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(Review)

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[Intervention Review]

Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure

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ABSTRACT

Background

Women at risk of pre-eclampsia or gestational hypertension are sometimes advised to rest. Whether this, overall, does more good than harm is unclear.

Objectives

To assess the effects of rest or advice to reduce physical activity during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure.

Search methods

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

Selection criteria

Studies were included if they were randomised trials evaluating the effects of rest or advice to reduce physical activity for preventing pre-eclampsia and its complications in women with normal blood pressure.

Data collection and analysis

Two review authors independently selected trials for inclusion and extracted data. Data were double checked for accuracy.

Main results

Two small trials (106 women) of uncertain quality were included. Both recruited women with a singleton pregnancy at moderate risk of pre-eclampsia from 28 to 32 weeks' gestation. There was a statistically significant reduction in the relative risk of pre-eclampsia with four to six hours rest per day (one trial, 32 women; relative risk (RR) 0.05, 95% confidence interval (CI) 0.00 to 0.83), but not of gestational hypertension (RR 0.25, 95% CI 0.03 to 2.00), compared to normal activity. Rest of 30 minutes per day plus nutritional supplementation was associated with a reduction in the risk of pre-eclampsia (one trial, 74 women; RR 0.13, 95% CI 0.03 to 0.51) and also of gestational hypertension (RR 0.15, 95% CI 0.04 to 0.63). The effect on caesarean section was unclear (RR 0.82, 95% CI 0.48 to 1.41). No other outcomes were reported.

Authors' conclusions

Daily rest, with or without nutrient supplementation, may reduce the risk of pre-eclampsia for women with normal blood pressure, although the reported effect may reflect bias and/or random error rather than a true effect. There is no information about outcomes such as perinatal mortality and morbidity, maternal morbidity, women's views, adverse effects, and costs. Current evidence is insufficient to

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support recommending rest or reduced activity to women for preventing pre-eclampsia and its complications. Whether women rest during pregnancy should therefore be a matter of personal choice.

PLAIN LANGUAGE SUMMARY

Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure

Not enough evidence to say if rest is helpful in preventing pre-eclampsia and its complications for women with normal blood pressure during pregnancy.

Pre-eclampsia is a serious complication of pregnancy occurring in about 2% to 8% of women. It is identified by increased blood pressure and protein in the urine, but women often suffer no symptoms initially. It can, through constriction of the blood vessels in the placenta, interfere with food and oxygen passing to the baby, thus inhibiting the baby's growth and causing the baby to be born too soon. Women can be affected through problems in their kidneys, liver, brain, and clotting system. Rest has been proposed as being beneficial for women at increased risk of pre-eclampsia, including those with normal blood pressure. There are also possible adverse effects such as the potential for increasing the risk of blood clots in the legs, and the impact considerable periods of rest on women's lives and that of their families. The review of trials found two small studies, of not very good quality, and there were insufficient data to say what the potential benefits and harms might be. Further studies are needed, and in the meantime women will be guided by their own beliefs and reasoning, as well as those of their caregivers.

BACKGROUND

Hypertension (high blood pressure) is common during pregnancy. Around 10% of women will have raised blood pressure at some point before delivery. The hypertensive disorders of pregnancy comprise a spectrum of conditions that is usually classified into four categories: (i) gestational hypertension, a rise in blood pressure during the second half of pregnancy; (ii) pre-eclampsia, usually hypertension with proteinuria (protein in urine) during the second half of pregnancy; (iii) chronic hypertension, a rise in blood pressure prior to pregnancy or before 20 weeks' gestation, and (iv) pre-eclampsia superimposed on chronic hypertension (NHBPEP 2000). For women with uncomplicated mild to moderate hypertension, pregnancy outcome is similar to that for women with normal blood pressure. Outcome deteriorates if the blood pressure is very high, or pre-eclampsia develops. Pre-eclampsia is a multisystem disorder involving the liver, kidneys, brain, and placenta. It affects 2% to 8% of pregnancies (WHO 1988), and is associated with a substantive increase in morbidity and mortality for both the woman and her baby (DH 2002). Complications for the mother may include eclampsia (seizures), stroke, liver or kidney failure, and abnormal blood clotting, and problems for the baby include poor growth and preterm birth.

The cause of pre-eclampsia is uncertain, but current belief is that reduced blood supply to the placenta leads to abnormal function of endothelial cells lining blood vessels, possibly as a result of oxidative stress. Endothelial cell dysfunction results in generalised vasoconstriction, platelet activation and thrombosis, and decreased plasma volume, reducing blood supply to multiple organs. Pre-eclampsia is discussed in more detail in the generic protocol for this review (Generic Protocol 2005).

