Author’s response to reviews

Title: Molecular epidemiology of a hepatitis C virus epidemic in a haemodialysis unit: outbreak investigation and infection outcome.

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Author’s response to reviews: see over
Reviewer's report

Title: Molecular epidemiology of a hepatitis C virus epidemic in a haemodialysis unit: outbreak investigation and infection outcome.

Version: 4 Date: 2 July 2010

Reviewer: Nicola D Thompson

Reviewer's report:

Thank you for the opportunity to review the revised version of this manuscript, and for addressing the comments from the first review. This is a comprehensive and well written manuscript, documenting a large outbreak of HCV infection among hemodialysis patients linked to inadequate infection control practices within the unit. A clear and convincing case for patient-to-patient HCV transmission is presented by the Authors. This manuscript will be an important contribution to the literature, and quite clearly illustrated the need for adherence to Standard Precautions – including aseptic technique during the preparation and administration of injection medications (Safe Injection Practices), within the hemodialysis setting. Some additional revision to the discussion section of this manuscript will significantly improve this paper, and enhance this main message of the authors – see Minor Essential Revisions.

Minor Essential Revisions

1. There appears to be a lack of consistency in the logic related to one of the main messages of this manuscript - that multi-dose vials should be banned. The author’s reference in the discussion (refs 20 and 21) articles that are related to HCV transmission associated with the misuse of single dose vials; specifically where single dose vials are re-entered with a used syringe contaminating the vial, and subsequently the vial is used for another patient. In this case, the vial, while single-dose, is being used for multiple patients. Clearly, banning multi-dose vials does not prevent the type of outbreak described by the authors or elsewhere in the literature. It would seem a more effective message would be to emphasize the components of safe injection practices (use single dose vials wherever possible, limiting each vial to a single patient, AND using a clean needle and syringe for every injection), as stated by HICPAC.

The issue of “multi-dose vials” has already been a matter of discussion with both reviewers in the previous revision. In particular according to the other reviewer (JC Desenclos) sharing “multiple dose vials” is a relevant risk factor associated with hepatitis outbreak in Europe and USA and he insisted that the use of these devices should be banned (note 7 and 17 in this paper; previous remark N.7 and 10.6 by JC Desenclos). Also the HICPAC guideline 2007 state that “(...) The primary breaches in infection control practice that contributed to these outbreaks were 1) reinsertion of used needles into a multiple-dose vial or solution container (...)” (see for reference Siegel JD et al.; Am J Infect Control. 2007;35:S65-164 pages 68-69). To reduce the ambiguity of the text and to meet the remarks of both reviewers I changed the statement “banning of multi-dose vials” into “use of single-dose vials whenever possible” in the abstract/conclusion and the phrase “use of multi-dose vials” into “use of shared heparin
and saline solution vials” in table 3. In addition I rearranged the first paragraph page 11 to specify that, in the present paper, the phrase “multi-dose vials” is referred to “20 ml heparin vials and 250 ml saline solution vials”.

2. The authors do not specifically address the need for medications to be stored and prepared in a clean medication room or area. In the hemodialysis units, this area should separate from the patient treatment area where the risk for blood contamination is high. See CDC MMWR 2001 (p.21): Clean areas should be clearly designated for the preparation, handling, and storage of medications and unused supplies and equipment. Clean areas should be clearly separated from contaminated areas where used supplies and equipment are handled. Do not handle and store medications or clean supplies in the same or an adjacent area to where used equipment or blood samples are handled.

I added a sentence to address this point at page 13 lines 27-29 (reference is also provided as suggested see ref. 22)

3. Discussion, page 12: “The potential role of HCWs in the transmission was ruled out since no HCW was found to be anti-HCV positive.” This sentence needs clarification. HCWs did have a role in transmission (their lack of adherence to standard precautions). Please re-write this sentence to specifically state that infected HCW-to-patient transmission was ruled out.

The sentence has been modified according to the reviewer’s advice (page 12 last line and page 13 first line).

Discretionary Revisions

1. Methods/Auditing procedure: Inadequacies in the assistance – is not very clear what this means. Is it intended to mean, “Inadequacies in the practices of staff at the HD unit”? Please clarify what is meant by the assistance.

   The statement “Inadequacies in the assistance” has been changed into “Inadequacies in the practices of staff at the HD unit” as suggested.

2. Methods/Participants and clinical setting: Remove the last sentence starting Table 1. This data should be presented in the results and not methods section.

   Sentence has been removed as suggested. (Results section has already a reference to table 1 page 9 lines 4-5)

3. Results: Data on genotyping is presented in the 2nd paragraph, but the molecular epidemiology data is not presented until 4th paragraph on this page. It might be easier for the reader to understand the information in paragraph 2 if the molecular epidemiology information came before it.

   All data about genotype are in the “molecular epidemiology section” and the order of the sections has been already discussed in the previous revision by both the reviewers. However since it is a discretionary I would rather to keep the test as it is.

4. Results/Audit procedure, top of page 11: It appears as though the word shift and sessions are used interchangeable here. This section would be easier to understand if one word were used
throughout the paper (shift). Suggested changing; in previous sessions to ‘on the prior shift’ for the next sessions to ‘for the next shift’.

According to the reviewer’s advice “session” is changed into “shift” throughout the paper (highlighted in yellow).

5. Results/Audit procedure: This information “According to the Italian health regulation all HCWs should undergo compulsory blood-testing, including anti-HCV, once a year throughout their time in service [13-14].” has already been covered in the methods so in unnecessary here. Suggest dropping this sentence, and using reference 13-14 in the methods.

According to the reviewer’s advice the sentence has been dropped and reference used in methods section (references order has been rearranged accordingly).

6. Discussion, Page 12: Suggesting changing, “The retrospective cohort study showed that the 13 incident cases occurred by the end of September 2005 and for 10 of them HCV genotype was available in the clinical records (all genotype 2c).” To, “This investigation showed…” Drop the reference to table 2 is the discussion (should be in the results section).

All these changes have been done according to the reviewer’s advices.

7. The same for data presented on page 13 of the Discussion section (table 3, belongs in the results).

Since it is a discretionary I would rather to keep the test as it is.

8. Suggest changing, Nonetheless it may not be ruled out that during the emergency the area, to ‘It is also possible that during the bleeding emergency the area…’ Change, heparin doses used to be prepared, to ‘heparin doses were prepared’ Please change subjects to patients, in the sentence; We cannot clearly define how these subjects contracted

All these changes have been done according to the reviewer’s advices.

9. Some additional editing/proof reading of the manuscript is needed. See some edits below.

a. Abstract methods: The ‘i.e.’ is not needed before 10 out of 13; add dose to multi-vials, so that it is multi-dose vials

b. Methods/retrospective cohort study: ‘a 33-week’ instead of ‘a 33 weeks’; drop ‘from October 2005’ at the end of first sentence; add the work period: 24-week time ‘period’ before the onset

c. Methods/Molecular epidemiology: Use ‘we confirmed the’ instead of ‘confirm the’ Samples ‘HCV-RNA positive’ instead of ‘Samples that resulted HCV-RNA positive’

d. Methods/Prospective surveillance: ‘On those’ instead of ‘In those’

e. Results: top of page 10: ‘and was not further investigated’, instead of no further

f. Audit procedure, top of page 11: There is no need for the word ‘heparin’ to be between 10 doses respectively; suggest, ‘Interviews with patients’, instead of interviews of patients; drop the word ‘Remarkably’ from the start of this paragraph.
g. Discussion, Page 13: Drop the word ‘Virtually’; Drop ‘in the application’.

All these changes have been done according to the reviewer’s advices.

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