

Adverse cardiovascular events associated with triptans and ergotamines for treatment of migraine: Systematic review of observational studies

Cephalalgia

0(0) 1–14

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DOI: 10.1177/0333102414550416

cep.sagepub.com



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Abstract

Background: Apart from the underlying cardiovascular (CV) risk associated with migraine, both triptans and ergotamines can induce vasoconstriction and potentially increase the risk of serious ischemic events. Because of the low frequency of such events in eligible patients, randomized controlled trials are not exhaustive to assess the drug-related CV risk. Observational studies are, therefore, an essential source of information to clarify this matter of concern.

Aim: The aim of this study was to systematically review the available published observational studies investigating the risk of serious CV events in triptan or ergotamine users, as compared to unexposed migraineur controls.

Methods: We systematically searched MEDLINE and EMBASE electronic databases for cohort or case-control studies up to December 1, 2013. Studies retrieved from CDSR, DARE and HTA databases of the Cochrane Library were used for snowballing. Studies investigating the risk of any CV outcome in patients with a migraine diagnosis and exposed to triptans or ergotamines were considered for inclusion. Selection of studies, data extraction, and risk of bias assessment were conducted independently by two reviewers. Pooled odds ratios (ORs) with 95% confidence interval (95% CI) were computed using a random-effects model for studies and outcomes judged eligible for quantitative data synthesis.

Results: From a total of 3370 citations retrieved, after duplicate removal and screening, only four studies met the inclusion criteria (three nested case-control analyses and one retrospective cohort study). These studies investigated the risk of different CV outcomes associated with either the recency or the intensity of exposure to the studied drugs. As for the intensity of use, the pooled OR of serious ischemic events was 2.28 (95% CI 1.18–4.41; $I^2 = 0\%$) for ergotamine use (two studies), whereas for triptans (three studies) it was 0.86 (95% CI 0.52–1.43; $I^2 = 24.5\%$). Recent use of ergotamines was not significantly associated with any CV outcome (only one available study). Two studies investigated the risk of stroke related to recent triptan use: the first study reported an OR of 0.90 (0.64–1.26), and the second one suggested an increased risk of 2.51 (1.10–5.71). In this case, because of the high degree of heterogeneity, results were not pooled.

Conclusions: To date, few comparative observational studies have investigated the CV safety of migraine-specific drugs in clinical practice. Evidence gathered here suggests that intense consumption of ergotamines may be associated with an increased risk of serious ischemic complications. As for triptans, available studies do not suggest strong CV safety issues, although no firm conclusions can be drawn. In particular, evidence on stroke risk is conflicting. However, if an increase of the absolute stroke risk in recently exposed patients does actually exist, it must be small. Overall, residual uncontrolled confounding factors reduce the confidence in the risk estimates collected from the included studies. Further investigations are needed to better define the risk for rare but serious CV events related to triptan and ergotamine use for treatment of migraine.

Keywords

CV risk associated with migraine, ergotamine, triptans, migraine

Date received: 25 April 2014; revised: 9 June 2014; 29 July 2014; accepted: 15 August 2014

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