Restriction of activity and rest have traditionally been advocated during pregnancy for a variety of indications, including prevention and treatment of hypertension (Goldenberg 1994). Surveys conducted in Canada and USA on obstetrician and physician management of hypertensive disorders in pregnancy suggest that advice to stop work or to rest more, or both, is common when blood pressure is raised (Caetano 2004; Maloni 1998). This advice is based largely on findings from case-control studies, and the observation that when women are walking or moving about, they have a higher systolic blood pressure than when they have been sitting for some time. The issue of rest for women with hypertension during pregnancy is covered by another review (Meher 2005).

Women with normal blood pressure may also be advised to rest during pregnancy to reduce their risk of developing gestational hypertension or pre-eclampsia. In the past, another rationale for advising women that rest might reduce their risk of pre-eclampsia came from the belief that exercise would reduce uteroplacental blood flow, and bed rest would increase it. As pre-eclampsia is known to be associated with reduced placental perfusion, it was hypothesised that bed rest might therefore help prevent this syndrome (Mathews 1978). There is no information on how often women with normal blood pressure are advised to rest when they are at home. Nevertheless, it seems likely that women at high risk of pre-eclampsia would be offered this advice more often than those at low risk. Such advice may not come only from caregivers, but also from the lay literature, from friends and from family. Women with multiple pregnancy are at increased risk of hypertensive disorders in pregnancy. In the past, women with multiple pregnancy and

normal blood pressure were frequently advised to rest in hospital to improve pregnancy outcome, especially to reduce the risk of early birth and poor fetal growth. The effects of rest, including on hypertension, for women with a multiple pregnancy are covered by a separate review (Crowther 2001).

The relationship between rest, physical activity, and risk of pre-eclampsia is unclear and there is controversy over the potential effects of these interventions. In a cohort study of ambulatory blood pressure monitoring, women with normal blood pressure in their first pregnancy who were in paid employment had higher blood pressures and risk of developing pre-eclampsia than those who were not in paid employment (Higgins 2002). A meta-analysis of observational studies of occupational physical activity has also shown an association between physically demanding work and increased risk of hypertension and pre-eclampsia (Mozurkewich 2000). In contrast, observational studies of regular recreational physical activity during pregnancy report a reduced risk of pre-eclampsia (Marcoux 1989; Sorensen 2003), and it has been suggested that exercise may even help prevent pre-eclampsia (Weissgerber 2004). However, at present there is insufficient evidence from randomised trials evaluating aerobic exercise in healthy pregnant women (Kramer 2002), and in women at increased risk of pre-eclampsia (Meher 2006).

There may also be risks associated with rest. Prolonged reduction in physical activity increases the risk of deep vein thrombosis and pulmonary embolism. This is particularly so during pregnancy (Kovacevich 2000), when the risk is already considerably higher. In addition, restriction of activity may be stressful and disruptive to women's lives. It may lead to difficulty with caring for their family and may mean that they (or their partner) have to give up recreational activities or paid employment. Discontinuation of paid employment may have financial implications for both the woman and her family, as well as the employer.

Any advice for women to alter their lifestyle to reduce the risk of pre-eclampsia needs to be supported by reliable evidence that the benefits of following such advice outweigh the harms or inconveniences associated with it. It is therefore important to evaluate the effects of rest for preventing pre-eclampsia and its complications.

OBJECTIVES

To assess the effects of rest, or any advice to restrict physical activity during pregnancy, for preventing pre-eclampsia and its complications in women with normal blood pressure.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised trials evaluating rest, or advice to rest, for women with normal blood pressure were included. Trials with quasi-random design were excluded.

Types of participants

Pregnant women with normal blood pressure were included, regardless of gestation at trial entry. Whenever possible and

relevant, women were grouped on the basis of their risk of developing pre-eclampsia at trial entry as follows.

(a) High risk: defined as having one or more of the following: diabetes, renal disease, thrombophilia, autoimmune disease, or previous severe or early onset pre-eclampsia (for multiple pregnancy, see [Crowther 2001](#)).

(b) Moderate risk: defined as none of the above, but having either previous pre-eclampsia that was not severe or early onset (or severity unspecified), or a first pregnancy and at least one of the following: teenager or over 35 years age, family history of pre-eclampsia, obesity (body mass index of at least 30), increased sensitivity to Angiotensin II, positive roll-over test, abnormal uterine artery doppler scan.

