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Aspirin for vascular dementia (Review)
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Aspirin for vascular dementia

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ABSTRACT

Background

Aspirin is widely prescribed for patients with a diagnosis of vascular dementia. In a survey of UK geriatricians and psychiatrists 80% of patients with clinical diagnoses of vascular dementia were prescribed aspirin. However, a number of queries remain unanswered. Is there convincing evidence that aspirin benefits patients with vascular dementia? Does aspirin affect cognition and behaviour, or improve prognosis? Does the risk of cerebral or gastric haemorrhage outweigh any benefit?

Objectives

To assess the randomised trial evidence for efficacy and safety of aspirin in the treatment of vascular dementia.

Search methods

We searched ALOIS: the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 12 March 2012 using the terms: aspirin OR “acetylsalicylic acid”. ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases, numerous trial registries and grey literature sources.

In addition, relevant websites were searched and some journals were handsearched. Specialists in the field were approached for unpublished material and any publications found were searched for additional references.

Selection criteria

Randomised controlled trials investigating the effect of aspirin for vascular dementia were eligible for inclusion.

Data collection and analysis

Retrieved studies were analysed independently by both review authors. Methodology and results were critically appraised and outcomes scanned included cognition, behavioural change, mortality and institutionalisation.

Main results

No trials were eligible for inclusion in this review.
Authors’ conclusions

The most recent search for references to relevant research was carried out in March 2012. No trials were found for inclusion in this systematic review.

Low-dose aspirin is frequently used as ‘treatment as normal’ in control groups and as a baseline treatment in pharmacological trials. There is still no good evidence that aspirin is effective in treating patients with a diagnosis of vascular dementia.

There is increasing concern that low-dose aspirin is associated with increased risk of haemorrhages.

Further research is needed to assess the effect of aspirin on cognition, and on other outcomes such as haemorrhages, mortality, institutionalisation and behaviour.

However, the feasibility of such research is limited by a number of factors, including the widespread use of low-dose aspirin for secondary prevention of cerebrovascular and cardiovascular conditions, and its low cost and lack of patent, which limit commercial interest in investing in these studies. In addition, there is increasing evidence of its potential to cause harm from haemorrhages, especially gastric and cerebral haemorrhages that can be fatal.

PLAIN LANGUAGE SUMMARY

There is no evidence that aspirin improves the symptoms of vascular dementia

Low-dose aspirin can improve the prognosis of heart disease and stroke, possibly by reducing clot formation within the blood vessels and helping to maintain or improve blood flow to the heart and brain. Many doctors assume that aspirin will also provide some benefit for people with vascular dementia.

This systematic review shows that there is no evidence to suggest that aspirin is useful for people with vascular dementia. It is possible that vascular dementia and stroke are caused by different pathological processes. Practitioners need to be aware of the risks of aspirin, such as haemorrhages, which can be fatal.

BACKGROUND

Description of the condition

Dementia is a syndrome consisting of a cluster of symptoms. The core feature is cognitive impairment, which may include deterioration in memory, verbal and non-verbal intellectual abilities, spatial orientation, attention, recognition and interpretation of perceptions. There may also be changes in personality, motivation, and regulation of emotions and behaviour. Each individual’s symptom profile will depend on the areas of brain affected. The condition progresses and occurs in clear consciousness.

Vascular dementia is a subtype of dementia and “is the result of infarction of the brain owing to vascular disease, including hypertensive cerebrovascular disease. The infarcts are usually small but cumulative in their effect. Onset is usually in later life” (ICD 10 2010).

This term includes multi-infarct dementia, arteriosclerotic dementia, vascular dementia of acute onset, subcortical vascular dementia, mixed cortical and subcortical vascular dementia, leukoariosis and Binswanger’s disease.

Description of the intervention
Aspirin is acetylsalicylic acid. It has analgesic, anti-pyretic, anti-inflammatory and anti-platelet clumping properties. In the 5th century BC Hippocrates used the bitter powder from willow bark, which contains salicylic acid, as an anti-pyretic and analgesic. There are worldwide historical examples of its use, for instance by Native Americans, Middle Eastern civilisations and in medieval England.

In 1828 the French pharmacist Leroux isolated salicylic acid, which is also found in the wild flower, meadowsweet. Hoffmann, working for Bayer, synthesised and sold aspirin as a powder and in 1899 this was patented. Eleven days later Bayer also patented the opiate heroin. In 1915 aspirin tablets were created and in 1917 the patent expired.

