ISRCTN80468181 https://doi.org/10.1186/ISRCTN80468181

Can taking a zinc supplement during pregnancy reduce the symptoms of depression both before and after the baby is born?

Submission date
12/06/2018

Recruitment status
No longer recruiting

Registration date
18/07/2018

Overall study status
Completed

Last Edited
17/07/2018

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Perinatal depression is a depressive illness that affects women in pregnancy around childbirth or within the first year following birth. It is experienced as persistent low mood and it is estimated to affect 10-15% of women in the UK. The cost to health and social services is estimated at £1.8 billion for each one-year cohort of births in the UK and it is one of the leading causes of deaths amongst new mothers. Besides being difficult for affected women, perinatal depression can have negative effects on the growth and development of their babies and affect the well-being of the entire family. Research shows a clear relationship between zinc deficiency and the development of mood disorders. Evidence also suggests that zinc supplementation helps to reduce the symptoms of depression in both animals and humans. It is recognised that women who are pregnant and breastfeeding are at risk of lower levels of zinc because of the high demand from the developing and feeding baby. Studies in the perinatal period are however limited, highlighting the need to carry out a study to determine whether the same anti-depressant effects are seen in this group of women. To make the future study as successful as possible the aim of this study is to first test the practicality of the study design.

Who can participate?
Pregnant women

What does the study involve?
At assessment participants are classified as either having a history of depression or onset of depression in pregnancy and as either users or non-users of antidepressants. The women not taking an antidepressant are randomly allocated to take either a placebo (dummy supplement) or zinc. The women taking an antidepressant are also randomly allocated to take either antidepressant and zinc or antidepressant and placebo. On a daily basis for the duration of their pregnancy and for 4 weeks after giving birth, participants take either a placebo or a zinc tablet on its own or with an antidepressant depending on which group they are assigned to. At five different time points they have a blood test to measure their zinc levels, and complete a food diary and questionnaires that evaluate the amount of zinc consumed from their diet and their mood. Adherence is measured by counting pills. Participants are also provided with a diary so

they can record the date and time the tablet is taken, side effects experienced and any missed days. The researcher contacts the participants by telephone on a fortnightly basis to discuss any side effects or issues with adherence. Likewise, the participants have both telephone and email access to the researcher and their midwife should they have any concerns about their supplement use. The diaries are also collected at the scheduled appointments.

What are the possible benefits and risks of participating?
The potential benefits to the study participants include: closer supervision and monitoring of their mental health; an awareness of their dietary intake; a reduction of depressive symptoms; and new knowledge. There is an awareness of potential drug-zinc interactions and these will be identified through regular assessment and managed on a case by case basis in collaboration with the clinical team. Too much zinc may be harmful, symptoms include: nausea, vomiting, loss of appetite, stomach cramps, diarrhoea and headaches. When people take too much zinc for a long time, they sometimes have problems such as low copper levels, lower immunity, and low levels of HDL cholesterol (the “good” cholesterol). Thus, women's individual overall supplement intake will also be assessed to ensure that it does not exceed the safe upper limit of 40 mg per day.

Where is the study run from?
Ashford and St Peter's Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2018 to July 2019

Who is funding the study?
University of Surrey (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
ZnPND PhD Project

Study information

Scientific Title
Can taking a zinc supplement during pregnancy reduce the symptoms of perinatal depression?

Acronym
ZnPND

Study objectives
Zinc supplementation either together with or without antidepressant drugs improves the symptoms of depression in pregnancy and the postnatal period.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Single-centre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Perinatal depression

Interventions
At assessment women will be classified as either having a history of depression or onset of depression in pregnancy. Antidepressant use is found to be a prognostic variable. Hence, at the

recruitment women will be classified as either users or non-users of antidepressants and subdivided into two groups:
• Women not taking antidepressants
• Women taking antidepressants

To control for the effect of antidepressant use which is a confounder a stratified randomisation will be used so that the randomisation scheme is performed separately for antidepressant users and for non-users. The treatment (zinc) and the control (placebo) will be randomised to participants within each stratum.

The women not taking an antidepressant will be randomly allocated into one of two arms and given either:
• Placebo alone
• Zinc alone

The women taking an antidepressant will also be randomly allocated into one of two arms and given either:
• Antidepressant and zinc
• Antidepressant and placebo

To avoid the potential sources of bias, double blindness or masking will be adopted in allocating treatments. Neither the participants nor the researchers will know which participant belong to which group. Randomisation codes will be generated by the web based application called sealed envelope available at https://www.sealedenvelope.com/.

