Introduction
Ergotamine is an alkaloid derivative of ergot. It is a powerful vasoconstrictor, working mainly as an alpha adrenoceptor agonist, and probably also has partial agonist actions at serotonin (5-HT) receptors.\(^1\)

The 2004 WHO Model Formulary recommends its use for the treatment of acute migraine attacks, to be considered only when attacks are unresponsive to non-opioid analgesics (paracetamol, aspirin or other non-steroidal anti-inflammatory drugs). The Formulary, which recommends that the product is not used in children, includes no alternative to ergotamine for the treatment of acute migraine where non-opioid analgesics have failed.

Product and Dosage
Ergotamine is listed in the Formulary as the tartrate in 1mg tablets.\(^2\) The suggested dose (in adults) is 1–2mg at the first sign of an attack, maximum 4mg in 24 hours. If the dose needs to be repeated, there should be an interval of no less than 4 days between doses. The maximum dose is 8mg in any 1 week, and the treatment should not to be used more than twice in any 1 month.\(^2\)

Absorption of ergotamine from the gastrointestinal tract is poor and may be further decreased by the gastric stasis that occurs during migraine attacks. Moreover, there is considerable individual variation in the bioavailability of ergotamine.\(^1\) Ergotamine is sometimes used together with caffeine with the aim of improving absorption of ergotamine, although it is not clear whether such enhancement occurs.\(^1\)

Evidence of value
There are few published randomised controlled trials assessing the use of ergotamine in the treatment of acute migraine. A meta-analysis of placebo-controlled trials was not able to demonstrate a benefit from oral ergotamine.\(^3\) Ergotamine has been compared with acetylsalicylic acid in a published randomised controlled trial. The trial, which involved 250 people with acute migraine, found that ergotamine 2mg + caffeine 200mg was significantly less effective in relieving headache than was lysine acetylsalicylic acid 1,620mg + metoclopramide 10mg (headache relief in 61% vs. 77% of patients, \(p=0.01\)). The combination was also less likely to have reduced nausea and vomiting after 2 hours (in 40% vs. 65% of patients, \(p=0.001\)).\(^4\)

Assessments in reviews and standard texts do not recommend ergotamine as the preferred treatment of acute migraine unresponsive to non-opioid analgesics, and its place has been largely taken by the 5HT\(_1\) agonists (triptans eg sumatriptan).\(^1, 3, 6, 7\) Sumatriptan is more effective in relieving migraine headaches than oral ergotamine.\(^8\) However, triptans generally cost more than ergotamine. Some consider that ergotamine might have a role in the treatment of patients with prolonged attacks when recurrence of headache after treatment with a 5HT\(_1\) agonist is a problem,\(^6\) however there is no evidence to support this approach.
Adverse effects

After therapeutic doses, nausea and vomiting commonly occur as a result of the direct emetogenic effect of ergotamine and so it may exacerbate the nausea and vomiting that commonly develops as a migraine attack progresses; some people also experience abdominal pains. Weakness and muscle pains in the extremities, numbness and tingling of the fingers and toes may occur. Susceptible people, especially those with severe infections, liver disease, or occlusive peripheral vascular disease, may show signs of acute or chronic poisoning with normal doses of ergotamine.\(^1\) Overdose or chronic overuse of ergotamine may cause ergotism, a rare but life-threatening severe generalised vasospasm.\(^5\)

Ergotamine dependence can develop insidiously when ergotamine tartrate is used for more than 2 days a week, even if total daily or weekly dose recommendations are observed.\(^1\) Ergotamine-dependent patients have daily, or almost daily, migraine headaches, often referred to as ‘analgesic-induced headaches’ or ‘rebound headaches’, which are only relieved by ergotamine.\(^1\) Ergotamine is subject to international control under the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances.

Recommendation

Available evidence does not support the use of oral ergotamine in the treatment of acute migraine attacks. Evidence of its effects is sparse, its oral absorption is unreliable and it commonly causes adverse effects, which can be troublesome and sometimes dangerous, and which limit how much the drug can be used for an individual attack. Ergotamine tartrate should be deleted from the WHO Model List of Essential Medicines.

WHO should consider adding sumatriptan to the Model List for use in the treatment of acute migraine attacks unresponsive to non-opioid analgesics.

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References

Search Strategy

The medical literature was searched to identify guidelines, systematic reviews or meta-analyses related to ergotamine use in the treatment of acute migraine. Below is a list of electronic databases, websites and journals searched (date of search: 17.07.2004)

Sources Searched
The Cochrane Library
Clinical Evidence
Scottish Intercollegiate Guidelines Network
National Institute for Clinical Excellence
Prodigy
Guidelines International Network www.g-i-n.net
Drug and Therapeutics Bulletin
eTG complete (Therapeutic Guidelines)
Therapeutics Initiative www.ti.ubc.ca
British Medical Journal
Lancet
New England Journal of Medicine