Aspirin tablets are available worldwide but the dosages vary. For instance, in the UK it is available as 75 mg and 300 mg tablets, and 300 mg suppositories. The standard tablet in the US is 325 mg, the baby aspirin tablet is 81 mg and in Europe aspirin is available as 100 mg tablet (cardioaspirin). The recommended analgesic dose is 300 to 900 mg every four to six hours, while the recommended dose for secondary prevention of thrombotic cerebrovascular and cardiovascular disease is 75 to 300 mg daily. Low-dose aspirin is generally defined as 75 to 300 mg/day.

How the intervention might work

Aspirin causes a non-competitive, irreversible inhibition of cyclooxygenase (COX) 1, 2 and 3. Its actions vary with the dose. At low doses (75 to 300 mg/day) it irreversibly blocks COX 1, which is necessary for thromboxane A2 (TXA2) synthesis. Lowered thromboxane levels reduce platelet stickiness and reduce vasoconstriction. Hence, at low doses (300 mg/day or less) aspirin reduces the formation of intravascular clots and emboli and improves peripheral blood flow. Low-dose aspirin has little effect on prostaglandins.

Although aspirin is metabolised after a few hours, platelets are unable to synthesis more COX 1 so this effect lasts several days until more platelets are manufactured.

At high doses (1.2 to 3.6 g/day) aspirin acts predominantly on COX 2, which converts arachidonic acid to prostaglandins throughout the body. Thus at high doses, aspirin, like nonsteroidal anti-inflammatory drugs, reduces prostaglandin synthesis and has anti-pyrexial, anti-inflammatory and analgesic properties, and can cause gastritis. The anti-inflammatory effects are mediated by vasoconstriction. There is little effect on platelet stickiness.

Thus, aspirin affects the balance between TXA2, which promotes aggregation of platelets and local vasoconstriction, and prostacyclin (PGI2), which inhibits aggregation. At low doses, aspirin decreases TXA2 synthesis without significantly reducing PGI2 synthesis, thus reducing platelet aggregation and promoting local vasoconstriction. By this mechanism or others, low-dose aspirin can improve outcomes for patients after a stroke or myocardial infarction.

Aspirin is widely prescribed for the management of stroke and myocardial infarction with a view to preventing further episodes. APT 1994 found that long-term anti-platelet treatment given to people who have suffered transient ischaemic attacks or mild ischaemic strokes reduced the proportional risk of non-fatal stroke by one third and fatal stroke by one fifth. It was also suggested that although there is some evidence that aspirin increases risk of intracranial haemorrhage, the overall stroke rate is still reduced.

Many clinicians assume that aspirin may benefit patients with vascular dementia by similar mechanisms and it is widely prescribed for these patients (Dennis 1998). In one study of practice by geriatricians and psychiatrists in the UK, more than 80% of patients with cognitive impairment and vascular risk factors were prescribed aspirin. In one survey of Canadian specialists in sub-cortical vascular dementia (Molnar 1998), 86% of respondents prescribed aspirin.

A retrospective case note analysis of patients with vascular dementia showed a statistically insignificant trend towards both increased life expectancy and time to institutionalisation in those regularly taking low-dose aspirin (Devine 2003).

Aspirin has complex pharmacological actions that could affect the progress of dementias.

If the aetiology of dementia is ischaemic, as proposed in vascular dementia, the pharmacological effects of low-dose aspirin predict a beneficial effect on symptoms and prognosis.

If the aetiology of any dementia is inflammatory then the mechanisms of aspirin treatment suggest that high-dose aspirin may be beneficial and improve prognosis.

However, the pharmacological effects of aspirin also predict a possible worsening of symptoms.

It is possible that aspirin causes small cerebral haemorrhages that could stimulate the amyloid cascade, a theoretical model for Alzheimer’s disease.

There is increasing concern that aspirin is linked to cerebral haemorrhages that may be primary or secondary. Again these are predicted by its known actions on platelets and small blood vessels.

It is well known that aspirin can cause gastric haemorrhages, probably via its anti-prostaglandin actions, and that these can be fatal. As aspirin has a range of pharmacological effects it is possible that it will be found to influence the progress of different dementias in different ways, either beneficially or adversely.

