction

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ABSTRACT

Objective: To characterise consumer adverse drug reaction (ADR) reports for phosphodiesterase type 5 (PDE5) inhibitors.

Methods: We included ADR reports submitted by adults to the European ADR database (EudraVigilance) from 2007 to 2011. ADRs were classified according to type, seriousness and age and sex of consumers. The unit of analysis was one ADR.

Findings: Totally, 328 ADRs were reported for sildenafil and vardenafil, and only 5% of these were serious. The largest number of reported ADRs was found for sildenafil, i.e., "lack of efficacy" and/or "drug efficacy decreased" (n = 134) and "headache" (n = 21).

Conclusion: ADRs reported by consumers for PDE5 inhibitors were relatively low, and only few ADRs were serious.

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INTRODUCTION

Phosphodiesterase type 5 (PDE5) inhibitors were launched in the late 1990s for treatment of erectile dysfunction (ED), and since then prescribing of these medications, particularly sildenafil has increased dramatically.[1,2] Internet prescribing and direct-to-consumer advertising has also contributed to increasing consumers' focus on the possibility of medical treatment of their ED.[3] Despite the large number of users, no studies have hitherto systematically analysed users' experiences with side effects from the use of PDE5 inhibitors.[4] Consumer reporting of adverse drug reactions (ADRs) has been introduced in national ADR reporting systems in order to increase knowledge about ADRs which were not reported by health care professionals.[5] Previous studies of ADRs reported to national ADR reporting systems showed that consumers contribute with knowledge about ADRs that was not previously provided by pharmaceutical companies or health professionals.[5,6] By 2012, consumer ADR reports were officially accepted in five European countries: Denmark, The Netherlands, Norway, Sweden and the United Kingdom.[5] The aim of this study was to characterise ADRs reported by consumers for PDE5 inhibitors in Europe.

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METHODS

We analysed European ADR data reported from 2007 to 2011 with respect to medications, type and seriousness of reported ADRs and age and sex of consumers. The unit of analysis was one ADR. We used data from the European ADR database, EudraVigilance (EV), maintained by the European Medicines Agency which contains information about

ADRs reported in the EU, including those reported to pharmaceutical companies.[7] Before ADR reports were submitted to the EV database, they were assessed by staff at the national pharmacovigilance centres and/or pharmaceutical companies and categorised by degree of seriousness and type of ADR.[8] Seriousness of reported ADRs was classified according to international criteria. ADRs were classified serious if they led to death, were life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or a congenital anomaly/birth defect and other medically important conditions.[8] Data were placed at the disposal of this study in anonymous form with encrypted personal identification.

RESULTS

From 2007 to 2011, a total of 7,437 individual ADR reports containing information about 35,349 ADRs reported by consumers were found in EV. Of these, 244 ADR reports corresponding to 328 ADRs were reported for PDE5 inhibitors. Approximately 5% of these ADRs (n = 18) were serious, including two fatal cases reported for sildenafil ("cytogenetic abnormality" and "exposure via semen"). One half of all ADRs were reported for men (n = 277) and 4% of ADRs for women. One third of ADRs (n = 96) was reported in 18-64-year-olds, followed by 19% of ADRs (n = 59) in patients above 64 years of age. For approximately one half of all reported ADRs, information about age and sex of the patient was not provided. Almost all ADRs were reported for sildenafil, and only two ADR reports were found for vardenafil. The ADRs reported for vardenafil were "lack of efficacy" and amnesia.

Table 1 display the characteristics of ADRs reported for sildenafil by number, type and seriousness. The largest number of reported ADRs was "lack of efficacy" and/or drug efficacy decreased" (n = 134) followed by "headache" (n = 21) and "erythema" (n = 11).

Table 1: Adverse drug reactions reported for sildenafil by consumers to the European EudraVigilance database, 2007-2011

Adverse drug reaction (s)	Total number (serious)
Lack of efficacy/drug efficacy decreased	134 (1)
Headache	21 (2)
Erythema	11
Dyspepsia	9
Erectile dysfunction	9
Flushing	9
Incorrect dose administered	6
Palpitations	5 (1)
Pyrexia	5
Abdominal pain upper	4
Myalgia	4
Rash	4
Ocular hyperaemia	3
Visual impairment	3
Nausea	3
Fatigue	3
Blood pressure decreased	3
Dizziness	3
Nasal congestion	3
Tinnitus	2
Blindness	2 (1)
Conjunctivitis	2
Vomiting	2
Chest pain	2
Drug/food interaction	2 (1)
Hangover	2
Accidental exposure	2
Heart rate increased	2
Muscle spasms	2
Migraine	2
Paraesthesia	2
Somnolence	2
Others	60 (12)
Total	328 (18)

DISCUSSION

A low number of consumer ADR reports were located for PDE5 inhibitors in the EV database. The majority of reports were for sildenafil, probably since this product was the first among the PDE5 inhibitors to be marketed in Europe. The number of reported cases was relatively low compared to sales figures.[1-3] A large number of ADR reactions such as "lack of efficacy" and/or drug efficacy decreased" was reported, probably because this side effect can easily be assessed, and is very obvious compared to many other types of ADRs. Sildenafil was not licensed for use in women, hence consumer ADR reports submitted by women were found in the EV database. We don't know whether this result can be explained by misclassification of reports in the regulatory agencies, or whether the medication in rare cases is used off-label by women. The strength of our study is that the material consisted of all consumer reports submitted to the EU ADR database over a 5-year-period. However, as it has not been mandatory to report consumer data to EV, except from serious reports, more data are expected to be present with the national pharmacovigilance agencies. The study design and results are based on spontaneous reports. A major limitation is that we do not know the causality of these ADRs, and this should be borne in mind when interpreting the results. Also, the large number of non-serious ADRs, which from a

clinical point seems irrelevant, questions the value of consumer reports in pharmacovigilance.

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AUTHORS' CONTRIBUTION

L Aagaard and EH Hansen designed the study, analysed the data and wrote the first version of the manuscript. L Aagaard did the sampling. Both authors approved the final version of the manuscript.

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