REVIEW

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Antioxidant administration on the incidence of preterm premature rupture of membranes: a literature review

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ABSTRACT

One of the obstetric issues that can lead to consequences for both the mother and the unborn child is premature rupture of membranes (PROM). In Indonesia, 35% of pregnancies ended in preterm rupture of the membranes in 2013. The incidence of preterm pregnancy is 2% of all pregnancies, while the incidence of term pregnancy ranges from 6 to 19%. At 37 weeks gestation, the phrase "premature rupture of membranes" is used. Preterm premature rupture of membranes (PPROM) is the term used to describe when the membranes burst before birth in women whose gestational age is less than 37 weeks. It is believed that the pathophysiology of premature membrane rupture involves reactive oxygen species (ROS). The result of premature membrane rupture is anticipated to be impacted by antioxidant supplementation.

Keywords: Premature Rupture of Membranes, Antioxidant, Vitamin C.
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INTRODUCTION

The amniotic membrane rupturing before delivery is known as premature rupture of membranes (PROM). Under normal circumstances, the amniotic membrane breaks in the process of labor. Furthermore, rupturing the membranes before labor symptoms appear and waiting an hour before they do is known as premature rupture of the membranes. Premature rupture of membranes is used at ≥37 weeks of gestation. Preterm premature rupture of membrane (PPROM) is the term used to describe a rupture of the amniotic membrane before birth in a mother whose gestational age is less than 37 weeks.[1]

According to data from the World Health Organization (WHO), 70% of cases of premature rupture of membranes (PROM) occur in term pregnancies, with the frequency of PROM worldwide ranging from 5–10% of all births. A further 1% of cases are preterm. 30% of cases of preterm rupture result in preterm birth.[2] Between 4.5 and 6% of pregnancies in Indonesia result in PROM. The reported incidence of PROM in various Indonesian hospitals varies greatly; Sardjito Hospital has a 5.3% incidence, Hasan Sadikin Hospital has a 5.05% incidence, RSCM has an 11.22% incidence, Pringadi Hospital has a 2.27% incidence, and Kariadi Hospital has a 5.10% incidence.[3]

The cause of premature rupture is still unknown and has multifactorial dimensions. Infection is thought to be a predisposing factor for premature rupture of membranes, which can occur directly in the amniotic membrane or as an ascending infection of the vagina or cervix. In addition, things that are thought to be related to the occurrence of premature rupture of membranes include cervical incompetence, abnormalities of the amniotic membrane, fetal position abnormalities, pregnancy at the age of less than 20 years and more than 35 years, blood group factors, parity/multigravida factors, smoking, low socioeconomic conditions, antepartum hemorrhage, history of abortion and preterm birth, previous history of premature rupture of membranes, nutritional deficiencies during pregnancy such as copper or ascorbic acid deficiency, uterine overdistension, narrow pelvis, excessive maternal activity, and trauma obtained from sexual intercourse, internal examination, or amniocentesis.[1,4,5]

The risk ratio for antioxidant supplementation in these pregnancies was 0.95 (95% CI 0.66-1.3) for PROM and 0.87 (0.47-1.60) for PPROM, according to the study by Duckworth et al. When examined by single/multiple pregnancy subgroups, antioxidants had no discernible impact on either PROM or PPROM. Contrary to expectations, Spinato JA, et al. stated that vitamin C and E supplementation in this dose combination may be associated with an increased risk of PROM and PPROM.[6,7] Therefore, this study aims to antioxidant administration on the incidence of preterm premature rupture of membranes.

METHODS

The literature review approach was used to write this essay, which entailed looking for both domestic and foreign literature that was pertinent to the chosen study topic. Reputable sources like PubMed and ScienceDirect provided the data for

this study, which came from publications published between 2010 and 2024. Certain keywords were used to identify the articles, including "Antioxidant," "Vitamin C," "Vitamin E," "PPROM," and "Premature Rupture of Membranes." The quality and relevance of the selected articles were assessed based on inclusion and exclusion criteria. The inclusion criteria consisted of articles that were relevant to the keywords used in the search, and the relationship between oxidative stress, antioxidants (vitamin C, vitamin E), and the incidence of PPROM was discussed. The exclusion criteria were articles that did not provide full access to research content.

