Reviewer's report

Title: Latent and subclinical tuberculosis in HIV infected patients: a cross-sectional study

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Reviewer: Jack Barker

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Comments to the authors

Thank you for asking me to review your paper. I think it is fairly straightforward paper auditing the introduction of interferon-gamma release assays is a test for latent and clinical tuberculosis in an HIV clinic in the East End of London. You show that you can get the test done, you can investigate the patients with a positive tests and you can get them to complete chemoprophylaxis.

You do not include any costs and you do not have any control groups so we cannot really be confident about the effectiveness of the intervention.

Having said that it is relevant as we appear to be moving into the phase of trying to eliminate tuberculosis in low prevalence countries.

It is an interesting read.

Review

Latent and subclinical tuberculosis in HIV-infected patients: a cross-sectional study

Kall et al

• Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
• Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Abstract

Background

Methods

Results

I think you can remove the statement “but this was unrelated to CD 4 count"

Conclusions

The T-Spot TB test help to identify HIV-positive patients with subclinical TB. Patients with latent TB had high chemoprophylaxis completion rates.

Background
Can you check the sentence “interferon-gamma release assays have a higher sensitivity and specificity for TB than the tuberculin skin test, particularly in patients with lower CD 4 counts and those from areas with a low incidence of TB”

I wonder whether you can break this up-I suspect the sensitivity is greater in patients with low CD 4 counts but not in patients from areas with a low incidence of TB whereas the specificity may be greater in areas with a low incidence of TB but not in those with low CD 4 counts. I hope you get my meaning.

I think you can drop the word “pragmatic” in the 2nd paragraph.

Methods

Could you give me one sentence on why patients on HAART receive isoniazid were as those who are not on HAART receive rifampicin and isoniazid? It would seem important as one of your conclusions was that the patients successfully complete chemoprophylaxis and duration of treatment would seem to be a determinant of this.

Can you clarify this sentence for me that starts with “if active TB was excluded…….” You mention that the TB regimen included rifampicin and pyrazinamide as though this was more important than the fact that it included rifampicin and isoniazid-which it probably did. Does the reference (14) suggest that rifampicin and pyrazinamide are more effective chemoprophylaxis in HIV-positive patients than rifampicin and isoniazid? Otherwise I'm not sure why you are making the point about rifampicin and pyrazinamide.

Results

You can remove the “at” in the “a positive result occurred at more frequently among patients…..” sentence.

“One individual without any symptom (sic) and a normal chest radiograph had a positive immunospot and sputum culture grew Mycobacterium tuberculosis” - I guess this brings to mind the fact that there is no control group in this study. Who knows what would have happened if you have done bronchial lavage on all the patients. We don't really know that the immunospot is being ineffective sieve.

I feel a bit uncomfortable about the paragraph relating to a false positive result. I don't think the immunospot is any more false positive in this patient than it is in any of the other patients who had a positive test and did not have clinical tuberculosis. I suppose if the patient had a positive sputum smear for acid-fast bacillus this might have been a false positive test for Mycobacterium tuberculosis disease because the sputum smear is being used as a test for clinical pulmonary tuberculosis. Currently I do not think we are using the immunospot as a test for TB disease although as you report it might have this benefit at times. The specificity for this in your cohort is very low. Approximately 3/50 patients with a positive test.

I do not understand the significance of the sentence….“And another stopped at 6
months although the CD 4 count was 131 cells per microlitre” is the duration of chemoprophylaxis meant to be related to the CD 4 count?

Discussion

“Screening of those who were asymptomatic diagnosed 10% of all TB HIV coinfection”-where does this statement come from? Is their data to support this in the results section?

“To date this is the largest study…” -I cannot validate this. I trust you that it is true.

“Thus, screening amongst those with HIV…” I think a “thus” statement should follow from a previous statement. I think you’re probably trying to say that the incidence of clinical disease amongst those screened is as high as amongst those screened in contact tracing exercises? If this is what you are saying, you should probably say it.

“A study in Tanzania” has this sentence got the arrowhead in the right direction? Do you mean CD 4 count greater than 200 or CD 4 count less than 200?

“The rate at which those with a positive immunospot…..” I think there is a word missing from this sentence-possibly tuberculosis?

“The interferon-gamma release assays were more accurate…….” I never really know what accurate means in this context. Do you mean had a higher positive predictive value? Perhaps you can help me?

“We would therefore estimate that over the period of the study…..” I'm afraid I don't understand how you made this calculation. Do you mean by giving the patient is highly active antiretroviral therapy or do you mean by giving them chemoprophylaxis against tuberculosis? How did you do the calculation?

You don't say anything about the costs of screening all of the bronchoalveolar lavage protocol. It does not sound cheap.

“A systematic review of isoniazid preventive therapy…….” I don't understand this sentence- do you mean a systematic review of patients who developed tuberculosis after they had received isoniazid preventive therapy……?

Conclusions

I think this statement is too broad. It's a relatively small, single centre study and the prevalence of latent infection will as you say be critically dependent on where patients come from. I suspect an HIV clinic in central Canada would yield very different results. So I think you should say “screening for TB in an HIV clinic in London, UK, yielded……”

“This yield of latent and active tuberculosis was greater than that typically found in contact tracing exercises. This should encourage health care workers to implement IGRA based TB screening in the HIV clinic.”
Figure 1
I think there should be 36-22+4 in the indeterminate box. So I think that this should be 18

Figure 2
I take from the emphasis put in the paper on the relationship between CD 4 count and immunospot result that there is thought to be a relationship between these 2. Do you mention this in the introduction?

Table 2
what are the stars relate to? There does not appear to be any text relating to this table. It doesn’t tell us whether this is a multivariate analysis or whether these are individual analyses.

Table 3: I’m not sure that weight gain in someone with a schizoaffective disorder can be assumed to be related to treatment of tuberculosis. It is highly likely that other things were going on at this time in this patients life. It is possible that the editors will choose to remove this table.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**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