(c) Low risk: defined as pregnancy that does not qualify as either high or moderate risk.

(d) Undefined risk: when the risk is unclear or not specified.

Women were excluded if they had hypertension or established pre-eclampsia.

If a trial included women with pre-eclampsia or non-proteinuric hypertension as well as women with normal blood pressure, where possible, we planned to include only women with normal blood pressure. For trials that did not report results separately for the two groups, we planned to include them in the review but present them as a separate subgroup. No such studies were identified, however.

Types of interventions

We included the following comparisons:

1. rest or advice to restrict activity versus unrestricted activity;
2. rest or advice to restrict activity combined with other interventions, versus unrestricted activity; and
3. rest or advice to restrict activity versus any other interventions for preventing pre-eclampsia.

Studies were included regardless of where or how women were advised to rest. Studies were excluded if the intended duration of the intervention was for less than one week. This cut off was taken because it is unlikely that such a brief intervention could influence pregnancy outcomes, based on what is known of the pathophysiology of pre-eclampsia.

Types of outcome measures

The following outcomes were included. The definitions used for each outcome are summarised below. Trials that used acceptable variations of these definitions, or that did not define their outcomes were still included, and definitions, where available, are described in the table 'Characteristics of included studies'. If an important outcome was not reported, authors were contacted whenever possible.

For the woman

Main outcome

(1) Pre-eclampsia: hypertension (blood pressure at least 140 mmHg systolic or 90 mmHg diastolic) with proteinuria (at least 300 mg protein in a 24 hour urine collection or 30 mg/dL in a single sample or 1+ on dipstick or 30 mg/mmol urine protein/creatinine ratio).

Other outcomes

(2) Death: during pregnancy, childbirth, or up to 42 days after end of pregnancy.

(3) Severe morbidity: including eclampsia, liver or renal failure, haemolysis elevated liver enzymes and low platelets syndrome, disseminated intravascular coagulation, stroke and pulmonary oedema. These outcomes will be reported individually, and as a composite measure where the information is available.

(4) Severe pre-eclampsia: pre-eclampsia with two or more signs or symptoms of severe disease, such as severe hypertension, severe proteinuria (usually 3 g/24 h, or 3+ on dipstick), visual disturbances, exaggerated tendon reflexes, upper abdominal pain, impaired liver function tests, high serum creatinine, low platelets, fetal growth restriction, or reduced liquor volume.

(5) Early onset of pre-eclampsia: pre-eclampsia at or before 33 completed weeks.

(6) Severe hypertension: blood pressure at least 160 mmHg systolic or 110 mmHg diastolic.

(7) Gestational hypertension: blood pressure at least 140 mmHg systolic or 90 mmHg diastolic, after 20 weeks' gestation.

(8) Use of antihypertensive drugs or need for additional antihypertensive drugs.

(9) Abruption of the placenta or antepartum haemorrhage.

(10) Elective delivery: induction of labour or caesarean section.

(11) Caesarean section: emergency and elective.

(12) Postpartum haemorrhage: blood loss of 500 ml or more.

(13) Side-effects: any adverse events related to rest: thromboembolism, muscle atrophy, bone loss, rest stopped due to side-effects.

(14) Use of health services: antenatal clinic visits, visit to day care unit, antenatal hospital admission, intensive care (admission to intensive care unit, length of stay, ventilation, dialysis).

(15) Women's experiences and views of rest.

For the Child

Main outcomes

(1) Death: including all deaths before birth and up to discharge from hospital.

(2) Preterm birth: birth at or before 37 completed weeks' gestation.

(3) Small-for-gestational age: growth below the 3rd centile, or lowest centile reported.

Other outcomes

(4) Apgar score at five minutes: low (less than seven) and very low (less than four) or lowest reported.

(5) Endotracheal intubation or use of mechanical ventilation.

(6) Neonatal morbidity: respiratory distress syndrome, chronic lung disease, sepsis, necrotizing enterocolitis, retinopathy of prematurity, and intraventricular haemorrhage.

(7) Long-term growth and development: blindness, deafness, seizures, poor growth, neurodevelopmental delay and cerebral palsy.

(8) Use of hospital resources: admission to neonatal intensive care unit, duration of hospital stay after delivery.

Economic outcomes

1. Costs to health services: short term and long term, for both mother and baby.

2. Costs to the woman, her family, and society associated with rest.

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 (January 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.

For details of the additional searching we undertook for the initial version of the review, see: [Appendix 1](#)

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors assessed potentially eligible studies for inclusion. We resolved any differences in opinion by discussion. If important data were missing, we attempted to contact the trialists for further information.