On a daily basis for the duration of their pregnancy and for 4 weeks post giving birth, women will be required to take either a placebo or a single 10mg zinc tablet, on its own or adjunct to an antidepressant depending on which group they are assigned to (see above).

At five different time points they will also be required to have a blood test to measure their zinc levels, complete a food diary and questionnaires that evaluate both the amount of zinc consumed from diet and mood.

Adherence will be measured by pill counts, the standard for monitoring patient adherence for both experimental and clinical drugs (Lee et al. 2007). Upon starting the study each woman will receive a supply of either zinc supplements or placebo and unbeknown to her more tablets will be supplied than needed. At the scheduled study appointments women will be asked to return any excess supplements. Pill counts will be calculated by the PhD researcher as the number of pills taken (the number of pills dispensed minus the number of pills counted) to confirm adherence. The number of pills expected to have been taken will be calculated by multiplying the daily dose by the number of days since the date dispensed. The supply will then be replenished accordingly until the next appointment and so forth until the end of the study. The women will also be provided with a diary so they can record the date, time the tablet is taken, side effects experienced and any missed days. The PhD researcher will contact the women by telephone on a fortnightly basis to discuss any adverse reactions and/or issues with adherence. Likewise, the women will have both telephone and email access to the PhD researcher and their midwife in between time should they have any concerns about their supplement use. The diaries will also be collected at the scheduled appointments.

Intervention Type
Supplement

Primary outcome measure
Severity of depressive symptoms, measured using the Edinburgh Post Natal Depression Score at 6-12 weeks baseline, 20 weeks/anomaly scan, 28-30 weeks, birth visit up to 10 days post delivery, and 4 weeks post delivery

Secondary outcome measures
Measured at 6-12 weeks baseline, 20 weeks/anomaly scan, 28-30 weeks, birth visit up to 10 days post delivery, and 4 weeks post delivery:
1. Zinc levels in the blood, measured using a blood test
2. Zinc intake from diet, measured using the Zinc Food Frequency Questionnaire and 4-day food and drink diary

Overall study start date
11/06/2018

Completion date
31/07/2019

Eligibility

Key inclusion criteria
1. Pregnant women irrespective of age, ethnicity, socioeconomic status, pregnancy status (primigravida or multigravida)
2. Pregnant women may be prescribed an antidepressant or not
3. Pregnant women may be taking supplements or not

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
On average, it is estimated there will be between 4 and 8 women per month who fulfil the inclusion/exclusion criteria based on the number of women currently referred to the perinatal mental health specialist midwife. Recruitment will be implemented over a 10 month period and this will provide 40-80 potential participants. Due to the length of the study duration (10 months) and particularly due to the nature of study population, i.e. mothers who recently delivered a baby, a drop out of rate of 50% is anticipated, which is slightly higher than in a usual setting. Nevertheless, the required sample of between 25-50 participants as recommended for feasibility studies by Sim and Lewis (2012) and Julious (2005), will be achievable to investigate the distribution and key parameters of the outcome measures.

Key exclusion criteria
Women infected with HIV will be excluded. Whilst they are particularly susceptible to zinc deficiency, the HIV virus also requires zinc and excessive dietary zinc has been linked with declining CD4 cell counts and reduced survival. Baum et al. (2010) carried out a RCT of zinc

supplementation to prevent immunological failure in HIV-infected adults and whilst no serious side effects were reported, the dose was significantly lower than the suggested therapeutic dose for this study. More research is needed; hence women who are HIV positive will be excluded.

Date of first enrolment
20/08/2018

Date of final enrolment
19/07/2019

Locations

Countries of recruitment
United Kingdom

Study participating centre
Ashford and St Peter's Hospitals NHS Foundation Trust
Peter's Hospital
Chertsey
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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/00ks66431

Funder(s)

Funder type
University/education

Funder Name
University of Surrey

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Publication of the study protocol is planned. When both the quantitative and qualitative results have been interpreted and integrated, the dissemination strategy is to share the findings with existing academic/clinical networks and study participants, through conference presentation and publication in a high-impact peer reviewed journal, specific to maternal, child and family mental health. The Pre and Post Natal Depression Advice and Support (PANDAS) website along with our PPI advisers will be used to identify support groups to reach out to the women specifically at risk of perinatal depression and discuss the outcomes with them directly. Social media will also be used as a platform to share the findings.

Intention to publish date
31/07/2020

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date