

Pergolide and pathologic gambling

Introduction

Pergolide (Permax[®]) is on the Dutch market since July 1991. Recently, the therapeutic indication was restricted to second-line treatment by a medical specialist of patients with Parkinson's disease in need of treatment with a dopamine agonist.

The Netherlands Pharmacovigilance Centre Lareb received two reports of pathological gambling, possibly reflecting a compulsive disorder, in association with the use of pergolide. Pathological gambling is not mentioned in the SPC of Permax[®] [1].

Reports

The first report from a neurologist concerns a female aged 50 years, with pergolide monotherapy because of m. Parkinson. She developed pathological gambling and increased libido within two months after dosage increment from 3 dd 0.5mg to 3 dd 1mg. Unfortunately, no additional data could be retrieved but the neurologist's statement was that this association is not unusual.

The second report from a consumer concerns a male aged 58 with levodopa/carbidopa (? dd 50/12.5) since about two years, pergolide (? dd 1mg) since eight years, and entacapone (? dd 400mg). He reported pathological gambling, but the date of onset is unknown. Additional information revealed that his neurologist recognised pathological gambling as a pergolide-associated ADR.

Other sources of information

Literature

Bergh *et al.* describe that CSF-levels of dopamine and related substances in persons with pathological gambling (not using dopamine agonists) differ from controls. He suggests that the dopaminergic system, possibly mediating positive and negative reward, and the noradrenergic system, possibly mediating selective attention, have changed in pathological gambling [2].

Geschwandtner *et al.* describe two patients with m. Parkinson with pathologic gambling, deterioration of Parkinson's disease and addiction to dopaminergic medication. Latency period in the first patient was within 3 months, but could not be determined in the second patient due to non-compliance. As most likely explanation, they consider overstimulation (by abuse) of mesolimbic dopamine receptors by dopaminergic drugs [3].

Molina *et al.* describe 12 patients with Parkinson's disease and pathological gambling. The gambling behaviour appeared more often in the "on" periods of motor fluctuations and worsens with levodopa therapy, suggesting that it could represent a behavioural manifestation of pharmacologic treatment [4].

Driver-Dunckley *et al.* retrospectively researched 1,884 files from patients with Parkinson's disease, and found 9 (1:209) cases with pathological gambling, all with pramipexole (incidence 1.5%) or pergolide (incidence 0.3%). All started after dopamine agonist dosage increase and resolved with dosage reduction. According to these authors, the incidence of pathological gambling in the general population is between 0.3 and 1.3% [5].

Seedat *et al.* describe a patient with slowly progressive pathological gambling since using pergolide and selegiline for m. Parkinson. Treatment followed with risperidone, which caused deterioration of Parkinson symptoms, followed by adjuvant low dose levodopa/carbidopa [6].

Polard *et al.* describe a patient with use of SSRIs for 15 years because of chronic depression. An idiopathic M. Parkinson developed. Treatment followed with bromocriptin, and later levodopa was added. Because of pathological gambling levodopa was replaced by levodopa/carbidopa, without result [7]. In September another study on anti-Parkinson drugs will be published [8].

Databases

The database of the Netherlands Pharmacovigilance Centre Lareb contains no other reports of (pathological) gambling in association with other drugs.

Gambling is not a term of the WHO dictionary. Compulsion-like terms were not disproportionately present in association with pergolide. For this reason, The WHO-database does not support this association.

Mechanism

The general impression from literature is that the grade of stimulation of dopaminergic receptors as needed for control of m. Parkinson symptoms, may imply overstimulation of those cerebral areas that control behaviour.

Conclusion

Two reports initiated research for the association between use of pergolide and pathological gambling, that seems well known in literature and well known by involved physicians.

Intensive dopamine agonist therapy is associated with pathological gambling, as supported by two case reports and literature data.

References

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