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[Intervention Review]

Antibiotic therapy for preventing infections in people with acute stroke

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ABSTRACT

Background

Stroke is the main cause of disability in high-income countries and ranks second as a cause of death worldwide. Infections occur frequently after stroke and may adversely affect outcome. Preventive antibiotic therapy in the acute phase of stroke may reduce the incidence of infections and improve outcome. In the previous version of this Cochrane Review, published in 2012, we found that antibiotics did reduce the risk of infection but did not reduce the number of dependent or deceased patients. However, included studies were small and heterogeneous. In 2015, two large clinical trials were published, warranting an update of this Review.

Objectives

To assess the effectiveness and safety of preventive antibiotic therapy in people with ischaemic or haemorrhagic stroke. We wished to determine whether preventive antibiotic therapy in people with acute stroke:

- reduces the risk of a poor functional outcome (dependency and/or death) at follow-up;
- reduces the occurrence of infections in the acute phase of stroke;
- reduces the occurrence of elevated body temperature (temperature $\geq 38^\circ\text{C}$) in the acute phase of stroke;
- reduces length of hospital stay; or
- leads to an increased rate of serious adverse events, such as anaphylactic shock, skin rash, or colonisation with antibiotic-resistant micro-organisms.

Search methods

We searched the Cochrane Stroke Group Trials Register (25 June 2017); the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 5; 25 June 2017) in the Cochrane Library; MEDLINE Ovid (1950 to 11 May 2017), and Embase Ovid (1980 to 11 May 2017). In an effort to identify further published, unpublished, and ongoing trials, we searched trials and research registers, scanned reference lists, and contacted trial authors, colleagues, and researchers in the field.

Selection criteria

Randomised controlled trials (RCTs) of preventive antibiotic therapy versus control (placebo or open control) in people with acute ischaemic or haemorrhagic stroke.

Data collection and analysis

Two review authors independently selected articles and extracted data; we discussed and resolved discrepancies at a consensus meeting with a third review author. We contacted study authors to obtain missing data when required. An independent review author assessed risk of bias using the Cochrane 'Risk of bias' tool. We calculated risk ratios (RRs) for dichotomous outcomes, assessed heterogeneity amongst included studies, and performed subgroup analyses on study quality.

Main results

We included eight studies involving 4488 participants. Regarding quality of evidence, trials showed differences in study population, study design, type of antibiotic, and definition of infection; however, primary outcomes among the included studies were consistent. Mortality rate in the preventive antibiotic group was not significantly different from that in the control group (373/2208 (17%) vs 360/2214 (16%); RR 1.03, 95% confidence interval (CI) 0.87 to 1.21; high-quality evidence). The number of participants with a poor functional outcome (death or dependency) in the preventive antibiotic therapy group was also not significantly different from that in the control group (1158/2168 (53%) vs 1182/2164 (55%); RR 0.99, 95% CI 0.89 to 1.10; moderate-quality evidence). However, preventive antibiotic therapy did significantly reduce the incidence of 'overall' infections in participants with acute stroke from 26% to 19% (408/2161 (19%) vs 558/2156 (26%); RR 0.71, 95% CI 0.58 to 0.88; high-quality evidence). This finding was highly significant for urinary tract infections (81/2131 (4%) vs 204/2126 (10%); RR 0.40, 95% CI 0.32 to 0.51; high-quality evidence), whereas no preventive effect for pneumonia was found (222/2131 (10%) vs 235/2126 (11%); RR 0.95, 95% CI 0.80 to 1.13; high-quality evidence). No major side effects of preventive antibiotic therapy were reported. Only two studies qualitatively assessed the occurrence of elevated body temperature; therefore, these results could not be pooled. Only one study reported length of hospital stay.

Authors' conclusions

Preventive antibiotics had no effect on functional outcome or mortality, but significantly reduced the risk of 'overall' infections. This reduction was driven mainly by prevention of urinary tract infection; no effect for pneumonia was found.

PLAIN LANGUAGE SUMMARY

Antibiotic therapy for preventing infections in people with acute stroke

Review question

Does preventive antibiotic therapy in people with acute stroke reduce the risk of dependency and death at follow-up, and does it reduce the infection rate?

Background

Stroke is the main cause of disability in high-income countries and ranks second as a cause of death worldwide. It is often followed by complications, especially infections, which occur in approximately 30% of people who have had a stroke. The occurrence of an infection may adversely affect clinical outcome after stroke. Preventive antibiotic therapy may reduce the number of infections, thereby improving stroke outcome.

Search date

This review is current to May 2017.

Study characteristics

We included eight studies on preventive antibiotic therapy, with a total of 4488 people with stroke: 2230 participants were randomised to preventive antibiotic therapy, and 2258 to control. The mean age of participants in the preventive antibiotics group was 74.2 years, and in the control group 74.8 years. In both groups, the percentage of men was 52%. Study interventions differed in all eight studies; in two studies, trialists selected the (type of) antibiotic according to local antibiotic policy, with the aim of treating pneumonia.

Key results

Preventive antibiotic treatment did not reduce the risk of dependency or death.

However, preventive antibiotic therapy did significantly reduce the occurrence of 'overall' infections from 26% to 19%. Regarding type of infection, findings were highly significant for urinary tract infections (4% vs 10%) but showed no effect on pneumonia (10% vs 11%).

No major side effects of preventive antibiotic therapy were reported.

Quality of the evidence

It has become possible to draw first 'overall' conclusions on the net effect of preventive antibiotic therapy in stroke; however, the decision of whether to use preventive antibiotic therapy in acute stroke should be reached with care. Studies were heterogeneous, and despite the large numbers of participants, results from a total of eight studies are limited. In two of these studies, risk of bias was considered to be high for three out of six criteria. Overall, reviewers considered the quality of evidence for the main outcomes of this review - looking at 'any' preventive antibiotic therapy, in 'any' dose, at any length of treatment - as high to moderate.