Reviewer's report

Title: Paediatric Investigators Collaborative Network on Infections in Canada (PICNIC) Study of Aseptic Meningitis

Version: 1 Date: 21 December 2005

Reviewer: Martha Lepow

Reviewer's report:

General

-----------------------------------------------------------------------------------------------

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

This is a retrospective, multicenter study with different laboratory capabilities for viral cultures and nucleic acid determinations. You may be too inclusive. The data are 8 years old and technology for diagnosis have changed with nucleic acid determinations being the standard in the U.S.

1. You should consider narrowing the inclusion to only those who had abnormal number of cells in the cerebrospinal fluid with a clinical presentation characteristic of enteroviral disease.

2. Once done, make a table by institution and age of subject with abnormal CSF.

3. Your “normal” cell count is much too high. At best infants < 28d may have as many as 30 WBC in the CSF – mainly lymphocytes or mononuclear cells. Any polymorphonuclear leukocytes in the CSF are abnormal. Over 28d, the white cell count should be less than 4 per cum/m. We suggest a table according to age of subject, CSF cell counts and % PMN. With many enteroviruses, polymorphonuclear leukocytes will be more common in day 1 or 2 than later in the illness.

4. At this point you can look at the group of 233 proven enteroviral meningitis by either viral isolation from stool, throat, CSF or PCR from CSF source according to center. Do other centers’ data correlate with those from Alberta who had 52% of the patients? There are seasonal variations, but epidemics occur due to one type of enterovirus and findings may be skewed because of different viruses may have different manifestations. Also different viruses may have circulated during the 2nd year of a study.

5. Omit any patients with underlying CNS disease (37) unless they are already excluded. Now you are ready to see whether you can combine the patients with positive viral studies with those with clinical aseptic meningitis. If so then the “other manifestations” can be looked at including CSF protein and sugar, fever, etc.

6. The age group of < 1 month should be looked at again as a group, especially those with low or absent cell counts and positive nucleic acid tests. Other have described similar findings, usually with absent cells in the CSF.

7. The virus types are interesting. Were Alberta types different from the others?

8. Length of stay – only 2 days is unusual. What were criteria for discharge?

9. Table with demographics is too detailed and data are covered in the text and exclude the figure.

Discussion – Shorten it. The neonatal comparisons are important. Today PCR is the standard for diagnosis. One of the weaknesses of your study was varying capabilities of the different centers and different results. Most other studies reported today in the literature will have positive RNA PCR as the major criteria. Bibliography should include only those published in the last 10 years with PCR because viral isolation from CSF has been poor, it is virus dependent, whereas PCR is specific for all RNA enteroviruses.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Reject because too small an advance to publish

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.