Why it is important to do this review

It is important to do this review to determine whether aspirin improves cognition or prognosis for patients with vascular dementia. This is important because it is a widely prescribed drug and has the potential risk of haemorrhage.
OBJECTIVES

To assess the randomised trial evidence for efficacy and safety of aspirin in the treatment of vascular dementia.

It primarily aims to assess cognitive, behavioural and global outcomes.

The secondary objective is to assess the effect of the aspirin on mortality, morbidity and institutionalisation.

METHODS

Criteria for considering studies for this review

Types of studies
Randomised controlled trials of aspirin for the treatment of vascular dementia are eligible for inclusion.

Types of participants
Participants of any age with a diagnosis of vascular dementia, as defined in the description of the condition (i.e. this term includes multi-infarct dementia, arteriosclerotic dementia, vascular dementia of acute onset, subcortical vascular dementia, mixed cortical and subcortical vascular dementia, leukoariosis andBinswanger’s disease).

Types of interventions
Trials assessing the effect of aspirin versus control (placebo or no placebo), with a minimum of six months’ follow-up, were considered for inclusion, regardless of dosage.

Types of outcome measures
Primary outcomes of interest were:
- cognition, using validated scales;
- behaviour, using validated scales;
- global function.

Secondary outcomes were:
- institutionalisation;
- morbidity, for example, gastric and cerebral haemorrhage;
- mortality.

Search methods for identification of studies

Electronic searches
We searched ALOIS (www.medicine.ox.ac.uk/aloi - created in part using a grant from the American Alzheimer’s Association) - the Cochrane Dementia and Cognitive Improvement Group’s Specialised Register on 3 March 2012. The search terms used were: aspirin OR “acetylsalicylic acid”.

ALOIS is maintained by the Trials Search Co-ordinator of the Cochrane Dementia and Cognitive Improvement Group and contains studies in the areas of dementia prevention, dementia treatment and cognitive enhancement in healthy. The studies were identified from:
1. monthly searches of a number of major healthcare databases: MEDLINE, EMBASE, CINAHL, PsycINFO and Lilacs;
2. monthly searches of a number of trial registers: ISRCTN; UMIN (Japan’s Trial Register); the World Health Organization (WHO) portal (which covers ClinicalTrials.gov; ISRCTN; the Chinese Clinical Trials Register; the German Clinical Trials Register; the Iranian Registry of Clinical Trials and the Netherlands National Trials Register, plus others);
3. quarterly search of the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library);
4. six-monthly searches of a number of grey literature sources: ISI Web of Knowledge Conference Proceedings; Index to Theses; Australasian Digital Theses.

To view a list of all sources searched for ALOIS see About ALOIS on the ALOIS website.

Additional searches were performed in many of the sources listed above to cover the timeframe from the last searches performed for ALOIS to ensure that the search for the review was as up-to-date and as comprehensive as possible. The search strategies used can be seen in Appendix 1.

The latest searches of July 2011 and March 2012, retrieved a total of 267 and 57 results respectively. After a first-assess and a de-duplication of these results the authors were left with 35 and 10 references from each search to assess further.

In addition, relevant websites and journals were searched for trials.

Searching other resources
Specialists in the field were approached for unpublished material and any publications found were searched for additional references.
Data collection and analysis

Selection of trials
Two review authors (GR, MO) independently considered the studies identified by the search against the inclusion criteria.

Data extraction
As there were no studies suitable for inclusion in this systematic review, data were not formally extracted.

RESULTS

Description of studies
See: Characteristics of excluded studies.
There were no studies eligible for the review.

Risk of bias in included studies
There were no included studies.

Effects of interventions
There were no studies eligible to be included, as updated in March 2012.

DISCUSSION

Low-dose aspirin has been widely prescribed for patients with a diagnosis of vascular dementia for many years. It is often assumed that because it has confirmed benefit in stroke, it will have benefit in vascular dementia. However, there is some evidence that the pathogenesis of these two conditions may differ. Furthermore, aspirin is often considered a safe treatment although evidence is accruing that it has significant risks of haemorrhage. Therefore both the advantages and disadvantages of prescribing low-dose aspirin for patients with vascular dementia must be considered.

There were no eligible studies that could be included in this review. The Meyer 1989 study was excluded on detailed inspection of its methodology. We had wished to assess cognitive, behavioural and global outcomes in addition to mortality, morbidity (specifically haemorrhages) and institutionalisation data, but this was not possible.

