Reviewer’s report

Title: Leg elevation decreases the incidence of post-spinal hypotension in cesarean section: a randomized controlled trial

Version: 0 Date: 03 Jan 2017

Reviewer: Frederic Mercier

Reviewer's report:

GENERAL COMMENTS :

- This randomized study aims to investigate the use of passive leg raising (versus control) just AFTER onset of spinal anesthesia for elective Cesarean section on incidence of hypotension.

- The strengths of the study are the following :

1- it is a randomized controlled study with an adequate sample size calculation (p 6) including 75 parturients / group.

2- the use of passive leg raising (or more accurately "leg elevation" in the present study) after spinal anesthesia to try to prevent hypotension during Cesarean section has been investigated only once 23 years ago (ref. 9 quoted by the authors) and yielded a negative result but likely because of inadequate power (hypotension incidence of 39% vs. 53% in the control group with n=32 vs. n=31 parturients).

3- the present study retrieves conversely a positive effect of leg elevation (35% vs. 59%), which is an interesting finding, because it is a simple and no-cost maneuver particularly in low-resource countries.

- But there are also weaknesses :

1- a RL pre-load (10 ml/kg) was used whereas this is ineffective and clearly no longer recommended. Most experts recommend using a crystalloid co-load or a colloid pre-load (Ngan Kee, Curr Opin Anaesthesiol 2010 - Mercier, Curr Opin Anaesthesiol 2012 - Mercier Br J Anaesth 2014)

2- the vasopressor used is ephedrine, whereas there is a wide consensus since a decade at least to using phenylephrine (instead of ephedrine) as first-line vasopressor in elective Cesarean section. This is probably due to unavailability (or cost issue?) of phenylephrine in Egypt but
nevertheless this limits the external validity of the present study for high-income countries where prophylactic phenylephrine + effective crystalloid coload or colloid preload are used.

These limitations need to be better detailed and acknowledged in the Discussion section of the manuscript.

SPECIFIC COMMENTS:

Introduction:

* 3rd and 4th sentences (Lines 8 to 18):

The 3rd sentence is correct, i.e., "decreased vascular tone (due to spinal-induced sympathetic blockade) leading to decreased systemic vascular resistance and decreased venous return". But consequently, the next sentence (4th) is inappropriate, because increasing vascular tone by vasopressors not only increases systemic vascular resistance (via its action on arterial tone) but also increases venous return (by constricting capacitance vessels, namely on the splanchnic venous system) (see Ngan Kee et al., Anesthesiology 2015 Apr;122(4):736-45 with the Discussion section in page 742)

Thus, increasing venous return may be achieved both with vasopressor and fluid administration. Please, modify accordingly.

* Lines 26 to 36:

The Passive Leg Raising (PLR) maneuver has been described by intensivists (your ref. 5 & 6 are adequate): it is a well defined / specific maneuver where the whole body is lowered from the semi-recumbent position to the supine position, by tilting the bed (see Fig. 1 in your ref. 6 where Monnet and Teboul describe precisely the maneuver). Thus, what you described here in the introduction along with your ref. 5, 6 & 7 is actually the PLR maneuver but contrarily to what you suggest in your last sentence, this is not what you have been using in your study. Indeed, as detailed in your Methods section at the top of page 5, you did not tilt the whole body of your parturient but rather only raise their legs for 30 cm using two standard pillows. This is a maneuver rather similar to the one described by Rout et al. in 1993 (your ref. 9) and it will be more appropriate as he did to entitle it as "leg elevation". This nuance is not purely semantic because the full PLR maneuver (which also include the trunk tilting) is likely more effective to mobilize venous blood from the large splanchnic compartment than leg elevation alone (see Monnet and Teboul, Crit Care 2015 Jan 14;19:18).

It is not a problem that you used a simple leg elevation maneuver in your study instead of the PLR maneuver per se, because obviously the latter cannot be performed easily in this Cesarean
section setting. But you need to modify your manuscript to remove this potential confusion/misunderstanding.

It will be also useful/interesting that you provide the average angle obtained with the leg elevation you used.

Methods :

* Page 4, line 37 : As I mentioned in my general comments, Ringer's lactate pre-load is no longer recommended (although still too much used routinely) because it has been wellshown to be poorly effective or ineffective and even potentially counterproductive (Ngan Kee, COIA 2010 - Mercier, COIA 2012 - Mercier BJA 2014). Thus, you should acknowledge this limitation in the Discussion section (pages 10-11).

* Page 4, line 46 : please, remove the capital letter of "Bupivacaine" (i.e., write "bupivacaine") and change "ug" to "µg" (or "mcg").

* Page 5, line 27-28 : please, convert "drops per minute" to international units (for ex : units / h).

* Page 5, line 36 : demographic data are not (secondary) "outcome" parameters ; they are "baseline" data.

* Page 5, line 48 : an interval of 3 min for arterial blood pressure recording is a too long interval to optimally detect hypotension from onset of spinal anesthesia during Cesarean section until delivery of the newborn. All or at least most studies on spinal anesthesia for Cesarean section have used a 1-min interval. This should also be acknowledged as a study limitation in the Discussion section.

Results :

* Table 1 : Please, provide the p value, even when "NS". For example, Nausea & Vomiting is probably less in the "PLR" group (this would make sense, given that hypotension incidence and ephedrine requirements are both less) but does not reach statistical significance likely because of insufficient power on this secondary outcome.
Discussion:

* Page 9, line 10: "this means that PLR decreased the incidence of hypotension by 63%". It seems you are making confusion between odds ratio and relative risk. The incidence of hypotension in your study decreased from 58.7% to 34.7% as shown in your Table 1. This means that it decreased by \((0.587 - 0.347) / 0.587 = 0.409 = 40.9\%\) (not 63%).

* Page 9, lines 12 to 15: this last sentence of the 1st paragraph appears useless; it is methodological information you already provided adequately in the Methods section (in the middle of page 5 along with the definition of the primary outcome).

* Page 9, 2nd paragraph: again, as I mentioned already above, please use "PLR" only when you refer to the actual PLR maneuver described in the literature you are quoting. But as soon as you refer to the maneuver you used in your study, please use "leg elevation" instead.

* Page 9, line 38: I was unable to retrieve the 150-mL volume of blood mobilized from the calves" that you are mentioning here. In the study you quoted (ref. 8) of Rutlen et al. (Circulation, 1981), it is stated that leg elevation produced a 34 ± 4% decrease in counts from the radiolabeled intravascular space (with the counts being proportional to blood volume). Please explain where you find the information on the "150-mL volume of blood mobilized from the calves" you mentioned or alternatively modify your manuscript if inaccurate.

* Page 10, line 41: I guess you intended to write "the use OF expensive and sophisticated…"

* Page 10, one line below: I agree it is "simple, rapid and effective". However you should make more clear in this comment, that the effectiveness, although well proven here, is not huge (nor mild): it is moderate (a decrease by 41% of the incidence of hypotension, with ephedrine requirement that are halved but unexpectedly low even in the control group).

* You may also add in this Discussion section that the (true) PLR maneuver has been already investigated (and quote Meirowitz et al., IJOA 2012; 21: 324-8) in parturients undergoing Cesarean section but solely to try to predict hypotension (rather than to prevent it like in the present study) and in this case, it was found ineffective.

* Page 10, last paragraph on "study limitations": see by previous comments above; some other limitations should also be acknowledged.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls? 
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown? 
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? 
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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