

Tramadol and hallucinations

Introduction

Tramadol (Tramal[®]), a (weak) synthetic opioid, has been approved for the Dutch market on December 21st, 1992. Tramadol induces analgesia by binding to the μ -opioid receptor and by inhibition of the reuptake of norepinephrine and serotonin [1]. Tramadol is used as a step two analgesic on the WHO pain treatment ladder.

The adverse reaction profile of tramadol is similar to the other opioids. The most frequently occurring adverse reactions are dizziness, nausea, constipation and pruritis [2].

The SPC of Tramal[®] mentions *changes in the cognitive and sensory capacity (e.g. the ability of making decisions and disturbance of perception)* as an infrequent adverse reaction with an incidence of less than 0.1% [3]. Hallucination is not stated in the SPCs of Tramal[®], Tramagetic[®], Zaldiar[®] or Tramagetic-once daily[®], but it is mentioned in the SPC of Tramal retard[®] [4-7].

Reports

Up to February 2004, Lareb received 18 reports of hallucinations on tramadol (10 reports from pharmacists and 8 reports from general practitioners). The characteristics of these reports are summarized in table 1, three reports will be discussed in more detail below.

Table 1. Characteristics of cases of hallucination reported to Lareb

Parameter	Value	Comment
Age	72 years (mean)	9 are older than 80
Gender	F: 83% M:17%	
Daily dose	132 mg (mean)	In 1 to 4 doses. Dose unknown in 1 case
Time to onset	6 days (mean)	8 less than 2 days
Outcome	12 recovered (67%)	Unknown in 6 cases
Formulation	2 retard, 1 solution, 15 capsule	

Patient A

This report concerns a 78-year-old female, who used tramadol (50 mg once a day) for unspecified pain. She developed visual pseudo-hallucinations 5 days after starting tramadol. She saw people moving in her room, which, she realized were not present at that time. Concomitant medication was omeprazole, diclofenac and prednisone. Patient used the tramadol for one month, and after withdrawal, she fully recovered.

Patient B

An 89-year-old woman was using tramadol (50 mg 3 to 4 times a day) for unspecified pain. After two days, she began to see a yellow-green beetle and abnormal cats. Concomitant medication was metoprolol and naproxen. The tramadol has been withdrawn the next day, outcome is unknown.

Patient C

A 40-year-old female developed hallucinations (not specified), photopsia, vomiting, syncope and a cold feeling two days after starting tramadol 100 mg once a day. Concomitant medication was not reported. She fully recovered after discontinuation of the tramadol.

Other sources of information

Literature

A literature search on hallucinations related to the use of tramadol yields three articles. Both auditory and visual hallucinations have been described secondary to tramadol administration [8]. Hallucinations have also been associated with morphine and other opioids [9,10].

Databases

On February 31, 2004, the database of the Netherlands Pharmacovigilance Centre contained 18 reports on tramadol concerning hallucinations. The database of the WHO Uppsala monitoring centre contains 303 reports of hallucinations in association with tramadol.

Table 2. Overview of data of case/non-case approach of Lareb and WHO database

Database	n reports tramadol with hallucination	Reporting rate (%)	n reports tramadol total	ROR (95% CI)
Lareb	18	5.7	318	6.7 (4.1– 10.9)
WHO	303	3.8	7966	4.9 (4.4 – 5.5)

Mechanism

The mechanism of opioid-induced hallucinations is unknown, although the effect seems to be dose dependent. In general, elderly are more susceptible to psychiatric adverse drug reactions.

Conclusion

Lareb received 18 reports of hallucinations in association with tramadol. These associations are disproportionately present in both the WHO and Lareb databases. Case reports in literature are supportive. Most of the Lareb reports concern elderly patients, with other psychotropic drugs as concomitant medication. Although these factors are possible confounders, in practice tramadol is used especially in this group of patients. The hallucinations occurred within a week after start and disappeared in most patients after stop of tramadol.

References

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