There are difficulties in assessing the effect of aspirin in vascular dementia. Vascular dementia is often diagnosed with reference to a history of stroke or myocardial infarction and such patients are likely to be taking aspirin already. This presents difficulty in constructing a placebo-controlled trial.

AUTHORS’ CONCLUSIONS

Implications for practice
This review alerts the physician to the fact that despite the widespread prescription of aspirin in patients with vascular dementia, there is no empirical evidence to support this practice.

Implications for research
There is a case to be made for a multicentre randomised double-blind placebo-controlled trial assessing the effect of aspirin on cognition. In addition, the behavioural and global domains need to be assessed. Mortality, morbidity and institutionalisation data should also be measured.

However, the risk of potentially fatal haemorrhage associated with low-dose aspirin may make such a study unethical.

It would also be useful to research the mechanism underlying the effects of aspirin on the neurobiological bases of cognition, for instance blood flow studies, neuroimaging and detailed neuropsychological testing.

ACKNOWLEDGEMENTS

We would like to thank Peter Smith and Simon Williams for their support for the original review. We also wish to thank Jacqueline Birks (statistics), Dymphna Hermans (Coordinator and Trials Search Coordinator), Katherine Hicks (Review Coordinator) and Owain Bennallack (consumer editor).

Vittoria Lutje performed the 2008 update search.
Annal Noel-Storr performed the 2012 searches and Sue Marcus helped with the editorial process.
REFERENCES

References to studies excluded from this review

AD 2000 [published data only]

ASPREE 2008 [published data only]

Broe 2000 [published data only]

Guekht 2011 [published data only]

Henderson 1997 [published data only]

Meyer 1989 [published data only]

Moretti 2008 [published data only]

Price 2008 [published data only]

Richard 2010 [published data only]

Sturmer 1996 [published data only]

Szekely 2008 [published data only]

Teramoto 2010 [published data only]

Thoonsen 2010 [published data only]

Yining 2011 [published data only]

Zhai 2010 [published data only]

Additional references

APT 1994

Dennis 1998
Devine 2003

ICD 10 2010

Molnar 1998

References to other published versions of this review

Rands 2000

* Indicates the major publication for the study
### Characteristics of excluded studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD 2000</td>
<td>This was a randomised open-label trial of low-dose aspirin in 310 community-resident patients with probable Alzheimer’s dementia and was part of a trial of donepezil. There were no significant benefits in terms of cognition or functional abilities but the risk of haemorrhage was significantly greater in the treatment group (risk ratio 4.4; 95% confidence interval 1.5 to 12.8; P = 0.007)</td>
</tr>
<tr>
<td>ASPREE 2008</td>
<td>A history of dementia was 1 of the key exclusion criteria in this protocol</td>
</tr>
<tr>
<td>Broe 2000</td>
<td>This was a community survey, not a treatment study. 50 drugs or drug groups were categorised and their use by people with Alzheimer’s and vascular dementias analysed</td>
</tr>
<tr>
<td>Guekht 2011</td>
<td>3 related papers found in search; all of them had aspirin as basic treatment for patients in control and treatment groups, with cerebrolysin as the trial drug (2008 to 2011)</td>
</tr>
<tr>
<td>Henderson 1997</td>
<td>This study was a community survey and was not specific for vascular dementia</td>
</tr>
<tr>
<td>Meyer 1989</td>
<td>The method of randomisation was alternate entry, with 4 cases who were intolerant of aspirin allocated to the next control group slot (personal communication described in this Cochrane review 1999)</td>
</tr>
<tr>
<td>Moretti 2004</td>
<td>The comparison was aspirin and nimodipine versus rivastigmine</td>
</tr>
<tr>
<td>Price 2008</td>
<td>At entry into the study the participants did not have dementia</td>
</tr>
<tr>
<td>Richard 2010</td>
<td>Excluded because aspirin is only 1 element of multicomponent vascular care intervention, and the outcome is radiological</td>
</tr>
<tr>
<td>Sturmer 1996</td>
<td>The study was a survey and not specific for vascular dementia</td>
</tr>
<tr>
<td>Szekely 2008</td>
<td>This was a large cohort study and people with vascular dementia were a very small group within it. Not a randomised controlled trial, natural controls only</td>
</tr>
<tr>
<td>Teramoto 2010</td>
<td>This study evaluated the primary prevention of aspirin in older Japanese people with risk factors for cerebrovascular and cardiovascular disease. Dementia and cognitive assessments were not included in their primary or secondary end points. The enrolment was completed in June 2007 and follow-up was an average of 4 years so results are imminent. Their results will be of interest in terms of risk of haemorrhages in the aspirin-treated group. So far only rationale, design and baseline data are available</td>
</tr>
<tr>
<td>Thoonsen 2010</td>
<td>Poster presentation of a systematic review of the 2 papers suggesting that the pooled risk ratio of intracranial haemorrhage in dementia patients using aspirin was 7.67 (95% confidence interval 1.73 to 34.1; P = 0.007)</td>
</tr>
<tr>
<td>Yining 2011</td>
<td>Excluded because aspirin was treatment as normal in both control and intervention groups</td>
</tr>
</tbody>
</table>
Zhai 2010 | Aspirin was administered to all patients in both groups
DATA AND ANALYSES

