Haemodynamic control during spinal anaesthesia: fluids & vasopressors, new insights & evidence

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Interim Chief, Division of Women’s Anesthesia

OAA Three Day Course, November 2014
Objectives

- Efficacy of fluid loading strategies
- Choice of vasopressors
- Optimal dosing
- Impact on outcomes
Acute Hydration for Prevention of Hypotension of Spinal Anesthesia in Parturients

Stuart B. Wollman, M.D.,* and Gertie F. Marx, M.D.†

Note: After hypotension 1000 cc D 5% in L/R was given.
A Reevaluation of the Role of Crystalloid Preload in the Prevention of Hypotension Associated with Spinal Anesthesia for Elective Cesarean Section


Crystalloid preload: 20 ml/kg over 15-20 min

- Preloading: 55%
- No Preloading: 71%

P=0.07

Rout CC. Anesthesiology 1993; 79: 262-9
Techniques for preventing hypotension during spinal anaesthesia for caesarean section (Review)

Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Colloid</th>
<th>Crystalloid</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardoso 2004 a</td>
<td>25</td>
<td>25</td>
<td>1.00 [0.93, 1.08]</td>
<td></td>
</tr>
<tr>
<td>Dahlgren 2005</td>
<td>37</td>
<td>56</td>
<td>0.78 [0.62, 0.97]</td>
<td></td>
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<tr>
<td>French 1999</td>
<td>10</td>
<td>80</td>
<td>0.26 [0.14, 0.49]</td>
<td></td>
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<tr>
<td>Karinen 1995</td>
<td>5</td>
<td>13</td>
<td>0.63 [0.28, 1.41]</td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8</td>
<td>30</td>
<td>0.50 [0.25, 0.99]</td>
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</tr>
<tr>
<td>Ozkan 2004</td>
<td>13</td>
<td>25</td>
<td>0.93 [0.56, 1.55]</td>
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</tr>
<tr>
<td>Perumal 2004</td>
<td>13</td>
<td>20</td>
<td>0.93 [0.60, 1.43]</td>
<td></td>
</tr>
<tr>
<td>Selvan 2004</td>
<td>20</td>
<td>40</td>
<td>0.71 [0.47, 1.09]</td>
<td></td>
</tr>
<tr>
<td>Siddik 2000</td>
<td>8</td>
<td>20</td>
<td>0.50 [0.28, 0.89]</td>
<td></td>
</tr>
<tr>
<td>Ueyama 1999</td>
<td>10</td>
<td>24</td>
<td>0.56 [0.31, 0.99]</td>
<td></td>
</tr>
<tr>
<td>Yorozu 2002</td>
<td>27</td>
<td>32</td>
<td>1.14 [0.89, 1.45]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>365</td>
<td>333</td>
<td>0.70 [0.51, 0.96]</td>
<td></td>
</tr>
</tbody>
</table>

Total events 176 225
Heterogeneity: Tau² = 0.23; Chi² = 104.72, df = 10 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.20 (P = 0.03)
Coloading vs. Preloading

\[ \Delta CO (\%) \]

Spinal anesthesia

- Infusion before the block
- Infusion after the block

Time (min.)

Kamenik M. Anesth Analg 2001;92:710-714
Crystalloid preload vs. coload

- 50 women randomized to 20 ml/kg of crystalloid solution as preload or coload

- Significantly more women in coload group did not require vasopressor therapy (p=0.047)

- The coload group required a lower median dose (P=0.03) and a lower median number (P=0.04) of ephedrine doses

### Preload or coload for spinal anesthesia for elective Cesarean delivery

Pré-charge ou co-charge lors de rachianesthésie pour un accouchement non urgent par césarienne: une méta-analyse

Arnab Banerjee, MD · Renato M. Stocche, MD, PhD · Pamela Angle, MD · Stephen H. Halpern, MD

