Haemodynamics using transthoracic echocardiography in women with untreated severe preeclampsia in South Africa

AT Dennis, RA Dyer, M Gibbs, L Nel, J Castro, J Swanevelder

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Dublin Ireland May 2014
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Disclosures

none
Overview

1. Rationale for the study
2. Aims
3. Method
4. Results
5. Conclusions
6. Acknowledgements
Rationale for the study

Preeclampsia is a life-threatening hypertensive disease of pregnancy

6.5 million women affected each year

Major cause of stroke, heart failure, kidney impairment, haemorrhage and premature birth


Rationale for the study

Pathophysiology – there is a need to conduct scientific observations on women with untreated disease in order to understand heart function and the underlying mechanisms for the cardiac changes.

Published online 11 June 2008 | Nature 453, 840-842 (2008) |
doi:10.1038/453840a

News Feature

Translational research: Crossing the valley of death
Rationale for the study

Australia (2008-2013)
Maternal Mortality Ratio
6/100,000 live births

- Healthy pregnant women
- Women with untreated preeclampsia (mild and severe)
- Women with treated preeclampsia

Preeclampsia – preserved systolic function, reduced diastolic function, non-dilated ventricle
Lower cardiac outputs compared with treated women

# Rationale for the study

## Australia (2008-2013)

**Maternal Mortality Ratio**

6/100,000 live births

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- Women with treated preeclampsia

Preeclampsia – preserved systolic function, reduced diastolic function, non-dilated ventricle

Lower cardiac outputs compared with treated women

## The Netherlands (1991)

Visser and Wallenburg

Pulmonary artery catheter

87 women untreated preterm severe preeclampsia

Preeclampsia – reduced cardiac output in women with untreated preeclampsia compared with treated women, increased left ventricular stroke work index

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Rationale for the study

South Africa
Maternal Mortality Ratio
140/100,000 live births

Do women with preeclampsia in high MMR countries represent a different phenotype and disease severity?

Aim

To determine heart function in women with severe untreated preeclampsia in a high MMR setting

http://www.who.int/research/en/
Method

Institutional ethics approval & written consent

Transthoracic echocardiography in pregnant women ACTRN12613000992707, HREC 442/2013 University of Cape Town and The Groote Schuur Hospital and The University of Melbourne and The Royal Women’s Hospital – AT Dennis, RA Dyer, M Gibbs, L Nel, J Castro, J Swanevelder

Prospective observational study performed during a 4 month period from August – December 2013 (investigator availability)
Total number of women recruited: 126

All women recruited with preeclampsia: 43
- 8 excluded
- 20 treated

Included women with preeclampsia: 35
- Women with untreated preeclampsia: 15

Term pregnant women with HIV infection: 36
- 6 excluded

Term healthy pregnant women: 47
- 7 excluded

Term pregnant HIV infection: 30

Term healthy pregnant: 40
Included women with preeclampsia

- 35 Women with untreated preeclampsia
- 15

All women recruited with preeclampsia 43

20 treated

8 excluded

Term pregnant women with HIV infection 36

6 excluded

Term healthy pregnant women 47

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Total number of women recruited 126

Term pregnant HIV infection 30

Term healthy pregnant 47
Method

**South Africa subgroup** - 15 HIV negative women with single fetus, not in labour, no signs of pulmonary oedema, no pre-existing hypertensive, cardiac or renal disease, untreated severe preeclampsia:

severe disease defined as systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 100 mmHg, central nervous system symptoms, proteinuria, premature birth
Method

Compared with

Australian subgroup

– 19 women with single fetus, not in labour, no signs of pulmonary oedema, no pre-existing hypertensive cardiac or renal disease, untreated severe preeclampsia (published data)

- 40 healthy pregnant women (published data)
Method

Rested
Left lateral position
3-lead electrocardiograph
Blood pressure measured (mmHg)
Standardised echocardiography examination (ASE) image acquisition
two investigators (A Dennis, L Nel)
Offline measurements
Method

Variables were compared using t-tests with Welsh’s correction or Fisher’s exact test for proportions, inter-observer measurements were compared using Bland Altman methodology.
Results

Haemodynamics were able to be assessed in all women (100%)

Interobserver measurements:
95% of measurements are within 0.20 cm (10%) of mean left ventricular outflow tract diameter
95% of measurements are within 2.3 cm/sec (11%) of mean velocity time integral
## Results

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<th>South Africa Untreated severe preeclampsia n = 15</th>
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<td>Age (years)</td>
<td>30 ± 6.1</td>
<td>26 ± 7.7</td>
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<td>Body mass index (kg/m$^2$)</td>
<td>32 ± 7.4</td>
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<td>Nulliparous</td>
<td>26 (65)</td>
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<td>Gestation (weeks)</td>
<td>35 ± 4.9</td>
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<td>125 ± 12.7</td>
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*60% of women were anaemic
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Cardiac output

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p = 0.011  p = 0.040

Cardiac output (ml/min)
Cardiac output

Healthy pregnant
Preeclampsia

Cardiac output (ml/min)