THE ROLE OF ANTIOXIDANTS IN THE PREMATURE RUPTURE OF MEMBRANES

Preterm and term pregnant women who experience premature membrane rupture are more likely to experience pregnancy problems. The mother, fetus, or newborn are all at risk of infection following membrane rupture. After premature rupture of the membranes for more than 24 hours, the risk of newborn infection rises to 3% to 5% if there is clinical chorioamnionitis.[8]

Each component of the chorioamnion, a multifaceted layer made up of supporting tissue and epithelial cells, plays a crucial function in metabolism, which is necessary for the physiological integrity of the developing fetus. Collagen gives the amnion its strength. Research is currently ongoing to determine how endogenous and external processes might degrade the embryonic membrane. Local membrane disruption is also caused by external causes, such as impacts from microbial, host, or nicotine-induced metabolism that lowers antiprotease activity, and endogenous factors, such as local differences in membrane thinning or collagen.[8]

A balance of intrinsic elements that control the synthesis and breakdown of connective tissue preserves the chorioamnion's strength and integrity. Matrix metalloproteinases regulate the chorioamnion's collagen breakdown. The release of matrix metalloproteinases is regulated by tissue inhibitors of metalloproteinases or TIMPS.[8]

Reactive oxygen species (ROS), which are unstable chemicals that are constantly produced in the body, are thought to cause tissue damage that results in PROM. Reactive oxygen species activity may represent a reversible pathophysiological route that might cause premature membrane rupture, according to a 2001 proposal by Woods et al. Reactive oxygen species produced by the body's reaction to different conditions including illness, smoking, bleeding, or cocaine use, they believed, may activate collagenolytic enzymes and eventually compromise the integrity of embryonic membranes.[9,10] It is believed that exposing the chorioamnion to ROS increases matrix metalloproteinases, which causes membranes to rupture too soon. The generation of ROS and their removal are typically balanced. When prooxidants outweigh antioxidants, oxidative stress results.[8,11]

To maintain cellular integrity in the face of constant exposure to oxidant stress, the use of antioxidants may be considered. Antioxidants and ROS have a relationship through direct interactions, functioning as reducing agents by donating electrons to stabilize them, by activating enzymatic degradation pathways, or by limiting cofactors or catalysts required for ROS formation.[12]

Several important antioxidants can be obtained from food sources, such as vitamin C and vitamin E. Vitamin C has been known to play an important role in maintaining the integrity of the membranes (layers) that envelop the fetus and amniotic fluid. Since humans are unable to produce vitamin C (ascorbic acid), which is water soluble, this vital nutrient must be received from the diet. As is well known, one of the antioxidants is vitamin C. To reduce tissue damage brought on by free radicals, the body employs a variety of antioxidants. Collagen production is directly stimulated by ascorbic acid. By transferring a hydrogen atom with its lone electron to ROS, ascorbic acid also acts as a reducing agent. Collagen is made strong and stable by ascorbic acid.[8,12,13]

One of vitamin C's functions is to deliver hydrogen atoms with their single electron to ROS in order to strengthen and stabilize collagen. Oxidative stress happens when prooxidants outweigh antioxidants, which can lead to the premature rupture of membranes.[8] The eight substances that makeup vitamin E, which is fat-soluble, are referred to as tocotrienols and tocopherols. The primary component of vitamin E, alpha-tocopherol, is also its most physiologically active form. Lipid peroxidation is halted by alpha-tocopherol, the primary antioxidant. It keeps the antioxidant in place by inserting its long lipophilic hydrocarbon chain firmly into the lipid bilayer. To prevent reactive species from rupturing lipid bonds in the peroxidation chain reaction, the hydroxyl group on its chromanol head supplies the electrons required to stabilize ROS.[12]

An RCT study conducted by Gungorduk et al. was conducted to examine the effect of vitamin C and vitamin E supplementation on the latent period after preterm premature rupture of membranes. The study found that the duration of the latent period increased significantly in the vitamin-supplemented group compared to the placebo group. The gestational age at delivery also increased dramatically in the vitamin C and E-supplemented group compared to the placebo group. This is thought to be due to the role of vitamins as antioxidants associated with collagen metabolism and important in maintaining the integrity of the chorioamniotic membrane.[14]

The strengths of this study are high clinical relevance and reliable literature sources. The topic is highly relevant to obstetric clinical practice, especially in managing PPROM cases. Most of the references were from indexed scientific journals (PubMed, Scopus, etc.). The weakness of this study is that it is not a primary study. Being a narrative literature review, this article did not include direct patient data or quantitative statistical analysis.

CONCLUSION

Vitamin C and vitamin E are two of the many significant antioxidants that are found in the diet. It has been established that vitamin C is crucial for preserving the integrity of the membranes (layers) enclosing the embryo and amniotic fluid. Collagen production is directly stimulated by ascorbic acid. By transferring a

hydrogen atom with its lone electron to ROS, ascorbic acid also acts as a reducing agent. Collagen is made strong and stable by ascorbic acid.

AUTHOR CONTRIBUTION

All authors have contributed substantially during the conception of the manuscript, gathering and analyzing related literature, drafting and revising the manuscript, giving final approval, and have agreed to be accountable.

CONFLICT OF INTEREST

All authors declare there is no conflict of interest.

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