Cochrane Library

**Cochrane** Database of Systematic Reviews

# Plasma volume expansion for suspected impaired fetal growth (Review)

Say L, Gülmezoglu AM, Hofmeyr GJ

Say L, Gülmezoglu AM, Hofmeyr GJ.
Plasma volume expansion for suspected impaired fetal growth.
*Cochrane Database of Systematic Reviews* 1996, Issue 4. Art. No.: CD000167.
DOI: 10.1002/14651858.CD000167.

**www.cochranelibrary.com**




WILEY

# TABLE OF CONTENTS

[Intervention Review]

# Plasma volume expansion for suspected impaired fetal growth

Lale Say[1], A Metin Gülmezoglu[2], G Justus Hofmeyr[3]

[1]Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland. [2]UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland. [3]Department of Obstetrics and Gynaecology, East London Hospital Complex, University of the Witwatersrand, University of Fort Hare, Eastern Cape Department of Health, East London, South Africa

**Contact address:** Lale Say, Department of Reproductive Health and Research, World Health Organization, 20 Avenue Appia, Geneva, 1211, Switzerland. sayl@who.int.

**Editorial group:** Cochrane Pregnancy and Childbirth Group
**Publication status and date:** New search for studies and content updated (no change to conclusions), published in Issue 7, 2010.

**Citation:** Say L, Gülmezoglu AM, Hofmeyr GJ. Plasma volume expansion for suspected impaired fetal growth. *Cochrane Database of Systematic Reviews* 1996, Issue 4. Art. No.: CD000167. DOI: 10.1002/14651858.CD000167.



## ABSTRACT

### Background

Failure of the normal expansion of plasma volume in the mother is associated with impaired fetal growth and pre-eclampsia.

### Objectives

The objective of this review was to assess the effects of plasma volume expansion for suspected impaired fetal growth.

### Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (March 2010).

### Selection criteria

Randomized or quasi-randomized trials of plasma volume expansion compared to no plasma volume expansion in women with suspected impaired fetal growth.

### Data collection and analysis

Trial quality was assessed.

### Main results

No studies were included.

### Authors' conclusions

There is not enough evidence to evaluate the use of plasma volume expansion for suspected impaired fetal growth.

## PLAIN LANGUAGE SUMMARY

### Plasma volume expansion for suspected impaired fetal growth

Too little evidence to show whether it is beneficial for pregnant women to have extra plasma when the baby is growing more slowly than expected.

Plasma is the fluid that carries the blood cells in the body. The amount of plasma and blood cells (the blood) circulating in a woman's body can double during pregnancy. Sometimes, women whose babies are growing too slowly during pregnancy (impaired fetal growth) do not have as much blood circulating in their body as would be expected. Plasma volume expansion is where solutions are injected into the woman's bloodstream to increase plasma levels. No trials were found to show whether plasma volume expansion is beneficial for these women or their babies.

## BACKGROUND

Impaired fetal growth is the failure of a newborn to achieve its genetically determined growth potential, which may cause death as well as short or long-term childhood morbidity. It has been reported that 3% to 10% of neonates are small for corresponding gestational age and an estimated 30% of this is due to impaired fetal growth. Remaining 70% is due to constitutional factors such as maternal ethnicity, parity, weight and height (Lin 1998). The condition occurs with limited flow of nutrients and/or oxygen from mother to fetus as a result of fetal causes (e.g. chromosomal abnormalities, congenital malformations), placental factors (e.g. small placenta), or maternal factors (e.g. malnutrition, vascular/renal disease, drugs or other metabolic conditions) (Resnik 2002).

