TITLE: Gabapentin Tablets Versus Capsules: A Review of the Evidence Regarding Appropriate Use

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CONTEXT AND POLICY ISSUES:

Gabapentin is approved by Health Canada as an antiepileptic agent and it is also widely used off-label in the treatment of pain and in the management of several psychiatric conditions, including alcohol withdrawal and cocaine dependence.[1-4] The exact mechanism by which this central nervous system active agent exerts its antiseizure activity has not been identified.[1] In addition to its antiseizure activity, gabapentin has been shown to alter mood (e.g. elevation, euphoria) and may cause hallucinations in patients with epilepsy.[1,5] However, the potential for misuse and dependence with gabapentin is uncertain.

Gabapentin is supplied in 100 mg, 300 mg and 400 mg capsules and 600 mg and 800 mg tablets, although the capsule form is less expensive and more commonly used.[6] Reports have surfaced that the capsules are being inappropriately used (inhaled intranasally), particularly among certain patient populations.[7,8] This report will review the evidence regarding decreased risk of misuse of gabapentin tablets compared to capsules.

RESEARCH QUESTION:

What is the evidence regarding appropriate usage of gabapentin in tablet form versus capsule form?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, OVID's Medline and Embase, the Cochrane Library (Issue 3, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2000 and March 2010. No filters were applied to limit the retrieval by study type.

SUMMARY OF FINDINGS:

The literature search returned five observational case reports[7-10] that discuss the inappropriate use of gabapentin capsules. No higher quality evidence was identified.

Observational studies

In 2004, a report was published describing potential misuse of gabapentin among inmates in correctional facilities in Florida.[7] A recall of all dispensed prescriptions for gabapentin at one of the larger correctional facilities in the state revealed 19 of 96 prescriptions were in the possession of the intended patients. Subsequently, five inmates reported they were inhaling the powder from gabapentin (300 or 400 mg) capsules intranasally. All five inmates had psychiatric or pain diagnoses, as well as histories of cocaine abuse, but they reported being abstinent since their incarceration. Four of the five inmates reported obtaining an altered mental state or "high," similar to cocaine. In this instance, the intranasal inhalation of gabapentin may have been an attempt to alleviate cocaine withdrawal or craving. No evidence of further abuse was reported once gabapentin was removed from the formulary and prescribing was restricted to special cases. When gabapentin is prescribed, the Florida correctional facilities attempt to dispense single dose tablets when possible.[7]

Similar scenarios were reported among California inmates, which led to the removal of gabapentin from the formulary in that system as well.[9] The nature and prevalence of the misuse was not described in the case report. Of interest, it was noted from the California corrections facilities that tablet formulations of other medications (quetiapine and sustained release bupropion) were being crushed and inhaled intranasally by inmates.[9,11] Thus, both tablet and capsule formulations may be subject to misuse.

Case reports regarding the oral misuse of gabapentin have also been documented among patients with histories of alcohol abuse.[8,10] In the first case, a 67-year-old woman was taking 4200 mg daily of gabapentin (in addition to naproxen and amitriptyline) for pain associated with polyneuritis.[10] She self-titrated her dose to 7200 mg daily and she began seeking gabapentin from pharmacies and physicians in order to obtain more. When she was unable to obtain gabapentin and was switched to alternate pain medication, withdrawal symptoms developed, which resolved upon gabapentin administration. The second case involved a 33-year-old man who was taking twice his prescribed dose of gabapentin.[8] He would seek refills prematurely in order to calm his cravings for alcohol. Three days after he was denied further refills, symptoms of withdrawal, namely disorientation, agitation, tachycardia, hyperreflexia, and tremors emerged and he was hospitalized. In hospital he received lorazepam and haloperidol for his withdrawal symptoms to no effect. Symptoms, however, resolved on gabapentin administration. The third case, a 63-year-old man who was taking 4900 mg daily (almost three times his prescribed daily dose) of gabapentin, was hospitalized following days of fatigue, sedation and confusion that his physicians considered associated with months of high dose gabapentin use.[8] As in the previous case, the patient (who had similar withdrawal symptoms) was treated without success until gabapentin was administered. These reports[8,10] do not specify whether the tablet or capsule formulations were involved; however, misuse in these instances was unlikely to be determined by whether the medication was available in capsule or tablet form.

Limitations

The evidence for the misuse of gabapentin formulations is based on case reports and not on clinical or population-level data. These reports do not directly compare the rates of misuse between the gabapentin formulations. Also, there is no specified denominator with which to assess the frequency of misuse for either formulation.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

There is a paucity of primary studies comparing the potential for misuse of gabapentin capsules and tablets. There is evidence from case reports that gabapentin capsules may be subject to misuse in certain populations, particularly those with histories of substance abuse or dependency. It is conceivable, however, that gabapentin tablets would also be subject to intranasal misuse since the tablets can be crushed and the resulting powder inhaled. Furthermore, oral misuse has been reported and it is unlikely that the dosage form would be an important determinant of whether or not the agent was misused in these cases.

In addition, the capsule and tablet forms of gabapentin are supplied in different doses without overlap. Thus, directly substituting one for the other is not necessarily appropriate.

In summary, there is insufficient information to evaluate the extent of misuse of gabapentin capsules and insufficient data to confirm gabapentin tablets are associated with less frequent misuse than gabapentin capsules.

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