Reviewer's report

Title: Short course daily prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome (PREDNOS 2): protocol for a randomised controlled trial

Version: 5 Date: 5 April 2014

Reviewer: Jacques Lacroix

Reviewer's report:

Manuscript entitled “Short course prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome (PREDNOS 2): protocol for a randomized controlled trial” by Nicholas JA Webb et al.

Submitted to the journal “TRIALS”

Manuscript number: 9379553601102842

SUMMARY. – In this research protocol, Webb et al describe a double-blind randomized controlled trial (RCT) with 2 arms. The rationale of the study is that upper respiratory tract infections (URTI) are frequently associated with relapse of nephrotic syndrome. The hypothesis is that a 6-day course given to children with steroid sensitive nephrotic syndrome (SSNS) will reduce the number of relapses post URTI.

Three hundred children with relapsing SSNS will be randomized to take a 6-day course of prednisolone or of placebo each time they contract an URTI. Relapsing SSNS is defined by the occurrence of 2 or more relapses in the preceding year. A relapse is defined as the observation of edema and/or by the detection of proteinuria (Albustix +++) over 3 consecutive days. Randomization concealment is ensured. Compliance will be checked by counting pills used. Data will be collected on all co-interventions. Each patient will be followed during one year. Data on albuminuria will be annotated by parents in a diary. The primary outcome measure will be the number of relapses in each arm. Many important secondary outcomes measures are considered, like other immunomodulatory drugs used, adverse events, possible side effects of steroids (including effect on mood), quality of life, etc. There will be an economical analysis, as well as sub-group analyses of patients who will be grouped according to the other immunomodulatory drugs received at randomization.

MAJOR COMPULSARY REVISIONS

TITLE PAGE

• It is written on the title page: “For most recent version of the study protocol, please see the PREDNOS 2 website”. Does this mean that the manuscript does not report the latest version of the protocol?
METHODOLOGY
• Intervention and co-interventions. – Parents are told to start a 6-day course of steroids if their child shows clinical evidence of an URTI. An operational definition of URTI is provided to the parents, and they can call an investigator or a research assistant if they need someone to support their decision, which is great. However, is there any evidence that parents understand well the definition of URTI? Are there any data on the intra-rater and inter-rater reproducibility of the diagnosis of URTI by parents who use the diagnostic criteria of URTI provided by the investigators?
• How compliance will be checked for is well described, but what will be considered as adequate compliance is not defined.
• End Points and Main Outcome Measures. – The primary outcome measure is URTI-related relapse, which is defined as relapse that happens within 14 days of onset of URTI. How will be determined when the URTI started?

MINOR ESSENTIAL REVISIONS (not for publication).
Keywords.
• Please, add to the list of Keywords “randomised controlled trials”.
Competing interests.
• A section on possible competing interests must be added.
References.
The references must be formatted according to the editorial standards of the journal TRIALS.
• In each reference, all authors must be listed, up to 10 authors, before adding “et al”.
• The list of authors must be ended by a colon ( : ) rather than a period ( . ) (all references).
• The title must be printed in bold characters (all references).
• The name of the journal must be in italics (all references).
• Put a comma after year of publication, and volume must be printed in bold characters (example: 1999, 200:149-170).
• Delete month of issue, as well as number of issue, unless there is a supplement (references 3, 5, 6).
• Please, provide full range of pages (149-170 rather than 149-70) (most references).
• Reference 7. – J Pediatr or J Paediatr?
Tables.
• The legend of each table must include the definitions of all acronyms used.
DISCRETIONARY REVISIONS.
None.

REVIEWER
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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.