Vitamins C and E for Type 1 Diabetes Prevention in Women (DAPIT): A Randomised Placebo-Controlled Trial

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Abstract

Background: The use of antioxidants during pregnancy has not been shown to reduce pre-eclampsia in several trials, but the effect on women with diabetes is unknown. We planned to survey whether supplementation with nutrients C and E diminished frequency of toxemia in ladies with type 1 diabetes.

Methods: In a multicenter, randomized, placebo-controlled study, we recruited women from 25 UK antenatal metabolic clinics. Type 1 diabetes prior to pregnancy, presentation between 8 and 22 weeks of gestation, a singleton pregnancy, and age 16 or older were the eligibility criteria. Up until the time of delivery, women were assigned at random in a 1:1 ratio to receive either a matched placebo or 1000 mg of vitamin C and 400 IU of vitamin E (-tocopherol). Eight balanced blocks of patients comprised the stratified center of the randomization sequence. The treatment allocation was hidden from both trial personnel and participants. The essential endpoint was toxemia, which we characterized as gestational hypertension with proteinuria. Examination was by changed aim to treat. The ISRCTN number for this study is ISRCTN27214045.

Results: Between April, 2003, and June, 2008, 762 ladies were haphazardly apportioned to treatment gatherings (379 nutrient supplementation, 383 fake treatment). The primary endpoint was evaluated for 375 women who were given vitamins and 374 women who were given a placebo. Pre-eclampsia rates were the same in the vitamin (15 percent, n=57) and placebo (19 percent, 70) groups (risk ratio 0–81, 95% CI 0–59–112). There were no reports of adverse maternal or neonatal outcomes.

Conclusion: Supplementation with nutrients C and E didn't lessen hazard of toxemia in ladies with type 1 diabetes. However, additional research is needed to determine whether vitamin supplementation might be beneficial to women with low antioxidant status at baseline.

Keywords: Type 1 diabetes; Vitamin C and E; Antioxidants; Toxaemia; Supplements

Introduction

The hypothesis that oxidative stress plays a key part in the pathogenesis of pre-eclampsia was proposed in the late 1980s8 and has since been the focus of much research. Diabetes mellitus, specifically type 1 diabetes, is associated with increased oxidative stress and antioxidant depletion, which is partly related to prevailing blood glucose concentrations [1]. Increased oxidative stress in pregnant women with diabetes might account for rates of pre-eclampsia that Since pre-eclampsia is likely to be a heterogeneous disease, pathogenesis could differ between women with different risk factors, these findings led to several large trials of antioxidant treatment for pre-eclampsia prevention [2]. The results of these trials have shown no benefit of vitamin C and E supplementation during pregnancy. However, only three of these trials included women with diabetes, and each of these groups was small and poorly characterised Moreover, considering the expansion in oxidative pressure and cell reinforcement exhaustion that happen in diabetes, a valuable impact of cell reinforcement supplementation is conceivable in this gathering of patients [3].

We planned the Diabetes and Toxemia Mediation Preliminary (DAPIT) to survey whether supplementation with nutrients C and E diminished frequency of toxemia in ladies with type 1 diabetes.

Methods

Patients and the design of the study

DAPIT was a parallel-group, randomized, multicentre trial with a placebo control. Between April 2003 and June 2008, women were recruited from 25 antenatal metabolic clinics in Northern Ireland, Scotland, and northwest England. The final child was born in December of 2008. Type 1 diabetes prior to pregnancy, presentation between 8 and 22 weeks of gestation, a singleton pregnancy, and age 16 or older were the eligibility criteria. Women were excluded if they refused to participate, were enrolled in another study, were receiving warfarin treatment, or were known drug abusers. Supplements containing 500 mg or more of vitamin C or 200 IU or more of vitamin E daily were excluded from the study for women. The study included women with hypertension on a regular basis. Ethics approval was granted by the West Midlands multicentre research ethics committee (MREC 02/7/016). The patient information sheet was reviewed by participants at least 48 hours after they gave written informed consent [4].

Randomisation and masking

Participants were randomly allocated in a 1:1 ratio to receive 1000 mg vitamin C and 400 IU vitamin E or matched placebo daily from between 8 and 22 weeks' gestation until delivery. Vitamin C and identical placebo (calcium carbonate, microcrystalline cellulose, maltrodextrin, and stearic acid) tablets were manufactured by Thompson & Capper (Astmoor, Runcorn, Cheshire, UK). Natural-source vitamin E (α-tocopherol) and identical placebo (olive oil) capsules were manufactured by Eurocaps Limited (Dukestown, Tredegar, Gwent, UK) [5]. Victoria Pharmaceuticals (The Royal Hospitals, Belfast, UK) packaged tablets and capsules, 120 per bottle, according to a randomisation sequence generated in advance by Victoria Pharmaceuticals using PRISYM ID software (version 1.0009).