Assessment of study quality

Two review authors independently assessed the quality of each trial using the criteria outlined in the Cochrane Reviewers' Handbook ([Alderson 2004](#)). Methods used for generation of the randomisation sequence are described for each trial, where possible. Each study was assessed for quality of concealment of allocation, completeness of follow up, and blinding.

(1) Allocation concealment

A quality score for concealment of allocation was assigned to each trial, using the following criteria:

- (A) adequate concealment of allocation, such as telephone randomisation, consecutively numbered sealed opaque envelopes;
- (B) unclear whether concealment of allocation was adequate;
- (C) inadequate concealment of allocation such as random number tables, sealed envelopes that are not numbered or opaque.

(2) Completeness of follow up

Completeness of follow up was assessed using the following criteria:

- (A) less than 5% of participants excluded from analysis;
- (B) 5% to 10% of participants excluded from analysis;
- (C) more than 10% and up to and including 20% of participants excluded from analysis.

Studies were excluded if:

1. more than 20% of participants were excluded from analysis;
2. more than 10% of participants were not analysed in their randomised groups and it was not possible to restore participants to the correct group;
3. there was more than 10% difference in loss of participants between groups.

Data were analysed based on the group to which the participants were randomised, regardless of whether they received the allocated intervention or not. Where data were missing, we sought clarification from the authors.

(3) Blinding

Blinding was assessed using the following criteria:

1. blinding of participants (yes/no/unclear or unspecified);
2. blinding of caregiver (yes/no/unclear or unspecified);
3. blinding of outcome assessment (yes/no/unclear or unspecified).

Data extraction and data entry

Two review authors independently extracted data. We entered data onto the Review Manager software ([RevMan 2003](#)), and double checked them for accuracy.

Statistical analyses

We carried out statistical analyses using the Review Manager software ([RevMan 2003](#)). We presented the results as summary relative risk with 95% confidence intervals. As there was only one trial in each comparison, there was no need to assess heterogeneity. When more data become available, the I^2 statistic will be used to assess heterogeneity between trials. In the absence of significant heterogeneity, results will be pooled using a fixed-effect model. If substantial heterogeneity is detected (I^2 more than 50%), we will explore possible causes and will perform subgroup analyses for the main outcomes. Heterogeneity that is not explained by subgroup analyses may be modelled using a random-effects analysis, where appropriate.

Sensitivity analyses

Our prespecified sensitivity analysis was to explore the effects of trial quality assessed by concealment of allocation, by excluding studies with clearly inadequate allocation of concealment (rated C). This analysis has not been conducted due to the small number of included trials. It will be included in future updates when sufficient data become available.

Subgroup analyses

The prespecified subgroups were based on:

1. risk of pre-eclampsia at trial entry (high, moderate, low, or undefined);
2. allocated duration of rest (less than four or four or more hours per day); and
3. type of physical activity at trial entry (paid employment, recreational sport, or household duties only).

Only the main outcomes listed above will be included in the subgroup analyses.

These subgroup analyses were not performed due to insufficient data but will be included in future updates, should more data become available.

RESULTS

Description of studies

Two studies were included in this review (total 106 women). One study was conducted in Colombia ([Herrera 1993](#)), and the other in USA ([Spinapolice 1983](#)). See 'Characteristics of included studies' table.

Both studies included nulliparous women with a singleton pregnancy, normal blood pressure and a positive roll-over test. According to the criteria used in our protocol, all participants were therefore at moderate risk of pre-eclampsia. The women were enrolled between 28 and 32 weeks' gestation. Their baseline level of activity at trial entry is not reported for either trial. In one study ([Spinapolice 1983](#)), some participants were in paid employment, but the level of physical activity in this employment is not stated. For the other study ([Herrera 1993](#)), there is no information about baseline activity at trial entry, although it is reported that women in the control group did not have regular daytime rest.

One trial compared four hours per day of rest with unrestricted activity. The other compared two 15-minute periods of rest each day plus a nutrient supplement (soy protein, calcium and linoleic acid) three times per week with unrestricted activity plus placebo. For both trials, rest was lying in the left lateral position at home, but not necessarily in bed. Neither required women to stop working.

Neither trial reported data on compliance with the advice to rest. Although one study ([Spinapolice 1983](#)) states that the participants were visited by nursing staff three times a week to ensure compliance with rest, no information is available about what the nurses observed during these visits. Also, there is little information about women's baseline activity level or the activity level during the trial in the control group.

