Interactive case report

Treating nausea and vomiting during pregnancy: case progression

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Last week (31 January, p 276) we presented the case of Ms Reynolds, a 25 year old woman who presented to her general practitioner when eight weeks pregnant complaining of nausea and vomiting with light headedness. After an unsuccessful trial of prochlorperazine, she asked about alternatives to conventional drugs. We invited responses on which therapeutic options are safe to consider or recommend in pregnancy, what study design might provide evidence for their relative efficacy in an individual patient, and what proportion of patients and pregnant women use complementary therapies. To look at the discussion of the case so far go to bmj.com

One of us (NH) is interested in complementary medicine and suggested a trial of vitamin B-6 (pyridoxine) to relieve the patient's symptoms. We searched Medline (1996 onwards, limiting our search to review articles) using the MeSH terms "hyperemesis gravidarum" or "nausea" or "vomiting" and "pregnancy." We obtained 77 studies. We also searched the Cochrane Library and *Clinical Evidence*. We limited the search to systematic reviews of randomised controlled trials¹ or evidence based review articles with explicit search strategies and quantitative assessment of treatment effects.²⁻³ The available evidence from three placebo controlled trials of vitamin B-6 shows that vitamin B-6 does not reduce vomiting (odds ratio=0.91, 95% confidence interval 0.6 to 1.4) but does reduce nausea (change in a 10 cm visual analogue scale; weighted mean difference 0.9 cm, 95% confidence interval 0.4 to 1.4 cm).¹

We suggested to Ms Reynolds that an objective way to assess whether vitamin B-6 was effective in reducing her symptoms was to undertake an n of 1 trial.⁴ In such a trial a patient undergoes pairs of treatment periods (one period of each pair with the active drug and one with placebo, assigned at random, with both patient and health professional blind to treatment allocation).⁴ Because of the paucity of evidence on the use of vitamin B-6, we judged that this trial method was ethical.

We had already obtained vitamin B-6 and matching placebo capsules and had secured approval from an ethics committee to undertake an n of 1 trial in patients with nausea and vomiting during pregnancy. The dose (10 mg three times a day) was within safe suggested levels in pregnancy according to the Food Standards Agency and matched the doses used in previous trials.

Ms Reynolds had five treatment pairs (two days active treatment, one day washout period, two days placebo), giving a total of 25 days of treatment. The hospital pharmacist alone was aware of treatment allocation. We measured Ms Reynolds's symptoms using a validated patient generated outcome measure—measure yourself medical outcome profile (MYMOP).⁵

Questions

1 How does the evidence obtained from the n of 1 trial differ from the evidence of randomised controlled trials?

2 How would you apply this evidence to other patients presenting with nausea and vomiting in pregnancy?

3 Can you think of other clinical dilemmas that would be helped by the use of n of 1 trials?

Please respond through bmj.com

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BMJ 2004;328:337

Ms Reynolds rated vomiting, dizziness, daily activity tasks, and general wellbeing as her most important symptoms. The reported reduction in nausea was not important to Ms Reynolds, who rated her other symptoms as more troublesome (figure). She completed a daily diary with each of these outcomes measured on an ordinal scale of 0 (as good as it could be) to 6 (as bad as it could be). We analysed each symptom over the five treatment pairs with a paired *t* test.⁴

Funding: This study was funded through an extended South and West Deanery registrar contract for NH through the Division of Primary Health Care, University of Bristol, and Dean Lane Family Practice, Bristol.

Competing interests: None declared.

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This is the second of a three part case report where we invite readers to take part in considering the diagnosis and management of a case using the rapid response feature on bmj.com. Next week we will report the case progression, and in four weeks' time we will report the outcome and summarise the responses

Day	1	2	3	4	5	6	7	8	9	10	11	12
Date	4/10/02	5/10/02	6/10/02	7/10/02	8/10/02	9/10/02	10/10/02	11/10/02	12/10/02	13/10/02	14/10/02	15/10/02
Symptom 1	4	3	5	5	4	6	5	4	3	3	4	2
Symptom 2	3	2	4	3	3	5	4	3	3	3	4	2
Activity (daily tasks)	5	4	5	5	4	5	4	4	4	4	4	3
General Wellbeing	4	3	5	5	4	5	4	4	4	4	3	3
Symptom 3												

Key: Score
0 1 2 3 4 5 6
As good as it could be As bad as it could be

Extract from Ms Reynolds's measure yourself medical outcome profile