Reviewer’s report

Title: Maternal occupational exposure and oral clefts in offspring

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Reviewer: Ronan Garlantezec

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In this case-malformed study the authors investigated the relationship between maternal occupational exposure and oral cleft. Assuming that a lot of pregnant women work during the windows of susceptibility of palate and lip formation, there is a need to better understand the relationship between occupational exposure and the occurrence of oral cleft. I am not sure that the present study add a lot considering several limitations (exposure assessment and choice of the control group) to the existing published ones in particular concerning solvents and pesticides exposure and need at least major revision.

Keywords: add occupational exposure.

Abstract and Introduction:

In the abstract and the introduction, the authors said that there is inconsistent results concerning occupational exposure to solvents and oral cleft. But in the literature review (line 68-71) they said that six studies reported an association between solvents exposure and oral cleft and two (including Lamon et al) did not. I not agree with the interpretation of Lamon et al study considered by the author as given 'negative' results. Please verify the interpretation of this study. Additional studies can be add in this literature review Holmberg 1982 in Finland, Cordier 1997 and Shaw 2003 (which is cited in the discussion).

In the line with this comment (interpretation of Laumon et al study) it's seems for me that most of existing studies are concordant for the association between maternal exposure to solvent and oral cleft (at least 7 positive studies vs 1 negative studies or 2 including Shaw 2003).

Lines 71-73: if there is some inconsistent results it can be also due to definitions of solvents (including oxygenated solvents or not), case assessment, study period (with changed in solvents uses) and study place.

Line 82-89 : It seems that the author put some methods information here, please remove this part to the corresponding method section.

Line 91-92 : The objective of the study include in addition to exposure to solvents and pesticides, exposure to metals, dusts, gases and fumes but there is no information in the literature review on
the existing (or not) studies concerning these exposure in relation the occurrence of malformations.

Methods Section:

Line 112: is it possible to add the percentage of informed consent.

Line 122: smoking and alcohol consumption preconceptionnal, beginning of pregnancy, anytime during pregnancy? Please specify.

Line 128-145: Definition of cases and control: I think it would be more logical to present first the definition of the case (P.135) and after that the exclusion criteria unemployed housewives….I think it's important to have an idea of the percentage of non-responder among the eligible cases and control. The number of non-responder are cited in the same way as for exclusion criteria (unemployed, housewife…). For me it's not the same.

In the case group, why have you include the Pierre Robin sequence?

Control group: the author choose as control group chromosomal/monogenic defects. Because the age of the parents is associated at least with chromosomal defects and because the advance age at pregnancy is very often associated with educational level and by consequence occupational exposure, I think that the control group is highly selected. Did the author conduct sensibility analyses with all other malformation as a control group?

Line 149: How did you defined periconceptional period did it include the windows of palate and lip formation?

Line 152: 'other' include the oxygenated solvents family (eg alcohols, cetone or glycol ethers)?

Line 177-180: it seems that the authors choose a restrictive criteria for selection of confounders included in the multivariate models (p=value of 5%). This criteria may be too restrictive and may lead to residual confounding but in light of the table 1 it include most of the potential confounder.

Results: It's not clear for me, why the table 1 is in the text and why table 2 is after the references.

Concerning the exposure description (line 235-242), it could be preferable to present the text in the same order that the table (any agents, and may be some information concerning solvents exposure which seems according to the literature review an important objective of this work, and then pesticides. …). Concerning solvents exposure, the most frequent exposure is the exposure to 'other' class of solvent. Is it possible to have some information about this class and the occupation mainly classified as exposed to this class in this study?
Discussion:

Line 276-280: It's not all the same studies that those present in the introduction. There is the need to check the literature review.

Line 284-285: I Don't understand why expert assessment could have led to differential recall bias. It may be concerned the self-reported on which expert evaluated the exposure? Please clarify.

In think that there is a prospective study in the literature cited, this kind of study is rare for studying malformation and may be some word on it could be important even if of course it have some limitations (the number of oral cleft ) but this study gives significant results with direct and indirect assessment methods of exposure.

Strengths and limitations:

Line 300-305: number of cases what about Desrosiers et al ? (>1000 I think). Shaw ? (preferable to have a larger sample size with a JEM assessment than a smaller one with expert assessment?)

Line 306: What about limitation of JEM exposure assessment comparing to expert assessment which is usually considered as the reference method in population based case-control study (Teschke et al OEM 2002). What about the fact that low and high exposure categories were merge in a single class. What could be the impact on the results? Is it possible for the more frequent exposure classes (any agents, solvents, other solvents, dusts, gases and fumes) to have the results by classes low and high?

Line 309-310: during pregnancy or during periconceptional period?

Line 311: What is the windows of susceptibility of oral cleft? Do you have any information concerning work change during pregnancies to avoid potential Hazards in the NL?

Line 325-326: … and may explained why the authors did not found associations with solvents exposure. Is it feasible to conduct a sensibility analysis with another group of malformed birth as control group.

Conclusion: line 343-345: in the text and in the table 2, the author reported a % of exposure to any agents >40% and for other solvents >20%, I think that it's not in accordance with the sentence in the conclusion (rare exposure)?

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