Trials of rest for women with a multiple pregnancy are described in a separate review ([Crowther 2001](#))

Ten studies were excluded. Nine studies were excluded because all women had hypertension at trial entry ([Cameron 1985](#); [Catalano 1997](#); [Crowther 1986](#); [Crowther 1992](#); [Leung 1998](#); [Mathews 1977](#); [Mathews 1982](#); [Sibai 1992](#); [Somers 1989](#)). In addition, in four of these studies all comparison groups had bed rest. Three of these studies compared an antihypertensive drug plus bed rest with bed rest alone ([Cameron 1985](#); [Catalano 1997](#); [Sibai 1992](#)). The fourth was a three-arm study in which bed rest alone was compared with bed rest and compliance enhancement training with and without biobehavioural intervention ([Somers 1989](#)). One

study was excluded because more than fifty per cent of the women randomised had miscarriages prior to 20 weeks' gestation; therefore, it was impossible to assess over half the participants for development of pre-eclampsia ([Harrison 1993](#)). See 'Characteristics of excluded studies' table.

Risk of bias in included studies

The quality of both trials is unclear. The methods used for allocation concealment were inadequately reported. Completeness of follow up was not reported in either trial. Clearly, blinding of participants to rest was not possible, although the caregivers were blinded in one trial. It is not reported whether the outcome assessor was blinded in either trial. Attempts to contact the trialists for further information were unsuccessful.

Effects of interventions

Comparison one: rest versus unrestricted activity

One trial (32 women) compared rest at home with unrestricted activity.

Pre-eclampsia

Rest was associated with a reduction in the relative risk of pre-eclampsia (relative risk (RR) 0.05, 95% confidence interval (CI) 0.00 to 0.83) compared to unrestricted activity.

Other outcomes

For women allocated rest, the RR of gestational hypertension was 0.25 (95% CI 0.03 to 2.00) compared to those allocated unrestricted activity. No other outcomes were reported.

Comparison two: rest plus nutrient supplementation versus unrestricted activity plus placebo

One trial (74 women) compared rest and nutrient supplementation at home with no restriction of activity and placebo pills.

Pre-eclampsia

Rest plus nutrient supplementation was associated with a reduction in the relative risk of pre-eclampsia (RR 0.13, 95% CI 0.03 to 0.51) compared to unrestricted activity and placebo.

Other outcomes

Rest plus nutrient supplementation was associated with a reduction in the RR of gestational hypertension (RR 0.15, 95% CI 0.04 to 0.63) compared to unrestricted activity and placebo. The relative risk of caesarean section was 0.82 (95% CI 0.48 to 1.41) with rest plus nutrient supplementation. No other outcomes were reported.

DISCUSSION

The aim of this review was to evaluate the effects of rest on development of pre-eclampsia and its complications in women with normal blood pressure. Data from the two included studies suggest that rest at home from 28 weeks' gestation onwards, with or without nutrient supplementation, may reduce the relative risk of pre-eclampsia for women with a singleton pregnancy at moderate risk. The confidence intervals are wide, however, suggesting that for rest alone the true effect could be anything between a 17% reduction and a 100% reduction ([Spinapolice 1983](#)),

and for rest plus nutrients, anywhere between a 49% and 97% reduction (Herrera 1993). As both trials were small and of uncertain quality, it is likely that at least some of these reported effects are due to the effects of bias and/or random errors, rather than to any true effect of rest. In view of our current understanding of pre-eclampsia as a multifactorial condition which originates in very early pregnancy, a large reduction in relative risk associated with rest from 28 weeks' gestation onwards seems implausible. Moreover, there is no information about other important outcomes such as perinatal mortality and morbidity, maternal morbidity, adverse events, women's views or costs. Therefore, it remains unclear whether rest or advice to rest for normotensive women is overall beneficial.

Neither trial reported data on compliance with the advice to rest, and there is little information about women's baseline activity level or the activity level during the trial in the control group. This information would have been important for understanding and interpreting the results of the studies, and is particularly relevant for trials that assess behavioral interventions.

Six trials (706 women) have evaluated rest in hospital compared with normal activity at home for women with a multiple pregnancy (Crowther 2001). There appeared to be a moderate reduction in the risk of hypertension, although this was borderline for statistical significance (RR 0.64, 95% CI 0.41 to 1.01). Data for pre-eclampsia were not reported.