Ultrasound evaluation of the fetus by measuring the abdominal circumference, head circumference, length of upper leg and interpreting these using standardised formulae allows the clinician to estimate the fetal weight, to relate this to the gestational age and to follow the growth progress. Ultrasound evaluation also allows to some extent to estimate the timing and the cause of the impairment. Symmetrical growth of the fetus is generally due to early problems such as chromosomal abnormalities, drugs, chemical agents or infection. Asymmetric growth usually results from inadequacy of substrates the fetus needs particularly later in pregnancy (Resnik 2002). In low-income settings where early pregnancy ultrasound is not available fetal growth can be monitored by serial symphysis fundus measurements. However, there is no proven effective treatment that can be applied once growth impairment is diagnosed. In general, when no apparent congenital abnormality exists, management is conservative by frequent growth measurements, smoking cessation if the mother smokes and early delivery when the fetus is thought be mature enough to survive outside the womb.

The outcomes of impaired growth are variable and usually related to the specific cause. For example, if the growth impairment is due to chromosomal anomalies or congenital abnormalities, the fetus is more at risk of a perinatal death. Other short-term outcomes may be moderate to mild metabolic problems (hypoglycemia, polycythemia, meconium aspiration, etc.) due to the chronic oxygen and nutrient deprivation. Depending on the severity and the duration of the condition, long-term outcomes may differ from normal to small decreases in IQ to an increased risk of cerebral palsy (Bernstein 2000).

A significant increase in intravascular volume is a characteristic of normal pregnancy. Failure of this physiological plasma volume expansion is associated with increased incidence of impaired fetal growth and of pre-eclampsia. There is thus a rational basis for attempting to treat impaired fetal growth by therapeutic plasma volume expansion in the mother using substances with high osmotic pressure.

## OBJECTIVES

To assess the effects of plasma volume expansion for suspected impaired fetal growth.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

All acceptably controlled evaluations of plasma volume expansion for suspected impaired fetal growth.

#### Types of participants

Women with suspected or potential impaired fetal growth.

#### Types of interventions

Plasma volume expansion to promote fetal growth.

#### Types of outcome measures

##### *Primary outcomes*

Fetal growth, birthweight, pregnancy duration, neonatal condition and complications, maternal complications.

### Search methods for identification of studies

#### Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (March 2010).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

### Data collection and analysis

Trials under consideration were evaluated for methodological quality and appropriateness for inclusion, without consideration of their results. Included trial data were processed as described in Clarke 2000.

## RESULTS

### Description of studies

There are no randomized trials which fit the inclusion criteria. Three studies were excluded (*see* Characteristics of excluded studies).

### Risk of bias in included studies

No trials included.

### Effects of interventions

Not applicable.

## DISCUSSION

*See* Authors' conclusions.

## AUTHORS' CONCLUSIONS

### Implications for practice

There is no evidence to support the routine use of plasma volume expansion in clinical practice for suspected impaired fetal growth.

### Implications for research

Randomized trials with adequate design and sample sizes are needed to evaluate the possible advantages and risks of plasma volume expansion for suspected impaired fetal growth.

## ACKNOWLEDGEMENTS

None.

# REFERENCES

## References to studies excluded from this review

**Bsteh 1995** *{published data only}*

Bsteh M, Tews G, John D. Hemodilution in treatment of intrauterine dystrophy [Haemodilution bei der behandlung der intrauterinen dystrophie]. *Geburtshilfe und Frauenheilkunde* 1995;**55**:83-6.

**Heilmann 1991** *{published data only}*

Heilmann L, Lorch E, Hojnacki B, Muntefering H, Forster H. Accumulation of two different hydroxyethyl starch preparations in the placenta after hemodilution in patients with fetal intrauterine growth retardation or pregnancy hypertension. *Infusionstherapie* 1991;**18**:236-43.

**Heilmann 1993** *{published data only}*

* Heilmann L, Tempelhoff G-Fv. Doppler sonographic results following hemodilution therapy. *Zeitschrift fur Geburtshilfe und Perinatologie* 1993;**197**:43-7.

Tempelhoff G-Fv, Heilman L. The effect of plasma volume expansion on the uteroplacental perfusion. *Clinical Hemorheology* 1993;**13**:729-36.

