Reviewer's report

Title: Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre placebo controlled randomised trial of a calcium channel blocker (nifedipine) and an alpha-blocker (tamsulosin): study protocol of the randomised controlled SUSPEND trial

Version: 2 Date: 21 January 2014

Reviewer: Josée Bouchard

Reviewer's report:

Dr. McClinton and colleagues are performing a randomized controlled trial including 1,200 patients to determine whether tamsulosin, nifedipine or placebo (400 patients per arm) have an effect on spontaneous passage of ureteric stones at four weeks. The authors anticipate that tamsulosin will be more effective than nifedipine to increase the percentage of spontaneous passage. The study will also look at the incremental cost per quality adjusted life years at 12 weeks.

Strengths and weaknesses: The study is an intention to treat, multicenter (25 centers), randomized controlled double-blinded study with adequate allocation concealment (telephone Interactive Voice Response randomization) which includes a larger number of patients than any previous study on the subject. The randomization algorithm will use center, stone size and location as minimization covariates, which is appropriate in the context. The power calculation is based on results reported in previous meta-analyses on the subject.

However, it is currently recommended in to use tamsulosin for four weeks to facilitate the spontaneous passage of uncomplicated ureteric stones less than 10 mm, so the main objective will not change current practice recommendations. In addition, the follow-ups at 4 and 12 weeks are based on postal questionnaires (and chart review), so the response rate may not be excellent. Formal follow-up visits would have been more accurate to assess the primary study objectives.

Major Revisions

1. The follow-ups at 4 and 12 weeks are based on postal questionnaires (and chart review), so the response rate may not be excellent. Formal follow-up visits would have been more accurate to assess the primary study objectives. What is the expected percentage of missing response rate based on enrolled participants so far? In addition, what is the percentage of participants seen in clinic at approximately four weeks after randomization?

2. In the UK, what is the percentage of patients who seek medical or surgical follow-up outside their primary physician office or initial hospital consultation? Could this affect the results of the study if a significant percentage of follow-up is missing?

3. The spontaneous passage of ureteric stones decrease progressively after 5
Will the authors look at the results based on stones less than 5, 5-7 (or 8) and 8-10 mm and not only less or more than 5 mm?

4. The authors mentioned that patients on digoxin and rifampin will be excluded from the study. However, this criterion is not listed in the 'official' exclusion criteria.

5. The authors mentioned that ‘Consideration of the frequency of monitoring reports, interim analysis and any criteria for stopping rules will be discussed and agreed with the DMC prior to recruitment starting.’ However, the recruitment has started in January 2011. Additional explanation should be provided on interim analysis.

6. The authors mentioned on page 5 that nifedipine is contraindicated in pregnancy. However, nifedipine is regularly used for hypertensive disorders in pregnancy (see Seely et al, NEJM 2011: 365:439-46).

7. Finally, what is the role of the funding source?

8. The cost-analysis should be reviewed by an expert in the field as judged by the Editor as I do not have this expertise.

Josee Bouchard

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests