Calcium antagonists for aneurysmal subarachnoid haemorrhage

NICE has developed the Cochrane Quality and Productivity topics to help the NHS identify practices that could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care. Each topic has been derived from a Cochrane systematic review that has concluded that the evidence shows that the practice is harmful or ineffective and should not be used, or that there is insufficient evidence to support widespread use of the practice.

Unless otherwise stated, the information is taken with permission from the Cochrane systematic review.

NICE summary of Cochrane review conclusions

Limited evidence suggests that oral nimodipine demonstrates increased benefits by reducing the risks of poor outcome and secondary ischaemia, with only modest risks. Evidence shows that the harms of intravenous calcium antagonists for aneurysmal subarachnoid haemorrhage may outweigh the benefits.

The intravenous administration of calcium antagonists should not be offered for routine use, given the limited evidence to support its use, higher costs and potentially higher risk of hypotensive effects.

Consider replacing intravenous calcium antagonists with oral nimodipine for routine use in the management of aneurysmal subarachnoid haemorrhages, which may lead to improved patient outcomes and patient safety through reduced adverse events.

The 'Implications for practice' section of the Cochrane review stated:

'Based on our conclusions, we recommend oral nimodipine (60 mg every 4 hours, to be continued for 3 weeks) as standard treatment in patients with aneurysmal subarachnoid haemorrhage. Although the evidence about the beneficial effect of nimodipine is not beyond all doubt, and is mainly based on one large study where aneurysms were treated with surgical clipping, we recommend oral nimodipine given the potential benefits and modest risks associated with it. Intravenous administration of calcium antagonists is more expensive and potentially hazardous in view of hypotensive effects, and is therefore not recommended.'

Details of Cochrane review

Cochrane review title

Calcium antagonists for aneurysmal subarachnoid haemorrhage

Citation

Dorhout Mees S, Rinkel GJE, Feigin VL, Algra A, van den Bergh WM, Vermeulen M, van Gijn J. Calcium antagonists for aneurysmal subarachnoid haemorrhage. Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD000277. DOI: 10.1002/14651858.CD000277.pub3

When the review content was assessed as up to date

18 July 2007

Quality and productivity category

Medicines management

Relevant codes	OPCS	ICD10	HRG
	I60	I60	AA23Z

Programme budget:

Neurological

Evidence

Relevance to the NHS

The Cochrane review considered randomised trials (RCTs) comparing calcium antagonists with control, and trials of a second calcium antagonist (magnesium sulphate) versus control in people already taking a calcium antagonist (oral nimodipine). Studies that assessed magnesium sulphate in the absence of nimodipine were included in the main analysis. The effect of adding magnesium sulphate to standard nimodipine treatment was analysed separately.

The meta-analysis included 16 studies with a total of 3361 patients. Overall, calcium antagonists significantly reduced the risk of poor outcome: the relative risk (RR) was 0.81 (95% confidence interval [CI] 0.72 to 0.92); the corresponding number of patients needed to treat to prevent one poor outcome was 19 (95% CI 1 to 51). For oral nimodipine alone the reduction in risk of poor outcome was statistically significant, RR 0.67 (95% CI 0.55 to 0.81) whereas for other calcium antagonists or intravenous administration of nimodipine the results were not significant. Calcium antagonists reduced the occurrence of secondary ischaemia and showed a favourable trend for reduction of case fatality. The addition of magnesium to nimodipine significantly reduced the clinical signs of secondary ischaemia, RR 0.66 (95% CI 0.45 to 0.96) and the reduction in poor outcome was approaching significance, RR 0.75 (95% CI 0.57 to 1.00).

If the largest RCT is excluded from the analysis, the results are no longer statistically significant, and therefore the evidence is not beyond all doubt. However, given the high likelihood of benefits and the modest risks associated with this treatment, the review authors concluded that 21 days of oral nimodipine at a dosage of 60 mg every 4 hours, started within the first 10 days, is beneficial for patients with an aneurysmal subarachnoid haemorrhage.

The addition of magnesium sulphate to oral nimodipine appears to be promising from this meta-analysis. A later trial of 327 patients randomised to receive either intravenous magnesium sulphate or saline placebo, in addition to oral nimodipine, found no significant difference in the proportion of patients with a favourable outcome (Wong, 2010). A further phase III RCT (MASH-II) is under analysis.

The use of oral nimodipine is now common practice in the management of aneurysmal subarachnoid haemorrhage in the NHS. This review re-emphasises that the substitution of this oral calcium antagonist with an intravenous formulation does not bring added benefit and may do harm due to associated hypotension.

Relevant NICE guidance and products

Stroke: diagnosis and initial management of acute stroke and transient ischaemic attack (TIA) –

NICE clinical guideline 68 (updated 2017)

This NICE guidance relates to the management of stroke, but does not directly consider the role of calcium antagonists in treating subarachnoid haemorrhage.

Other accredited guidance and products

Potential productivity savings

Estimate of current NHS use

Just over 4400 people in England are estimated to have aneurysmal subarachnoid haemorrhage each year. Most people will be treated with oral nimodipine. There is a strong possibility that some patients will receive nimodipine intravenously but it is not possible to estimate how many.

Level of productivity savings anticipated

The cost of oral nimodipine taken 60 mg every 4 hours for 21 days is £100.80.

The cost of intravenous nimodipine treatment (based on initially 1 mg/hour for 2 hours then increased to 2 mg/hour and continued for 5 to 21 days) is estimated at £323.68 for 5 days, £911.20 for 14 days and £1368.16 for 21 days (Dictionary of Medicines and Devices Browser Portal).

Based on these intravenous treatment costs, the saving per patient is estimated to range between £222.88 to £1267.36 depending on the duration of the intravenous nimodipine treatment.

Assuming an average length of stay of 14 days, the saving per patient would be £810.40.

Type of saving

Cash releasing

Any costs needed to achieve the savings

There is unlikely to be a cost barrier to change

Other information

The savings are likely to affect NHS provider Trusts

Potential impact on quality of NHS care

Impact on clinical quality

Clinical quality will be improved to a slight extent resulting in better outcomes anticipated for patients

Impact on patient safety

Improved patient safety, such as reducing the risk of adverse events, is anticipated

Impact on patient and carer experience

Not anticipated to have any impact on patient and carer experience

Likely ease of implementation

Time taken to implement

Can be achieved quickly: 0 to 3 months

Healthcare sectors affected

Affects one department or team

Stakeholder support

Evidence that all stakeholders fully committed and will be engaged in delivery

References

Dictionary of Medicines and Devices Browser Portal (2017)

National Institute for Health and Care Excellence (2017) CG98 Stroke: diagnosis and initial management of acute stroke and transient ischaemic attack (TIA)

Wong et al (2010) Intravenous magnesium sulfate after aneurysmal subarachnoid hemorrhage: a prospective randomized pilot study. Journal of Neurosurgery and Anesthesiology 2006; 18(2):142–8