There is little evidence that the nutrient supplements as used in the study by Herrera and colleagues (soy protein, calcium, and linoleic acid) influence the risk of pre-eclampsia. Calcium supplementation for prevention of pre-eclampsia is covered by a separate review (Hofmeyr 2002). Although the results of that review suggest that calcium supplementation reduces the risk of pre-eclampsia, the minimum dose of calcium for included studies is one gramme per day, whereas the dose in this trial was 300 mg three times per week. An interaction between the three supplements and rest remains possible, but would seem unlikely in the absence of evidence that any of the individual agents is beneficial.

Randomised trials evaluating bed rest for a variety of conditions outside pregnancy and during pregnancy have failed to demonstrate any clear evidence of benefit, and attention has been drawn to the potential hazards of recommending bed rest (Allen 1999). Caution is even more relevant for rest as a

potential preventative intervention. As for any prophylaxis, before recommending rest for preventing pre-eclampsia, we must first be sure that this advice does more good than harm for both mother and baby. Moreover, whether women rest or reduce their physical activity during pregnancy is normally a matter for personal choice. Women at increased risk of pre-eclampsia should not be advised to rest more than they would otherwise choose to unless there is sufficient evidence that this is beneficial, and adequate reassurance that it is not harmful. In the absence of such evidence, women should be allowed to make their own choices.

Further large randomised trials are needed if we are to have reliable evidence about the effects of rest on the risk of pre-eclampsia and its complications. As well as pregnancy outcomes, such trials should collect information on adverse effects, women's views, and costs to the women, society and the health services associated with restriction of activity. Better descriptions of women's patterns of activity and rest will give insight into how findings may be generalised to other women. Such trials would be most appropriate in settings where women with normal blood pressure who have an increased risk of pre-eclampsia are currently advised to rest during pregnancy.

AUTHORS' CONCLUSIONS

Implications for practice

Currently there is insufficient evidence to support recommending rest or restriction of activity to women with normal blood pressure to reduce their risk of pre-eclampsia and its complications. In the absence of such evidence, whether women rest or reduce their physical activity during pregnancy should be a matter of personal choice.

Implications for research

Any further trials should be large, and should collect information about perinatal mortality and morbidity, maternal morbidity, adverse effects associated with rest, women's views on restriction of activity, and costs. Trials should also describe women's baseline level of activity, the duration for which they rested, and whether they were able to rest for the allocated time period.

ACKNOWLEDGEMENTS

None.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Herrera 1993

Methods	Randomisation: computer-generated list. Allocation concealment: closed envelopes. No further information. Follow up: not reported. Blinding: participants blinded to nutritional supplements. Caregivers blinded, and blinding of outcome assessor not reported.
Participants	74 primigravidae women at 28-29 weeks' gestation with normal blood pressure, a positive roll-over test, and MAP at least 80 mmHg
Interventions	Exp: advised to rest at home in left lateral position for 15 minutes twice daily, and nutritional supplementation 3 times/week orally with soy protein 25 g, calcium 300 mg, and linoleic acid 300 mg, until delivery. Controls: no advice to rest, and placebo pills 3 times/week, containing ferrous sulphate 105 mg, until delivery.
Outcomes	Woman: gestational hypertension (BP $\geq$ 140/90 x 2, 6 hours apart), pre-eclampsia (gestational hypertension with $>$ 0.5 g/L proteinuria), caesarean section. Baby: mean values for gestational age, birthweight.
Notes	Control group did not report systematic daily rest. Compliance with rest: no information.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Spinapolic 1983

Methods	Randomisation: computer-generated list. Allocation concealment: closed envelopes. No further information. Follow up: not reported. Blinding: blinding of participants not possible, caregivers not blinded, and blinding of outcome assessor not reported.
Participants	32 nulliparous women at 28-32 weeks' gestation with normal blood pressure and a positive roll-over test.
Interventions	Exp: advised to rest at home in left lateral recumbent position for 4 hours daily until delivery. If MAP increased by at least 9 mmHg, the duration of rest was increased to 6 hours/day (1 participant). Seen every 2 weeks. Controls: no advice to increase rest. Seen every 2 weeks.
Outcomes	Woman: gestational hypertension (BP $\geq$ 140/90 or increase by 30/15 mmHg x 2 at least 6 hours apart), pre-eclampsia (not defined), induction of labour, mode of delivery. Baby: mean values for gestation at delivery, birthweight, Apgar score.
Notes	Data for all outcomes except gestational hypertension and pre-eclampsia were reported only for control group and not for intervention group. Compliance with rest: women in the experimental group had home visits by nurse 3 times/week to ensure compliance. No further information.