## Additional references

**Bernstein 2000**

Bernstein IM, Horbar JD, Badger GJ, Ohlsson A, Golan A. Morbidity and mortality among very low birth weight infants with intrauterine growth restriction. The Vermont Oxford Network. *American Journal of Obstetrics and Gynecology* 2000;**182**:198.

**Clarke 2000**

Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.1 [updated June 2000]. In: Review Manager (RevMan) [Computer program]. Version 4.1. Oxford, England: The Cochrane Collaboration, 2000.

**Lin 1998**

Lin C, Santolaya-Forgas J. Current concepts of fetal growth restriction: Part 1. Causes, classification, and pathophysiology. *Obstetrics & Gynecology* 1998;**92**(6):1044-55.

**Resnik 2002**

Resnik R. Intrauterine growth restriction. *Obstetrics & Gynecology* 2002;**99**(3):490-6.

* Indicates the major publication for the study

# CHARACTERISTICS OF STUDIES

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Bsteh 1995 | This study was excluded because all 20 pregnant women included in the study received haemodilution therapy with hydroxyethylstarch. 10 women were hospitalized while the other 10 were treated ambulatory. |
| Heilmann 1991 | 73 women with suspected impaired fetal growth and/or gestational hypertension were "randomized" to receive plasma volume expansion with either hydroxyethylstarch 10% (group A, n = 37) or haemofusin (group B, n = 36). Haematological, placental histological and neonatal features were compared between 36 of group A and 24 of group B, and 102 non-randomized controls. There was no randomized comparison between treatment (hydroxyethylstarch) and control groups. The comparisons were made between 2 types of volume expanders (hydroxyethylstarch 10% versus haemofusin) and with 102 non-randomized controls. There were thus no comparisons between treated and randomly allocated control groups on the basis of which to evaluate the effectiveness of plasma volume expansion. |
| Heilmann 1993 | Data not available in a suitable form (Doppler). Small study (6 women in each group). The treatment was given for 14 days after enrolment.<br><br>12 women (6 in each group) with a high Hb (> 13 g/dl), hematocrit (> 38%) and fetal aorta resistance index (> 0.75) underwent plasma volume expansion by 500 ml of hydroxyethylstarch (+ 500 ml of NaCl 0.9%) in a 'double- blind' fashion. The control group received 1000 ml of NaCl 0.9%. In both groups treatment continued for 14 days. The main outcome (Doppler resistance index) is not available in a suitable form for analysis. Plasma volume expansion caused a lowering of fetal aorta and uterine artery resistance index after 14 days. There was 1 case of intrauterine growth retardation in control group (diagnosed after delivery). |

## WHAT'S NEW

| Date | Event | Description |
|---|---|---|
| 23 April 2010 | New search has been performed | Search updated. No new trials identified. |

## HISTORY

Protocol first published: Issue 1, 1996
Review first published: Issue 1, 1996

| Date | Event | Description |
|---|---|---|
| 20 September 2008 | Amended | Converted to new review format. |
| 24 November 2006 | New search has been performed | Search updated but no new trials identified. |
| 30 June 2004 | New search has been performed | Search updated but no new trials identified. |

## CONTRIBUTIONS OF AUTHORS

Justus Hofmeyr wrote the original review for the Cochrane Pregnancy and Childbirth Database. Metin Gülmezoglu updated the review, and has been responsible for maintaining the review since 1995. Both review authors did the data extraction and contributed to the text of the review. Lale Say contributed to the recent update by checking the data entries and revising the text of the review.

## DECLARATIONS OF INTEREST

None known.

## SOURCES OF SUPPORT

### Internal sources

- University of the Witwatersrand, South Africa.
- HRP - UNDP/UNFPA/WHO/World Bank Special Programme in Human Reproduction, Geneva, Switzerland.
- UK Cochrane Centre, NHS R&D Programme, Oxford, UK.

### External sources

- No sources of support supplied

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Plasma Volume; Fetal Growth Retardation [*prevention & control]; Plasma Substitutes [*therapeutic use]

### MeSH check words

Female; Humans; Pregnancy