<table>
<thead>
<tr>
<th>Study</th>
<th>Co-load n/N</th>
<th>Preload n/N</th>
<th>OR (random) 95% CI</th>
<th>Weight %</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyer</td>
<td>15/25</td>
<td>21/25</td>
<td>12.04</td>
<td>0.29 [0.08, 1.09]</td>
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</tr>
<tr>
<td>Cardoso</td>
<td>9/40</td>
<td>5/20</td>
<td>13.14</td>
<td>0.87 [0.25, 3.06]</td>
<td></td>
</tr>
<tr>
<td>Mercier</td>
<td>15/24</td>
<td>12/24</td>
<td>14.78</td>
<td>1.67 [0.53, 5.27]</td>
<td></td>
</tr>
<tr>
<td>Bouchnak</td>
<td>29/30</td>
<td>26/30</td>
<td>5.18</td>
<td>4.46 [0.47, 42.51]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>68/119</td>
<td>64/99</td>
<td>45.13</td>
<td>0.99 [0.37, 2.67]</td>
<td></td>
</tr>
</tbody>
</table>

| % | 59 | 65 |

Test for heterogeneity: \( \chi^2 = 5.86, \text{df} = 3 (P = 0.12), \text{I}^2 = 48.8\%

Test for overall effect: \( Z = 0.02 (P = 0.99) \)
Colloid preload vs. coload

Hypotension with 500 ml HES

- Preload: 68%
- Coload: 75%

### The Incidence of Hypotension

<table>
<thead>
<tr>
<th>Study</th>
<th>Co-load n/N</th>
<th>Preload n/N</th>
<th>OR (random) 95% CI</th>
<th>Weight %</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colloid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teoh</td>
<td>15/20</td>
<td>18/20</td>
<td>7.75</td>
<td>0.33</td>
<td>[0.06, 1.97]</td>
</tr>
<tr>
<td>Carvalho</td>
<td>7/23</td>
<td>11/23</td>
<td>13.85</td>
<td>0.48</td>
<td>[0.14, 1.60]</td>
</tr>
<tr>
<td>Sahar Siddik</td>
<td>66/88</td>
<td>61/90</td>
<td>26.45</td>
<td>1.43</td>
<td>[0.74, 2.74]</td>
</tr>
<tr>
<td>Nishikawa</td>
<td>3/18</td>
<td>2/18</td>
<td>6.81</td>
<td>1.60</td>
<td>[0.23, 10.94]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>91/149</strong></td>
<td><strong>92/151</strong></td>
<td><strong>54.87</strong></td>
<td><strong>0.90</strong></td>
<td><strong>[0.43, 1.86]</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 4.26, df = 3 (P = 0.23), I² = 29.6%
Test for overall effect: Z = 0.29 (P = 0.77)
Management of SIH

- Labartino et al (1966)
  - 234 Caesarean Deliveries under SA
  - PE Infusion to manage SIH
  - “Especially reliable in these cases & simple to maintain a steady blood pressure”
Re-examining Phenylephrine

• Phenylephrine vs. Ephedrine in humans

• Effect on neonatal and maternal outcomes
Fetal Acidosis

No differences in
- Hypotension
- Hypertension

Neonatal Base Excess

Veeser M. Acta Anaesthesiol Scand 2012; 56: 810-16
Placental Transfer and Fetal Metabolic Effects of Phenylephrine and Ephedrine during Spinal Anesthesia for Cesarean Delivery


 Disclaimer: The information on this slide is used for educational purposes only and should not be used for clinical decision-making.

Diagram:
- UV/MA
- 2.0
- 1.5
- 1.0
- 0.5
- 0.0

Phenylephrine  Ephedrine

Umb A:
- PaCO₂
- Lactate,
- Glucose,
- E, NE with Ephedrine

Ngan Kee. Anesthesiology 2009; 111: 506-12
IS IONV DIFFERENT BETWEEN PE AND E?
## IONV with E vs. PE

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Ephedrine</th>
<th>Phenylephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ngan Kee 2008</td>
<td>Bolus</td>
<td>13 %</td>
<td>0 %</td>
</tr>
<tr>
<td>Prakash 2010</td>
<td>Bolus</td>
<td>13 %</td>
<td>4 %</td>
</tr>
<tr>
<td>Ngan Kee 2009</td>
<td>Infusion</td>
<td>35 %</td>
<td>2 %</td>
</tr>
<tr>
<td>Ngan Kee 2008</td>
<td>Infusion</td>
<td>40 %</td>
<td>0 %</td>
</tr>
<tr>
<td>Cooper 2002</td>
<td>Infusion</td>
<td>66 %</td>
<td>17 %</td>
</tr>
</tbody>
</table>