Spinapolic 1983 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

BP: blood pressure

Exp: experiment

MAP: mean arterial pressure

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Cameron 1985	<p>Women had hypertension. Comparison of labetalol with bed rest versus bed rest alone, in hospital.</p> <p>Methods: 'randomised'. No further information.</p> <p>Participants: 85 pregnant women with hypertension.</p> <p>Intervention: as above.</p> <p>Outcomes: blood pressure, proteinuria, biochemical and haematological tests, tests of placental function, adverse effects of therapy on mother and baby.</p>
Catalano 1997	<p>Women had mild pre-eclampsia. Comparison of nifedipine with bed rest versus bed rest alone, in hospital.</p> <p>Methods: 'randomly allocated'. No further information.</p> <p>Participants: 100 women at 26-36 weeks' gestation, with mild pre-eclampsia.</p> <p>Intervention: as above.</p> <p>Outcomes: blood pressure; prolongation of pregnancy; days of hospitalisation; preterm birth; mean birthweight; small-for-gestational age.</p>
Crowther 1986	<p>Women had hypertension.</p> <p>Methods: randomised controlled trial.</p> <p>Participants: 105 women with a singleton pregnancy at 28-38 weeks, with proteinuric hypertension.</p> <p>Interventions: strict bed rest in hospital versus voluntary ambulation around the hospital ward.</p> <p>Outcomes: severe hypertension; increase in proteinuria; fulminating pre-eclampsia; eclampsia; placental abruption; IOL; preterm delivery; low birthweight; passage of meconium; Apgar score; perinatal death; early neonatal death; stillbirth; endotracheal intubation; admission to special care nursery.</p>
Crowther 1992	<p>Women had hypertension.</p> <p>Methods: randomised controlled trial.</p> <p>Participants: 218 women with a singleton pregnancy at 28-38 weeks, with non-proteinuric hypertension.</p> <p>Interventions: some rest in hospital versus normal activity at home.</p> <p>Outcomes: severe hypertension; proteinuria; caesarean section; IOL; birthweight; small-for-gestational age; admission to intensive care nursery; length of stay in hospital; perinatal death; Apgar score at 1 and 5 minutes.</p>
Harrison 1993	<p>Three-arm trial comparing bed rest, HCG, or placebo for prevention of miscarriage. More than 50% women had miscarriage prior to 20 weeks' gestation, so it was not possible to analyse their data for development of pre-eclampsia. The blood pressure status of the women was not reported.</p> <p>Methods: 'randomly assigned' to treatment regimen in identical coded drug boxes. No further information.</p>

Study	Reason for exclusion
	<p>Participants: 61 women with a history of vaginal bleeding before the 8th week of gestational age.</p> <p>Interventions: 3-arm trial. Bed rest at home versus placebo (without bed rest) versus 5000 IU of HCG i/m twice a week until 12th week and weekly until 16th week.</p> <p>Outcomes: miscarriage; pre-eclampsia; abruption; premature labour; mode of delivery; neonatal death; birthweight.</p>
Leung 1998	<p>Women had hypertension. Large number of exclusions postrandomisation.</p> <p>Methods: randomised controlled trial.</p> <p>Participants: 90 women with a singleton pregnancy at 28-38 weeks, with non-proteinuric hypertension.</p> <p>Intervention: hospitalisation and bed rest versus normal activity at home with regular visits to day unit or outpatient clinic.</p> <p>Outcomes: hypertension, severe hypertension; proteinuria; mode of delivery; IOL; use of antihypertensive medication; women's views and preferences (questionnaire); birthweight; small-for-gestational age; admission to intensive care nursery; length of stay in hospital; stillbirth/neonatal death; Apgar score.</p>
Mathews 1977	<p>Women had hypertension. Large number of exclusions likely postrandomisation.</p> <p>Methods: participants 'allocated at random' to one of four groups using previously prepared cards contained in envelopes. No further information.</p> <p>Participants: 135 women with singleton pregnancy between 28 to over 38 weeks, with non-proteinuric hypertension.</p> <p>Intervention: (4 groups) bed rest in hospital with or without sedation (phenobarbitone 15 mg three times daily) versus normal activity at home with or without sedation.</p> <p>Outcomes: severe hypertension (BP > 109 mmHg); proteinuria; eclampsia; IOL; operative vaginal delivery; caesarean section; biochemical parameters; stillbirths and neonatal death; fetal distress during labour; Apgar score; small for gestation; preterm birth.</p>
Mathews 1982	<p>Women had hypertension.</p> <p>Methods: randomised controlled trial.</p> <p>Participants: 40 women with a singleton pregnancy at 26 to over 36 weeks, with proteinuric hypertension.</p> <p>Interventions: strict bed rest in hospital versus voluntary ambulation around ward in hospital.</p> <p>Outcomes: plasma urea and urate; serum human placental lactogen and oestriol; development of premonitory symptoms of eclampsia; hypertension; proteinuria; mode of delivery; perinatal death; gestation at delivery; birthweight; small-for-gestational age.</p>
Sibai 1992	<p>Women had hypertension. Comparison of nifedipine with bed rest versus bed rest alone, in hospital.</p> <p>Methods: randomised controlled trial.</p> <p>Participants: 200 women at 26-36 weeks' gestation with proteinuric and non-proteinuric hypertension.</p> <p>Interventions: as above.</p> <p>Outcomes: blood pressure; haematological and biochemical parameters; days in hospital; prolongation of pregnancy; preterm delivery; gestation at birth; mean birthweight; small-for-gestational age; placental weight; cord blood gas.</p>
Somers 1989	<p>Women had hypertension. Three-arm trial in which all three groups of participants had bed rest varying from 15.8 to 18 hours per day along with additional interventions.</p> <p>Methods: 'randomly' assigned. No further information.</p> <p>Participants: 45 women at 30 -36 weeks with hypertension, all prescribed restricted physical activity for hypertension.</p> <p>Interventions: 3-arms: bed rest at home versus bed rest and compliance enhancement training at home versus bed rest, compliance enhancement training, and bio-behavioral interventions at home.</p>