Comparison 1. Aspirin versus no aspirin

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Cognition</td>
<td>0</td>
<td>0</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>2 Behaviour</td>
<td>0</td>
<td>0</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>3 Global</td>
<td>0</td>
<td>0</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>4 Mortality</td>
<td>0</td>
<td>0</td>
<td>Peto Odds Ratio (Peto, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>4.1 Aspirin related</td>
<td>0</td>
<td>0</td>
<td>Peto Odds Ratio (Peto, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>4.2 Other causes</td>
<td>0</td>
<td>0</td>
<td>Peto Odds Ratio (Peto, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>5 Morbidity</td>
<td>0</td>
<td>0</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>5.1 Aspirin related</td>
<td>0</td>
<td>0</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>5.2 Other causes</td>
<td>0</td>
<td>0</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
</tbody>
</table>

APPENDICES

Appendix 1. Update search: July 2011

<table>
<thead>
<tr>
<th>Source</th>
<th>Search strategy</th>
<th>Hits retrieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ALOIS (<a href="http://www.medicine.ox.ac.uk/alois">www.medicine.ox.ac.uk/alois</a>)</td>
<td>Keyword search: aspirin OR &quot;acetylsalicylic acid&quot;</td>
<td>38</td>
</tr>
</tbody>
</table>
| 2. MEDLINE In-process and other non-indexed citations and MEDLINE 1950 to present (Ovid SP) | 1. Aspirin/  
2. aspirin.ti,ab.  
3. "acetylsalicylic acid".ti,ab.  
4. or/1-3  
5. Dementia, Vascular/  
6. VaD.ti,ab.  
7. "vascular cognitive impairment*".ti,ab.  
8. VCI.ti,ab.  
9. Dementia, Multi-Infarct/  
10. dementia*.ti,ab.  
11. or/5-10  
12. 4 and 11  
13. (2008* or 2009* or 2010* or 2011*). ed.  
14. 12 and 13 | 42 |

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3. EMBASE
1980 to 2011 week 30 (Ovid SP)

| 1. Aspirin/ |
| 2. aspirin.ti,ab. |
| 3. "acetylsalicylic acid".ti,ab. |
| 4. or/1-3 |
| 5. Dementia, Vascular/ |
| 6. VaD.ti,ab. |
| 7. "vascular cognitive impairment*".ti,ab. |
| 8. VCI.ti,ab. |
| 9. Dementia, Multi-Infarct/ |
| 10. dementia*.ti,ab. |
| 11. or/5-10 |
| 12. 4 and 11 |
| 13. (2008* or 2009* or 2010* or 2011*).em. |
| 14. 12 and 13 |
| 15. randomi?ed.ti,ab. |
| 16. randomi`.ti,ab. |
| 17. trial.ti,ab. |
| 18. placebo.ti,ab. |
| 19. groups.ab. |
| 20. or/15-19 |
| 21. 14 and 20 |

4. PsycINFO
1806 to July week 4 2011 (Ovid SP)

| 1. Aspirin/ |
| 2. aspirin.ti,ab. |
| 3. "acetylsalicylic acid".ti,ab. |
| 4. or/1-3 |
| 5. VaD.ti,ab. |
| 6. "vascular cognitive impairment*".ti,ab. |
| 7. VCI.ti,ab. |
| 8. Dementia, Multi-Infarct/ |
| 9. dementia*.ti,ab. |
| 10. exp Vascular Dementia/ |
| 11. or/5-10 |
| 12. 4 and 11 |
| 13. (2008* or 2009* or 2010* or 2011*).up. |
| 14. 12 and 13 |