Australia
n=40

Untreated severe
Australia
n=19

South Africa
n=15

p = 0.011

p = 0.040

*  

**
Cardiac output

Healthy pregnant
Australia
n=40

Preeclampsia
Untreated severe
Australia
n=19

Preeclampsia
Untreated severe
South Africa
n=15

Cardiac output (ml/min)

p = 0.040
p = 0.011

*  
**
Cardiac output

Healthy pregnant
Australia
n=40

Preeclampsia
Australia
n=19

Preeclampsia
South Africa
n=15

p = 0.011
p = 0.040

Cardiac output (ml/min)
Ejection fraction

p = 0.039  p = 0.980

Fractional shortening (%)

Healthy Pregnant  Preeclampsia  Preeclampsia
Australia  n=40  Untreated severe Australia  n=19  Untreated severe South Africa  n=15

*
Ejection fraction

Healthy Pregnant
Preeclampsia

Australia
n=40
Untreated severe
Australia
n=19

South Africa
n=15

* p = 0.039
p = 0.980

Fractional shortening (%)

Reduced ejection fraction

Healthy Pregnant
Preeclampsia
Preeclampsia

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Mitral valve E velocity/septal e' velocity ratio

Diastolic function

Healthy Pregnant Preeclampsia Preeclampsia

Australia
n=40

Untreated severe Australia
n=19

Untreated severe South Africa
n=15

p < 0.0001

p = 0.592

*
Reduced diastolic function

Diastolic function

- Australia: Healthy Pregnant (n=40)
- Australia: Untreated severe (n=19)
- South Africa: Untreated severe (n=15)

Statistics:
- p < 0.0001
- p = 0.592

Mitral valve E velocity/septal e' velocity ratio

* indicates reduced diastolic function
Ventricular dilatation

- Healthy Pregnant
  - Australia: n=40
- Preeclampsia
  - Untreated severe Australia: n=19
  - Untreated severe South Africa: n=15

`p = 0.923`
`p = 0.630`

Left ventricular end-diastolic diameter (cm)
Results

Untreated severe preeclampsia:
- Increased cardiac output (↑ in South African group)
- Increased contractility (↑ in South African group)
- Increased ejection fraction
- Preserved right ventricular systolic function
- Reduced diastolic function
- No ventricular dilatation
Limitations

1. small study
2. small geographical area
3. comparisons with healthy are with Australian women
Conclusions

1. Our observations suggest that severe preeclampsia is a hyperdynamic disease with
   - Increased cardiac output,
   - Increased contractility,
   - Preserved ejection fraction
   - Reduced diastolic function (Australia and South Africa)

2. Higher cardiac output and left ventricular stroke work index in South African women?
   - Anaemia - influence on haemodynamics/resting cardiac output/stress responses

3. In compensated disease (i.e. not in pulmonary oedema)
   - Our observations do not support the hypothesis that preeclampsia is associated with a reduction in systolic function
   - Or a dilated left ventricle

http://www.who.int/vmnis/anaemia/prevalence/summary/anaemia_status_summary/en
Conclusions

4. Transthoracic echocardiography can be used at the bedside to quantify heart function in individual women.

5. Further human research at the bedside to examine heart function in untreated women with preeclampsia is needed.
Acknowledgements

South Africa
Rob Dyer, Justiaan Swanevelder, Matthew Gibbs, Lynel Nel
Staff at Mowbray Maternity and Groote Schuur Hospitals

Australia
Julian Castro, Ioana Arhanghelschi, Andrew Buettner

GE Healthcare
Transthoracic echocardiography

University of Cape Town
Visiting Scholar Fund

Study participants

Human research ethics committee
## Stroke volume

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<td>1.96 ± 0.12</td>
<td>2.07 ± 0.21</td>
<td>0.077</td>
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<td>LVOT VTI (cm)</td>
<td>19.7 ± 3.6</td>
<td>23.7 ± 5.6</td>
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<td>LVOT VTI time (msec)</td>
<td>295 ± 35.6</td>
<td>326 ± 30.2</td>
<td>0.011</td>
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<td>LVOT VTI time/average cardiac cycle time</td>
<td>0.39 ± 0.05</td>
<td>0.45 ± 0.08</td>
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Interobserver variability
Left ventricular outflow tract diameter
n=40

LVOTd = left ventricular outflow tract diameter
Mean difference = -0.003 cm
Standard deviation (SD) = 0.099 cm
Upper limit = mean + 1.96 × SD = 0.197 cm
Lower limit = mean - 1.96 × SD = -0.197 cm
Mean LVOTd = 1.99 cm
95% interobserver measurements are within 0.20 cm (10 %) of mean LVOTd
Interobserver variability
Left ventricular outflow tract velocity time integral
n=40

VTI = velocity time integral
Mean difference = -0.251 cm/s
Standard deviation (SD) = 1.17 cm/s
Upper limit = mean + 1.96×SD = 2.03 cm/s
Lower limit = mean - 1.96×SD = -2.53 cm/s
Mean VTI = 21.15 cm/s
95% interobserver measurements are within 2.3 cm/s (11%) of mean VTI