Ngan Kee WD. Anaesthesia 2008; 63: 1319-26  
Ngan Kee WD. Anesthesiology 2009; 111: 506-12  
Ngan Kee WD. Anesth Analg 2008; 107: 1295-302  
Cooper D. Anesthesiology 2002; 97: 1582-9
OPTIMAL METHOD OF PE ADMINISTRATION
Prophylactic Phenylephrine Infusion for Preventing Hypotension During Spinal Anesthesia for Cesarean Delivery

Warwick D. Ngan Kee, MBChB, MD, FANZCA, Kim S. Khaw, MBBS, FRCA, Florence P. Ng, RN, BASc, and Bee B. Lee, MBBS, FANZCA
Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong, China

- PE infusion (100 μg/min) or PE boluses for ↓ BP (100 μg)
- LR at 5 ml/min
- ↓ incidence, frequency, and magnitude of ↓ BP
- ↓ IONV
- Similar Umbilical cord gases and Apgar scores

Ngan Kee WD. Anesth Analg 2004; 98: 815-21
DOES FLUID ADMINISTRATION REGIMEN MAKE A DIFFERENCE WITH PE INFUSIONS?
Rapid Coload
Maintenance Rate

PE Infusion 100 μg /min

Less PE with coload (56 vs. 42 mcg/min, p=0.008)
Transient reactive hypertension (47 %)

Ngan Kee. Anesthesiology 2005; 103: 744-50
WHAT SHOULD BE THE TARGET BLOOD PRESSURE?
Intraoperative Nausea/ Vomiting

Group 80 %: 40 %
Group 90 %: 16 %
Group 100 %: 4 %

P=0.006

Umb A pH: 7.30 (0.03), 7.30 (0.03), 7.32 (0.04), p=0.036
WHAT IS THE OPTIMAL PE INFUSION REGIMEN?
A Double-Blind, Placebo-Controlled Trial of Four Fixed Rate Infusion Regimens of Phenylephrine for Hemodynamic Support During Spinal Anesthesia for Cesarean Delivery

Terrence K. Allen, MBBS, FRCA,* Ronald B. George, MD, FRCPC,† William D. White, MPH,* Holly A. Muir, MD, FRCPC,* and Ashraf S. Habib, MBBCh, MSc, FRCA*

P=0.04 vs. PE 50, P=0.02 VS. PE 25

Number of Interventions

PE 0  PE 25  PE 50  PE 75  PE 100

Allen TK. Anesth Analg 2010; 111: 1221-9
A Double-Blind, Placebo-Controlled Trial of Four Fixed Rate Infusion Regimens of Phenylephrine for Hemodynamic Support During Spinal Anesthesia for Cesarean Delivery

Terrence K. Allen, MBBS, FRCA,* Ronald B. George, MD, FRCPC,† William D. White, MPH,* Holly A. Muir, MD, FRCPC,* and Ashraf S. Habib, MBBCh, MSc, FRCA*

![Box plot diagram]

\[ p = 0.01 \text{ vs PE 100} \]
A Randomized Controlled Trial of Variable Rate Phenylephrine Infusion With Rescue Phenylephrine Boluses Versus Rescue Boluses Alone on Physician Interventions During Spinal Anesthesia for Elective Cesarean Delivery

Sahar M. Siddik-Sayyid, MD, FRCA, Samar K. Taha, MD, Ghassan E. Kanazi, MD, and Marie T. Aouad, MD

- Hypotension: 20% (Variable Rate PE Infusion) vs. 90% (PE Bolus), P<0.001
- Hypertension: 15% (Variable Rate PE Infusion) vs. 0% (PE Bolus), P<0.001
- Nausea: 10% (Variable Rate PE Infusion) vs. 44% (PE Bolus), P=0.001

Median number of interventions: 0 vs. 3, p<0.001

Siddik-Sayyid S. Anesth Analg 2014; 118: 611-8
CAN'T YOU DO ANYTHING RIGHT?
Randomized comparison of closed-loop feedback computer-controlled with manual-controlled infusion of phenylephrine for maintaining arterial pressure during spinal anaesthesia for Caesarean delivery