5. CINAHL (EBSCOhost)

| S1 (MH “Aspirin”) |
| S2 TX aspirin |
| S3 TX “acetylsalicylic acid” |
| S4 S1 or S2 or S3 |
| S5 TX dementia* |
| S6 (MH “Dementia, Vascular”) OR (MH “Dementia, Multi-Infarct”) |
| S7 TX VaD |
| S8 TX vascular cognitive impairment* |
| S9 TX VCI |

1. Aspirin/ 
2. aspirin.ti,ab. 
3. "acetylsalicylic acid".ti,ab. 
4. or/1-3 
5. Dementia, Vascular/ 
6. VaD.ti,ab. 
7. "vascular cognitive impairment*".ti,ab. 
8. VCI.ti,ab. 
9. Dementia, Multi-Infarct/ 
10. dementia*.ti,ab. 
11. or/5-10 
12. 4 and 11 
13. (2008* or 2009* or 2010* or 2011*).em. 
14. 12 and 13 
15. randomi?ed.ti,ab. 
16. randomi`.ti,ab. 
17. trial.ti,ab. 
18. placebo.ti,ab. 
19. groups.ab. 
20. or/15-19 
21. 14 and 20

1. Aspirin/ 
2. aspirin.ti,ab. 
3. "acetylsalicylic acid".ti,ab. 
4. or/1-3 
5. VaD.ti,ab. 
6. "vascular cognitive impairment*".ti,ab. 
7. VCI.ti,ab. 
8. Dementia, Multi-Infarct/ 
9. dementia*.ti,ab. 
10. exp Vascular Dementia/ 
11. or/5-10 
12. 4 and 11 
13. (2008* or 2009* or 2010* or 2011*).up. 
14. 12 and 13

1. Aspirin/ 
2. aspirin.ti,ab. 
3. "acetylsalicylic acid".ti,ab. 
4. or/1-3 
5. VaD.ti,ab. 
6. "vascular cognitive impairment*".ti,ab. 
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8. Dementia, Multi-Infarct/ 
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10. exp Vascular Dementia/ 
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12. 4 and 11 
13. (2008* or 2009* or 2010* or 2011*).up. 
14. 12 and 13

1. Aspirin/ 
2. aspirin.ti,ab. 
3. "acetylsalicylic acid".ti,ab. 
4. or/1-3 
5. VaD.ti,ab. 
6. "vascular cognitive impairment*".ti,ab. 
7. VCI.ti,ab. 
8. Dementia, Multi-Infarct/ 
9. dementia*.ti,ab. 
10. exp Vascular Dementia/ 
11. or/5-10 
12. 4 and 11 
13. (2008* or 2009* or 2010* or 2011*).up. 
14. 12 and 13
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|  | S10 S5 or S6 or S7 or S8 or S9  
S11 S4 and S10  
S12 EM 2008  
S13 EM 2009  
S14 EM 2010  
S15 EM 2011  
S16 S12 or S13 or S14 or S15  
S17 S11 and S16 |  |
| 6. ISI Web of Knowledge - all databases [includes: Web of Science (1945 to present); BIOSIS Previews (1926 to present); MEDLINE (1950 to present); Journal Citation Reports] | Topic=(dement* OR VCI OR "vascular cognitive impairment*" OR VaD) AND Topic=(aspirin OR "acetylsalicylic acid") AND Topic=(randomly OR placebo OR groups OR trial OR RCT OR randomized OR randomised) AND Year Published= (2008-2011)  
43 |  |
| 7. LILACS (BIREME) | Aspirin AND dementia  
6 |  |
| 8. CENTRAL (The Cochrane Library) (Issue 4, Oct 2010) | #1 MeSH descriptor Aspirin explode all trees  
#2 aspirin  
#3 "acetylsalicylic acid"  
#4 (#1 OR #2 OR #3)  
#5 dementia*  
#6 "vascular cognitive impairment*"  
#7 VCI OR VaD  
#8 (#5 OR #6 OR #7)  
#9 (#4 AND #8), from 2008 to 2011  
21 |  |
| 9. Clinicaltrials.gov (www.clinicaltrials.gov) | Interventional Studies | dementia | aspirin OR acetylsalicylic | received from 01/01/2008 to 07/30/2011  
2 |  |
| 10. ICTRP Search Portal (http://apps.who.int/trialsearch) [includes: Australian New Zealand Clinical Trials Registry; ClinicalTrials.gov; ISRCTN; Chinese Clinical Trial Registry; Clinical Trials Registry - India; Clinical Research Information Service - Republic of Korea; German Clinical Trials Register; Iranian Registry of Clinical Trials; Japan Primary Registries Network; Pan African Clinical Trial Registry; Sri Lanka Clinical Trials Registry; The Netherlands National Trial Register] | Interventional Studies | dementia OR VCI OR VaD | aspirin OR acetylsalicylic | received from 01/01/2008 to 07/30/2011  
10 |  |
| TOTAL before de-duplication |  |  | 267 |
Feedback

Additional trials?