Qualified ladies who gave assent were doled out the following accessible number at that middle by research birthing specialists, and given their most memorable stock of preliminary medications — jugs of L-ascorbic acid tablets and vitamin E containers (nutrient gathering) or jugs of fake treatments (fake treatment bunch) — alongside a 7-day pill gadget to help adherence. Members were told to take one tablet and one container day to day until conveyance, and to leave unused pills in the jugs. Members went to preliminary visits at 26 (in no less than 2) weeks' and 34 (in something like) fourteen days' development, at which times tablets and containers were counted and the following stockpile apportioned. Unused tablets and containers were gathered during conveyance affirmation or at the 6-week post pregnancy preliminary visit, or were returned in postage prepaid envelopes [6].

Circulatory strain at randomisation was estimated with an English Hypertension Society approved mechanized instrument, (Omron M5-I, Omron Medical care, West Sussex, UK). The average of two measurements taken three minutes apart were recorded after the participant had been seated for five minutes [7]. At the end of the study, biological samples taken at baseline, 26 weeks, and 34 weeks were analyzed in a batch at Queen's University, Belfast's central laboratory for PAI-1 and PAI-2, plasma ascorbate concentrations, serum concentrations of -tocopherol (expressed per mmol of serum cholesterol), serum total cholesterol, HbA1c, and microalbumin and creatinine in the urine. The webappendix provides detailed information on laboratory analyses. For study participants, routine clinic visits six weeks after delivery and eight-week postpartum visits with their paediatrician, family doctor, or health visitor served as opportunities to collect follow-up information. The assessment of fixation, following, smiling, head control, tone, tendon reflexes, heart murmurs, and congenital abnormalities, in addition to the measurement of weight, length, and head circumference, comprised these data [8].

Results

Of the 762 ladies selected, 379 were arbitrarily designated to get nutrients C and E and 383 to fake treatment. 749 women were evaluated for pre-eclampsia in the original assigned group (375 vitamin, 374 placebo), and outcome data were available for 761 women (379 vitamin, 382 placebo). Eight women were enrolled outside of the 22-week gestational age limit (all were within 4 days of this threshold), and four patients were later reclassified as having type 2 diabetes. There were 12 deviations from the inclusion and exclusion criteria. The analysis included all 12 women [9].

Pre-eclampsia history, hypertension, antihypertensive treatment, and microalbuminuria were more common in the vitamin group than in the placebo group, despite the fact that most maternal baseline characteristics were the same between the two groups. Based on counts of returned pills from 618 women (n=45), 524 (85%) took at least 50% of their pills after delivery (or at the 34-week visit if no count was available after delivery), 434 (70%) took 80% or more, and 237 (38%) took all of their pills; 17 (3%), did not consume any. The median adherence rate for the vitamin C group was 95 percent (IQR 75–100), whereas the adherence rate for the placebo group was 96 percent (IQR 74–100); vitamin E, 93% [78–100] versus 93% [74–100] for the placebo).

Pre-eclampsia affected 127 (17%) women in total. The vitamin and placebo groups had the same risk of pre-eclampsia. Neither the risk of gestational hypertension nor the risk of a birthweight below the tenth centile for gestational age showed any significant differences between the groups. Figure 1 shows that the ratio of PAI-1 to PAI-2 did not differ between the groups at baseline (p=040), 26 weeks (p=032), or 34 weeks (p=078) [10].

We noticed no massive contrasts among nutrient and fake treatment bunches for any maternal result, including conveyance after a hypertension-related confirmation before 34 or 37 weeks, yet less children were conceived preterm (<37 weeks' growth) in the nutrient gathering than in the fake treatment bunch (table 3). For any clinical neonatal outcome, including fetal malformation, fetal loss, infant death, or miscarriage, there were no significant differences between the vitamin and placebo groups [11]. Both groups had comparable rates of admission to neonatal care, including intensive care, as well as respiratory diagnoses and other complications. The vitamin and placebo groups' mean birthweights are shown; there was no difference between the groups in the risk of birthweights of 2500 g or less (RR 082, 95% CI 056–120) and 4000 g or more (RR 025, 095–164). At birth or at follow-up, no significant differences in SD scores for weight, length, or head circumference were observed between infants in either group. Supplementation with vitamin C or E did not result in any adverse events or side effects in either the mother or the child [12].