W. D. Ngan Kee*, K. S. Khaw, F. F. Ng and Y. H. Tam

Median number of interventions: 10 vs. 2, p<0.001

Closed-loop double-vasopressor automated system vs manual bolus vasopressor to treat hypotension during spinal anaesthesia for caesarean section: a randomised controlled trial

B. L. Sng,¹ H. S. Tan² and A. T. H. Sia³
Closed-loop double-vasopressor automated system vs manual bolus vasopressor to treat hypotension during spinal anaesthesia for caesarean section: a randomised controlled trial

B. L. Sng, H. S. Tan and A. T. H. Sia

- Hypotension: 59% vs. 35%, P<0.001
- Hypertension: 13% vs. 8%, P=0.005
- Nausea: 10% vs. 1%, P=0.005

MAPE 9.8% vs. 8.5%, p=0.013

Sng BL. Anaesthesia 2013; 69: 37-45
WHAT IS THE OPTIMUM DOSE OF PE BOLUS?
Up-Down Determination of the 90% Effective Dose of Phenylephrine for the Treatment of Spinal Anesthesia-Induced Hypotension in Parturients Undergoing Cesarean Delivery

ED90= 147 mcg
WHAT IS THE EFFECT OF PE ON COP?
Hemodynamic Effects of Ephedrine, Phenylephrine, and the Coadministration of Phenylephrine with Oxytocin during Spinal Anesthesia for Elective Cesarean Delivery


A

<table>
<thead>
<tr>
<th>% change from pre-vasopressor value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ephedrine</td>
</tr>
<tr>
<td>Phenylephrine</td>
</tr>
</tbody>
</table>

Time (sec) after vasopressor administration

CO  HR  MAP

Dyer RA. Anesthesiology 2009; 111: 753-65
The Dose-Dependent Effects of Phenylephrine for Elective Cesarean Delivery Under Spinal Anesthesia

Adrienne Stewart, FRCA,* Roshan Fernando, FRCA,* Sarah McDonald, FRCA,† Rachel Hignett, FRCA,‡ Tanya Jones, FRCA,§ and Malachy Columb, FRCA‖

CO Change
PE25=7.8 %
PE50=15.2 %
PE100=22 %
HOW ABOUT BRADYCARDIA WITH PE?
PE Induced Bradycardia

• Baroreceptor reflex

• Vagolytics can lead to hypertension
IS THERE A BENEFIT FROM VAGOLYTIC PRETREATMENT?
Haemodynamic effects of glycopyrrolate pre-treatment before phenylephrine infusion during spinal anaesthesia for caesarean delivery

W.D. Ngan Kee, a S.W.Y. Lee, b K.S. Khaw, a F.F. Ng a

COP Changes over Time

**Fig 1. Cardiac Output Changes as Percentage of Baseline**
Data are median and interquartile range. Significant difference between groups (P<0.001).

BP and Nausea

- **Glycopyrrolate**
- **Control**

- **Hypotension**
  - Glycopyrrolate: 0%
  - Control: 0%
  - P=0.007

- **Hypertension**
  - Glycopyrrolate: 50%
  - Control: 30%
  - P=0.001

- **Dry Mouth**
  - Glycopyrrolate: 20%
  - Control: 15%

IS THERE A BENEFIT FROM MIXING PE WITH EPHEDRINE?
• As PE % decreased and E increased:
  – Faster HR
  – More hypotension/ IONV
  – Less hemodynamic stability
  – Lower pH and BE
Norepinephrine vs. Phenylephrine

- No differences in BP, higher bias with PE
- No differences in IONV
- Higher CO and HR with NE
- Umbilical vein pH and O$_2$ content higher with NE

Ngan Kee W. OAA Meeting 2014; O7
Conclusions: PHE vs. EPH

- Limited Efficacy of fluid loading
- PE vs. E
- PE prophylaxis vs. treatment
- Reactive Hypertension
- Lower HR and CO
- High risk pregnancies
Extraordinary Care – Through a Culture of Innovation