Summary
Peter Sandercock commented: “You don’t mention the results of the thrombosis prevention trial (Richards M, Meade TW, Peart S, Brennan PJ, Mann AH (1997) Is there any evidence for a protective effect of antithrombotic medication on cognitive function in men at risk of cardiovascular disease? Some preliminary findings. J Neurol Neurosurg Psychiatry 62:269-72.). A further trial is planned as a substudy to the AAA trial - contact Prof Gerry Fowkes (Gerry.Fowkes@ed.ac.uk). It may also be that the Womens health study: (Buring J, Hennekens C, for the Womens Health Study Research Group (1992). Women’s Health Study: study design. Journal of Myocardial Ischemia 4: 27-9) is looking prospectively at aspirin and cognitive function. There is also a small crossover study by Kellett, published as a letter to the BMJ some years ago, but never reported in full. I think it would be worth pursuing these and mentioning them in your next update.” (29/08/1999)

Reply
The review author replied:
“Thank you. We are aware of the studies referred to. There is increasing evidence that low dose aspirin benefits people with angina, MIs, CVAs, and various cancers but to date there is no specific evidence that it benefits cognitive function in people with vascular dementia”. (November 2003)

Contributors

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Gianetta Rands: grands@doctors.org.uk

What’s New

Last assessed as up-to-date: 4 March 2012.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 September 2012</td>
<td>New search has been performed</td>
<td>An update search was performed for this review on 30 July 2011 and 4 March 2012. No studies were found for inclusion</td>
</tr>
</tbody>
</table>
**HISTORY**


Review first published: Issue 2, 1999

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 May 2008</td>
<td>New search has been performed</td>
<td>Update search of 5 January 2008 retrieved several studies for consideration by the author. Three studies have been added to the list of excluded studies; no studies have been included</td>
</tr>
<tr>
<td>20 July 2005</td>
<td>New search has been performed</td>
<td>July 2005: an update search was performed resulting in two new references to one study (Moretti 2002). There was however, no placebo group with which to compare, so it is not known whether aspirin reduced rate of decline over the period of the trial. Therefore the results and conclusions of the review remain unchanged</td>
</tr>
<tr>
<td>19 November 2003</td>
<td>New search has been performed</td>
<td>November 2003: An update search was done and no new studies were found. The reviewers dealt with the peer reviewers' and consumer editor's comments. Comments and criticisms were added</td>
</tr>
<tr>
<td>20 August 2000</td>
<td>New citation required and conclusions have changed</td>
<td>Substantive amendment</td>
</tr>
</tbody>
</table>

**CONTRIBUTIONS OF AUTHORS**

GR: clinical and research input to reviews, drafting updates, correspondence, selection and assessment of studies, co-drafting of review, summaries of reviewed papers.

MO: co-author and reviewer of evidence.

SW: all correspondence on original review, drafting of review, searches, selection and assessment of studies.

AS: support on previous review processes.

Contact editor: Gordon Wilcock.

Consumer editor: Owain Bennallack.

The review was peer reviewed (November 2003).
DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources
- No sources of support supplied

External sources
- NHS R&D, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None.

NOTES

November 2003: an update search was done and no new studies were found. The review authors dealt with the peer reviewers’ and consumer editor’s comments. Comments and criticisms have been added.


March 2012: updated search. No new studies found. Excluded papers summarised and added. Increasing concerns about risks of low-dose aspirin noted.

INDEX TERMS

Medical Subject Headings (MeSH)
Anti-Inflammatory Agents, Non-Steroidal [*therapeutic use]; Aspirin [*therapeutic use]; Cognition Disorders [drug therapy]; Dementia, Vascular [*drug therapy; mortality]; Randomized Controlled Trials as Topic

MeSH check words
Humans