Discussion

Neither the PAI-1 to PAI-2 ratio, which is a measure of endothelial activation, nor the daily supplementation with vitamins C and E from early to mid-pregnancy did reduce the risk of pre-eclampsia, gestational hypertension, or low birthweight infants in women with type 1 diabetes. Although the numbers were small and neither analysis was significant with the more stringent interaction test that is recommended by CONSORT28, we noted no evidence that antioxidant supplementation was associated with any harm to mother or baby [13]. However, in two of 11 prespecified subgroup analyses, the risk of pre-eclampsia was significantly reduced in women with low antioxidant status at baseline who were randomly assigned to the vitamin group compared with women with similar antioxidant status assigned to the placebo. In fact, nearly all of the trends were favourable to the supplemented group.

Numerous large trials of antioxidant supplementation for the prevention of pre-eclampsia in women with low and high risk have already been completed. All of these studies utilized comparable doses of vitamins C and E, and the women were randomly assigned to treatment groups in the latter part of the first or second trimester. Pre-eclampsia as a primary or secondary outcome has consistently been found to be negative[14]. Increased rates of low birthweight, gestational hypertension, fatal loss, stillbirth, and premature membrane rupture were reported by researchers in some trials but were not

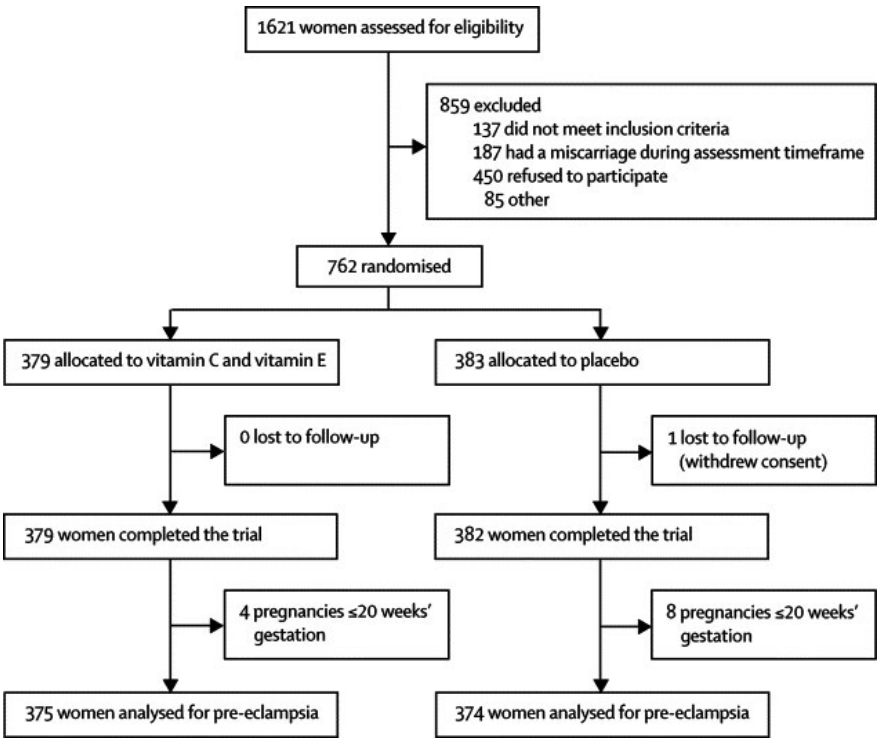

Figure 1: Trial profile.

confirmed in all studies, so their significance is unknown. A further trouble with a portion of these preliminaries is the heterogeneous idea of the populace under study. DAPIT varies from past preliminaries since it zeroed in on the job of cell reinforcements in a homogeneous gathering of painstakingly portrayed ladies with type 1 diabetes [15].

Conclusion

It's possible that the initial finding that antioxidant vitamins17 had a beneficial effect was a coincidental one. Women with a variety of pre-eclampsia risk factors were recruited for subsequent trials, and the presence of disparate disease processes and, as a result, pathophysiology may have reduced the likelihood of identifying a treatment effect. Our concentrate in a homogeneous populace of ladies with type 1 diabetes offers extra knowledge into sickness systems. The idea that oxidative stress is involved in the pathogenesis of pre-eclampsia remains plausible in principle, but women with vitamin deficiency may only benefit from vitamin supplementation; Nonetheless, this notion requires confirmation. Dietary mediation wealthy in different cell reinforcements could have benefits that can't be repeated by individual enhancements. On the other hand, remedy of cancer prevention agent nutrients at 8-22 weeks' incubation may be past the time to influence the neurotic interaction for most patients with diabetes. Cell reinforcement nutrients decrease paces of fetal mutation in rodents with tentatively prompted diabetes;30 be that as it may, testing of such a speculation in patients would require the presentation of supplementation previously or around origination in a lot bigger number of ladies.

Acknowledgement

None

Conflict of Interest

None

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