Risk of dementia and AD with prior exposure to NSAIDs in an elderly community-based cohort

Neurology
[April 22, 2009, early publication]

These authors are associated with the University of Washington School of Medicine

FROM ABSTRACT:

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) may prevent Alzheimer dementia (AD).

Methods: We analyzed the association of prior NSAID exposure with incident dementia and AD in the Adult Changes in Thought population-based cohort aged 65 years (median 74.8) at enrollment.

We studied 2,736 dementia-free enrollees for up to 12 years to identify dementia and AD.

Results: Contrary to the hypothesis that NSAIDs protect against AD, pharmacy-defined heavy NSAID users showed increased incidence of dementia and AD, by 66%.

Conclusions: These findings differ from those of other studies with younger cohorts. The relation of NSAID use and AD pathogenesis needs further investigation.

THESE AUTHORS ALSO NOTE:

Inflammatory mechanisms are probably involved in the pathogenesis of Alzheimer dementia (AD).

“NSAIDs are not helpful for people with established AD dementia.”

NSAIDs offer no benefit to people whose preclinical AD pathology is sufficiently advanced that they develop dementia symptoms within a few years.

This study is a prospective analysis of NSAID use and incident dementia or Alzheimer’s disease.
RESULTS

At initial assessment:
50% were light or no use of NSAIDs.
37% were moderate users of NSAIDs.
13% were heavy users of NSAIDs. [taking at least 1 NSAID per day for at least 16 months of a 2 year period].

At follow-up:
15% were heavy users.
38% were moderate users.

NSAID heavy users were 66% more likely to have dementia and 57% more likely to have AD.

DISCUSSION

“In a large cohort study of an elderly population-based sample, we observed no reduction in risk of dementia or AD among users of NSAIDs. Instead, we found that prior sustained NSAID exposure was associated with increased incidence of dementia and AD. This result was robust to comprehensive sensitivity analyses investigating features of both the design and analytic approach.”

“NSAIDs are not helpful for people with established AD, and rofecoxib [Vioxx] does not allay progression of milder cognitive symptoms to AD.”

There authors believe that their methodology of investigation of the relationship between ingestion of NSAIDs and dementia/AD is superior to other studies associations but with different conclusions doing the same, making their conclusions “a truer representation of the association of NSAIDs and dementia risk.”

**NSAID exposure and risk of Alzheimer disease**

Is timing everything?

Editorial

Neurology 2009;72:1–1

David A. Bennett, MD
Rachel A. Whitmer, PhD

A FEW KEY COMMENTS FROM THIS EDITORIAL

“Alzheimer disease (AD) is a large and growing public health problem and disease prevention represents the best long-term strategy for reducing its human and economic toll.”
“Presently no curative therapies exist, but even a small delay in disease onset would have significant public health implications.”

In this issue of Neurology, Breitner et al. suggest an increased rather than decreased risk of Alzheimer’s disease and dementia with the use of NSAIDs.

This study is important because it included “nearly 17,000 person-years of follow-up.”

**SUMMARY FROM USA TODAY**

April 23, 2009

By Mary Brophy Marcus

“A study in this week’s Neurology suggests that NSAID users do not have lower rates of dementia and that increased use of the pain relievers may actually raise the risk of cognitive decline.”

Researchers followed 2,736 persons who “were an average age of 75 at the study’s start. Participants were tracked for 12 years to see if they developed dementia, including Alzheimer’s disease.”

“Heavy users had a 66% higher risk of developing the condition [dementia] than those with low or no use.”

**KEY POINTS FROM DAN MURPHY**

**NOTE:**

These numbers represent only the use of prescription NSAIDs; over-the-counter use was more difficult to track and was assessed only indirectly. Sixteen different prescription NSAIDs were consumed, and 46% was one drug, Ibuprofen; a standard daily dose of prescription ibuprofen was defined as 1,200 mg per day. This is obtained by consuming two 600 mg prescription capsules per day.

<table>
<thead>
<tr>
<th>2,736 subjects use (1,200 mg per day) of prescription NSAIDs (rounded)</th>
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<tr>
<td>Light Use</td>
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<tr>
<td>&lt;30 standard doses / year</td>
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<tr>
<td>50%</td>
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<td>Moderate Use</td>
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<td>30-250 standard doses / year</td>
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<tr>
<td>Heavy Use</td>
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<td>&gt;250 standard doses / year</td>
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This indicates that as time progressed, subjects increased their use of NSAIDs. The consumption of NSAIDs in this patient population is astonishing.
1) “Alzheimer disease (AD) is a large and growing public health problem and disease prevention represents the best long-term strategy for reducing its human and economic toll.”

2) “Presently no curative therapies exist, but even a small delay in disease onset would have significant public health implications.”

3) This study is important because it included “nearly 17,000 person-years of follow-up.”

4) Astonishingly, this study showed that over 50% of senior citizens are consuming moderate to heavy doses of NSAIDs, and that there are very few elderly Americans who do not consume NSAIDs.

5) In this very well done study, elderly persons who were heavy users of NSAIDs were 66% more likely to have dementia and 57% more likely to have Alzheimer’s disease compared to nonusers of the drugs.

6) “In a large cohort study of an elderly population-based sample, we observed no reduction in risk of dementia or AD among users of NSAIDs. Instead, we found that prior sustained NSAID exposure was associated with increased incidence of dementia and AD. This result was robust to comprehensive sensitivity analyses investigating features of both the design and analytic approach.”

7) “A study in this week’s Neurology suggests that NSAID users do not have lower rates of dementia and that increased use of the pain relievers may actually raise the risk of cognitive decline.”

8) Researchers followed 2,736 persons who “were an average age of 75 at the study’s start. Participants were tracked for 12 years to see if they developed dementia, including Alzheimer’s disease.”

9) “Heavy users had a 66% higher risk of developing the condition [dementia] than those with low or no use.”

10) Although inflammatory mechanisms are probably involved in the pathogenesis of Alzheimer dementia, NSAIDs do not protect against such dementia, but instead increase the risk by 66%.