Reviewer’s report

Title: Analgesic and anti-inflammatory drug use and risk of bladder cancer: A population-based case control study.

Version: 2  Date: 12 March 2007

Reviewer: Henrik Toft Sørensen

Reviewer’s report:

General

This paper deals with an important public health issue, regarding which the existing epidemiological evidence is conflicting. The study is therefore important and provides some very interesting data based on a well-analyzed case-control set-up from New Hampshire, US. However the paper would benefit from a few clarifications.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The background section could be more precise. The reader would benefit from more information on the magnitude of the associations reported. A few other lines could, in contrast, be deleted without loss of information. It is e.g. not that relevant to get information on other sites than bladder cancer, especially since this issue is very briefly described and not very informative.
2. The study has a few potential problems that need to be addressed: a) selection bias, b) recall bias and c) limited information on some confounding factors.
3. There is a drop-out of 24% of the controls. Of the participating controls, 88% reported a history of use of pain medication. The impact of any potential selection bias could be discussed more thoroughly.
4. When reading the paper, it seems that phenacetin drugs have not been available since the 80s. However, the study includes bladder cancer cases diagnosed between 1998 and 2001. Therefore there might be asymmetry in the validity of the drug information between phenacetin and other drugs still available on the market. In addition, many of the phanacetin-induced bladder cases might have occurred before 1998, which will mean that the case-control design has some limitations. The impact and the direction of these two sources of bias should be thoroughly discussed in the paper.
5. On page 7 the authors write that the interviews for bladder cancer cases took place concurrently with the controls and, on average, within two years of the diagnosis (reference data of the cases and controls). The reader needs more details on this since it leaves a risk of recall bias.
6. It is a very important strength of the paper that the authors are able to stratify by cell type etc., although the data are spare.
7. The study includes limited data on social, occupational and lifestyle factors. The impact of such unmeasured and residual confounding should be covered.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

8. The references are written rather sloppily.
9. It would be nice to know some of the main brand names for phenacetin drugs.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests