

The Effect of Vitamin C on Premature Rupture of Membranes and Preterm Labor in Shiraz, Southern Iran

Dear Editor,

Premature rupture of the fetal membranes (PROM) affects 10–20% of all pregnancies and is the main known cause of preterm delivery and neonatal and maternal morbidity and mortality.¹ It may be related not only to physical trauma but also to biochemical processes.² Vitamin C plays a role in collagen metabolism and in maintaining mechanical strength of the chorioamniotic membranes throughout gestation,^{2,3} and also acts as a collagen posttranscriptional modifiers.⁴ Altered patterns of collagen synthesis and diminished concentrations of vitamin C at week 28th of gestation are associated with subsequent occurrence of PROM.^{2,5} Casanueva *et al.* found that 100 mg of vitamin C/day added to the usual diet was sufficient to maintain a leukocyte ascorbate concentration $>18\mu\text{g}$ (102 mol)/ 10^8 cells, and that this concentration is essential for the prevention of PROM.⁶

This study was performed in two referral hospitals affiliated to Shiraz University of Medical Sciences, Shiraz, southern Iran, from December 2005 to June 2006. The study was approved by the university Ethics Committee and a written informed consent was obtained from each subject. 130 women were eligible. Inclusion criteria were pregnant women with no acute or chronic disease, gestation age of 20 weeks, age >18 years, BMI >19.8 , singleton pregnancy, and no consumption of vitamin supplements. Exclusion criteria were *Gardnerella vaginalis* infection, major congenital anomalies and fetal growth restriction. The women were randomly assigned into two groups receiving vitamin C (100 mg/day) and the control group received placebo identically. Two groups were instructed to take one tablet with water before breakfast each day. Each woman's general data, past gynecologic and obstetric history and present obstetric history were recorded in a questionnaire. From weeks 20 to 36, the women were evaluated every 4 weeks. At each visit, a vaginal examination was performed, and a vaginal swab was taken for detection of *Gardnerella vaginalis*. *Gardnerella vaginalis* infection was diagnosed by homogenous vaginal discharge,

pH >4.7 and characteristic amine or fishy odor when 10% potassium hydroxide (KOH) was added to the specimen obtained from vaginal secretions (positive Whiff test). The diagnosis of leakage of amniotic fluid was made clinically, using the nitrazine paper method. Gestational age was estimated from the last menstrual period and ultrasonography. Preterm labor was defined when delivery occurred before 37 weeks of gestation. The association was assessed by Chi-Square test.

From 130 participating women, 90% completed the study (57 women in the case group and 60 in the control group). Among them, 27 pregnant women delivered due to premature rupture of membranes. Premature rupture of membranes was observed in 36.67% of women in the control group versus 8.77% in the case group ($p < 0.001$). Premature rupture of membranes in term deliveries occurred in 7.02% in the supplemented group versus 30.0% in the control group ($p = 0.001$). The incidence of preterm birth was observed in 36.67% in the case group versus 5.26% in the control group. There was no difference between the two groups in the incidence of preterm rupture of membranes (33.30% in the case group versus 57.10% in the control group with $p = 0.5$). The overall incidence of preterm labor was 8.55% in the case group, but there was no significant difference between the two groups (8.33% in the case group versus 8.77% in the control group).

Vitamin C supplementation was associated with PROM, but not with preterm rupture of membranes. Prevention of PROM and preterm labor is key in decreasing the rate of PROM and increasing the pregnancy outcome.⁷ Therefore, it is important to maintain a leukocyte ascorbate concentration $>18\mu\text{g}/10^8$ cell as this concentration protects against PROM.⁶ Our data showed that vitamin C supplementation prevents PROM. Wideman *et al.* showed that women with PROM had lower maternal plasma concentration of vitamin C compared to women who did not have any PROM.⁸ Tejero *et al.* showed that leukocyte concentrations of vitamin C in women with PROM were significantly lower than those in the healthy women.⁴

Barret *et al.* did not find any relationship between low vitamin C in amniotic fluid and preterm rupture of membranes.⁹ The present study did not support the presumption that vitamin C supplementation prevents preterm rupture of membranes either. Further studies need to be conducted with larger sample sizes in order to assess the relationship between vitamin C supplementation and preterm rupture of membranes.

In conclusion, our data support the fact that vitamin C supplementation 100 mg/day prevents premature rupture of membranes.

Acknowledgement

The authors would like to thank the Research Affairs of Shiraz University of Medical Sciences for financial support.

Keywords: vitamin C; Premature rupture of membranes; Preterm delivery; Southern Iran.

Conflict of interest: None declared.

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Received: December 15, 2007 Accepted: July 15, 2008

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