Study	Reason for exclusion
	Outcomes: mean arterial pressure; compliance with bed rest.

HCG: human chorionic gonadotropin

i/m: intramuscularly

IOL: induction of labour

IU: international units

DATA AND ANALYSES

Comparison 1. Rest alone versus unrestricted activity

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pre-eclampsia	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.05 [0.00, 0.83]
2 Gestational hypertension	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.00]

Analysis 1.1. Comparison 1 Rest alone versus unrestricted activity, Outcome 1 Pre-eclampsia.

Analysis 1.2. Comparison 1 Rest alone versus unrestricted activity, Outcome 2 Gestational hypertension.

Comparison 2. Rest plus nutrient supplementation versus unrestricted activity plus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pre-eclampsia	1	74	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.03, 0.51]
2 Gestational hypertension	1	74	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.04, 0.63]
3 Caesarean section	1	74	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.48, 1.41]

Analysis 2.1. Comparison 2 Rest plus nutrient supplementation versus unrestricted activity plus placebo, Outcome 1 Pre-eclampsia.

Analysis 2.2. Comparison 2 Rest plus nutrient supplementation versus unrestricted activity plus placebo, Outcome 2 Gestational hypertension.

Analysis 2.3. Comparison 2 Rest plus nutrient supplementation versus unrestricted activity plus placebo, Outcome 3 Caesarean section.

APPENDICES

Appendix 1. Search strategy

1. Bed rest
2. Bed Rest*ME
3. Rest*
4. Rest*ME
5. Inpatient
6. Outpatient
7. Hospital*
8. Ambulat*
9. Day next unit
10. Day next care next unit
11. (#1 OR #2 OR #3 OR #4)
12. (#5 OR #6 OR 7 OR #8)
13. (#9 OR #10)
14. (#11 OR #12 OR #13) AND (results of the search listed in the [Generic Protocol 2005](#))

Databases searched:

1. CENTRAL (*The Cochrane Library* 2005, Issue 3)
2. EMBASE (2002 to August 2005) (MeSH (ME) were changed to Emtree headings)

WHAT'S NEW

Date	Event	Description
18 January 2010	New search has been performed	Search updated. No new trials identified.

HISTORY

Protocol first published: Issue 2, 2005
Review first published: Issue 2, 2006

Date	Event	Description
20 September 2008	Amended	Converted to new review format and edited contact details.

CONTRIBUTIONS OF AUTHORS

The protocol for this review was based on the generic protocol of interventions for prevention of pre-eclampsia and its complications, which was drafted by Shireen Meher and Lelia Duley, with contributions from the Prevention of Pre-eclampsia Review Authors. Trials were assessed for inclusion by Shireen Meher and Lelia Duley independently. Data were extracted and entered into the Review Manager software by Shireen Meher and double checked for accuracy by Lelia Duley.

The review was drafted by Shireen Meher and Lelia Duley.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- The University of Liverpool, UK.
- The University of Oxford, UK.

External sources

- Health Technology Assessment, UK.
- Medical Research Council, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Bed Rest [*methods]; Blood Pressure; Dietary Supplements; Pre-Eclampsia [*prevention & control]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy