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Review Article

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A Review on Correlation of Vitamin A and D in Hypertensive Disorder of Pregnancy: Current Concepts

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ABSTRACT

Vitamin A is essential for the health of the mother as well as for the health and development of the fetus. Vitamin A deficiency has affected 19 million pregnant women with the highest burden found in the WHO regions of Africa and South-East Asia. Vitamin A is available in multiple vitamin formulations for prenatal care in some countries. When provided alone, the compounds most commonly used are retinyl palmitate and retinyl acetate in tablet form or oil-based solutions. Hypertension is common in pregnancy and causes high maternal mortality. This includes gestational hypertension, preeclampsia, severe preeclampsia, and pregnancy with chronic hypertension. Preeclampsia is a high-mortality disease among the common complication of hypertensive disorder of pregnancy. in particular, severe preeclampsia possess a serious threat to the safety of mothers and children, and there are great difficulties in the treatment of hypertensive disorders of pregnancy during clinical work. therefore, we are adequate in dealing with hypertensive disorders of pregnancy. Any adverse pregnancy outcomes associated with hypovitaminosis D should be accessed through the perspective of immune dysregulation both at the systemic and placental levels. It signifies the supplementation of vitamin D in pregnancy have a role in the improvement of maternal hypertensive complication and improve the fetal outcome.

Key-words: Hypovitaminosis D, Preeclampsia, PIHs, Severe Preeclampsia, Vitamin A, D

INTRODUCTION

Vitamin A deficiency also remains a public health problem among women, affecting an estimated 19 million pregnant women [1], with the highest burden found in the WHO regions of Africa and South-East Asia. During pregnancy, vitamin A is essential for the health of the mother as well as for the health and development of the fetus. This is because vitamin A is important for cell division, fetal organ and skeletal growth and maturation, maintenance of the immune system to strengthen defences against infection, and development of vision in the fetus as well as maintenance of maternal eye health and night vision [2,3].

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Thus, there is an increased need for vitamin A during pregnancy, although the additional amount required is small and the increased requirement is limited to the third trimester. Dietary sources of provitamin A include vegetables such as carrot, pumpkin, papaya, and red palm oil; animal foods rich in preformed vitamin A include dairy products (whole milk, yoghurt, cheese), liver, fish oils and human milk [3]. Scope and purpose Background WHO Guideline [3] Vitamin A supplementation in pregnant women Although pregnant women are susceptible to vitamin A deficiency throughout gestation, deficiency is most common in the third trimester due to accelerated fetal development and the physiological increase in blood volume during this period [4,5]. In a pregnant woman with moderate vitamin A deficiency, the fetus can still obtain sufficient vitamin A to develop appropriately, but at the expense of the maternal vitamin A stores. Vitamin A deficiency may also occur during periods when infectious disease rates are high and/or during seasons when food sources rich in

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vitamin A are low [6]. The prevalence of night blindness (a consequence of vitamin A deficiency) is also more common in the third trimester of pregnancy, and populations with a prevalence ≥5% are considered to have a significant public health problem of vitamin A deficiency [1,7]. It is currently estimated that 9.8 million pregnant women are affected by night blindness worldwide [1]. One study has suggested that 12 weeks of supplementation is needed to prevent a decline in serum retinol levels. Vitamin A is available in multiple vitamin formulations for prenatal care in some countries. When provided alone, the compounds most commonly used are retinyl palmitate and retinyl acetate in tablet form or oil-based solutions. Alternative forms of delivery include fish liver oils, β-carotene, and a combination of β-carotene and vitamin A. Recommended doses of vitamin A supplements are generally well tolerated by pregnant women [8,9]. βcarotene, a precursor of vitamin A, may be preferred over vitamin A supplements in pregnant women because excess of β-carotene is not known to cause birth defects.

Vitamin D3 (cholecalciferol) is naturally obtained through sunlight in the ultraviolet B (UVB) range of 290– 315 nm, through a membrane-enhanced thermal-dependent isomerization reaction, which results in 7-dehydrocholesterol conversion into vitamin D3, which then diffuses into the circulation through the capillary bed [10] and into circulation reversibly bound to the vitamin D binding protein (VDBP). In serum, the vast majority of vitamin D metabolites bind preferentially to VDBP, but they are also known to associate with serum albumin [10].

The teleological purpose of ongoing pregnancy is to fulfil its fundamental role of a successful, uncomplicated delivery, in conjunction with an optimal intrauterine environment for the developing fetus [11]. Vitamin D homeostasis during pregnancy is adapted to meet both these demands, first by stimulation of calcium absorption for adequate intrauterine bone mineral accrual of the fetus that substantially increases in the last trimester of pregnancy, and second, by enhancing systemic and local maternal tolerance to paternal and fetal alloantigens [12].

Pregnancy is characterized by three major adaptations in vitamin D homeostasis: a) an increase in maternal calcitriol, b) maternal 25(OH)D availability for optimal neonatal 25(OH)D status, and c) an increase in maternal VDBP concentrations. These changes are evident at both the systemic circulation and the placental level, suggesting that the placenta is the major site of vitamin D metabolism in pregnancy.

Review of Vitamin D and Hypertensive Disorders of Pregnancy- This narrative systematic review evaluates growing evidence of an association between low maternal vitamin D status and increased risk of hypertensive disorders. The inclusion of interventional, observational, and dietary studies on vitamin D and all hypertensive disorders of pregnancy is a novel aspect of this review, providing a unique contribution to an intensively-researched area that still lacks a definitive conclusion. To date, trial evidence supports a protective effect of combined vitamin D and calcium supplementation against preeclampsia [13]. Conflicting data for an association of vitamin D with gestational hypertensive disorders in observational studies arises from several sources, including large heterogeneity between study designs, lack of adherence to standardized perinatal outcome definitions, variable quality of analytical data for 25-hydroxyvitamin D (25(OH)D), and inconsistent data reporting of vitamin D status. While the evidence does appear to lean towards an increased risk of gestational hypertensive disorders at 25(OH)D concentrations <50 nmol/L, caution should be exercised with dosing in trials, given the lack of data on long-term safety. The possibility that a fairly narrow target range for circulating 25(OH)D for the achievement of clinically-relevant improvements requires further exploration. As hypertension alone, and not preeclampsia specifically, limits intrauterine growth, evaluation of the relationship between vitamin D status and all terms of hypertension in pregnancy is a clinically relevant area for research and should be prioritized in future randomized trials [13].

Vitamin A supplementation during pregnancy for maternal and newborn health outcomes- Vitamin A is a fat-soluble vitamin found in the liver, kidney, eggs, and dairy produce. Low dietary fat intake or intestinal infections may interfere with the absorption of vitamin A. Natural retinoids are required for a wide range of biological processes including vision, immune function, bone metabolism and blood production. In pregnancy, extra vitamin A may be required. Currently, the World Health Organization (WHO) and other international

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agencies recommend routine vitamin A supplementation during pregnancy or at any time during lactation in areas with endemic vitamin A deficiency (where night blindness occurs) [14].

It has been suggested that a low intake of vitamin A may be associated with complications in pregnancy such as the death of the mother or baby, increased infections for the mother or baby, low iron level for the mother or baby or having a baby with any of the following complications: early delivery, low birth weight or a congenital abnormality [14].

This review included 19 studies involving over 310,000 women. Seven trials were conducted in Africa, six in Indonesia, two in Bangladesh, and one each in Nepal, China, India, UK and USA. Most of the trials were conducted in populations considered to be vitamin A deficient (except USA and UK). The overall risk of bias was low to unclear in most of the trials, and the body of evidence was moderate to high quality. The findings indicate that routine supplementation with vitamin A (either alone or in combination with other supplements) during pregnancy did not reduce mother or newborn baby deaths. There is good evidence that antenatal vitamin Vitamin A supplementation during pregnancy for maternal and newborn outcomes, who live in areas. where vitamin A deficiency is common or who are HIV positive. The trials published so far did not report any side effects or adverse events. The available evidence suggests a reduction in maternal infection but these data are not of high quality and further trials would be needed to confirm or refute this [14].

Taking vitamin, A supplements during pregnancy does not help to prevent maternal deaths (related to pregnancy) or perinatal or newborn baby deaths. Taking vitamin, A supplements during pregnancy does not help to prevent other problems that can occur such as stillbirth, preterm birth, low birth weight of babies or newborn babies with anaemia. However, the risk of maternal anaemia, maternal infection and maternal night blindness is reduced [14].

Clinical observation indicators

Early prenatal follow-up and clinical problem of parturients- Prenatal examination of pregnant women in severe prenatal period should be strictly observed, such as interval time of prenatal examination, whether high salt diet, high fat diet, high sugar diet, weight change, oedema change, blood pressure fluctuation and self-change of urine and eggs; if pregnant women with severe preeclampsia find oedema, excessive weight gain, pre-hypertension change and low protein. Haemorrhage, lack of Vit A and D are warning signs of early-onset severe preeclampsia. Early Warning Information Should be Strengthened through Systematic Monitoring [12].

Monitoring and observation of pregnant women

- Demographic characteristics of pregnant and admitted women: age, number of pregnancies and births, family history, and past history of eclampsia [11].
- Continuous ambulatory blood pressure at admission, blood pressure changes and control, prenatal examination, termination of gestational weeks, perinatal condition, and general oedema of pregnant women [12].
- laboratory examination: blood routine (platelet count), urine routine (urine protein, 24-hour urine protein) to record 24-hour volume, electrolyte, liver function (serum high-density lipoprotein), serum total bilirubin, Indirect bilirubin, direct bilirubin, renal function test (uric acid, creatinine, urea), coagulation disorder and vitamin A and D serum levels, thyroid stimulating hormone (TSH), free triiodothyronine (FT3) [12] and free thyroid (FT4) were measured every 2 days. The changes in urinary protein and 24-hour urinary protein were examined. Color Doppler Ultrasound and Abdomine, Urinary System, Echocardiography, Understanding, whether there is Chest and Abdominal fluid or effusion, umbilical artery S/D [11,12].

Clinical Indicators of Observation- The fetal heart rate was monitored daily, the number of fetal movements was counted, and the changes in S/D value were observed by ultrasound every week. Amniotic fluid volume, placental maturity, placental abruption, intrauterine fetal death, etc. Complications were observed [13]. To observe the occurrence of placental abruption, heart, liver and kidney failure, pulmonary oedema, cerebral haemorrhage, persistent headache and upper abdominal pain, visual loss, or retinal detachment during pregnancy, and further decrease of platelet count leading to clinical complications such as HELLP syndrome, eclampsia, DIC and postpartum haemorrhage. Clinically, it is necessary to observe the birth weight, Apgar score and respiratory rate of early-

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onset neonates after delivery. Premature birth, neonatal respiratory distress syndrome, neonatal hypoxic-ischemic encephalopathy, neonatal death, neonatal rescue, transfer to the neonatal department, etc [14].

Treatment- Conventional interventions in the treatment of severe preeclampsia include restriction of activity, encouragement of left lateral position, restriction of sodium intake, vitamin supplementation, calcium supplementation, appropriate high-protein diet, sedation and so on. the magnesium sulfate injection loading dose was given, and 25% magnesium sulfate 16ml was added to 5% glucose injection 100 ml for intravenous drip within 30 minutes [15], and then 25% magnesium sulfate 60 ml was given for micro pump at the speed of 2 g/hr. the daily dose of magnesium sulfate 25 g was used for 48 hours. according to the blood pressure, 100 mg labetalol tid and 30 mg qid of nifedipine controlled release tablets were taken orally. During the treatment period, the blood pressure of the patients was observed strictly, and the drug dosage was adjusted whenever an abnormality was found. According to the 8th edition of Obstetrics and Gynecology, the target range of blood pressure control for patients with stage I hypertension was pointed out [16].

(1) Systolic and diastolic blood pressures should be controlled at 130-155 mmHg and diastolic pressure was no organ dysfunction in pregnant women.

(2) Systolic blood pressure control should be controlled in pregnant women with clinical complications of organ dysfunction. Total 130-139 mmHg, diastolic blood pressure control range 80-89 mmHg. strict blood pressure reduction should not be less than 120/80 mmHg [17].

Monitoring of severe preeclampsia: the common clinical fetal monitoring mainly monitors the fetal umbilical blood circulation, so there is more blood flow in the fetal umbilical artery. umbilical artery blood flow is the most sensitive. when severe preeclampsia occurs in pregnancy [18], the umbilical artery and umbilical vein contraction are obvious eventually leading to fetal placental circulation resistance, s/d ratio increased and ultimately fetal intrauterine hypoxia more sensitive. related research data show that there is statistical significance in the incidence of FGR. Routine examination of umbilical artery blood flow by doppler ultrasound is clinically routine to assist diagnosis and reflect in the uterus during severe preeclampsia. detection and treatment of fetal conditions, such as fetal ischemia, hypoxia, and fetal distress, can greatly improve the survival rate of pregnant women and perinatal babies [19].

Indications for termination of pregnancy [15-20]

1. If unstable blood pressure control occurs in the course of treatment, it will fluctuate greatly.
2. Proteinemia with massive pleural and pericardial effusion.
3. Heart failure, liver, and kidney failure
4. Continuous decrease of amniotic fluid with the frequent late deceleration of fetal heart rate revealed by fetal heart rate monitoring
5. Continuous decrease of platelets, intravascular hemolysis, jaundice, and hemoglobinuria.
6. Severe fundus haemorrhage with ICP
7. Occurrence of preeclampsia convulsion.

Selection of delivery process in early-onset and late-onset severe preeclampsia- Termination of pregnancy is the most effective method to treat preeclampsia and severe preeclampsia. The choice of delivery mode depends on the condition of the mother and infant, age and cervix. Cesarean section is the most common choice for the termination of pregnancy. Relevant domestic research data show that the mode of termination of pregnancy in severe preeclampsia has changed significantly from 1977 to 2010 [20,21]. The natural delivery rate in the early stage of pregnancy decreases year by year and the cesarean section rate increases year by year. However, the cesarean section rate in the early stage of pregnancy is higher than that in late-onset severe preeclampsia. The main termination mode of early-onset severe preeclampsia at the end of the 20th century is induced labour. The main reason is as flows: insufficient prenatal examination consciousness of pregnant women and no treatment of preeclampsia so the survival rate of perinatal infants delivered before 32 weeks is low, so most of them choose to abandon the fetus [22]. With the development of medical research, they have enough knowledge about the treatment of severe preeclampsia and expect that after 34 weeks of treatment, the survival rate of perinatal infants will increase significantly, and cesarean section will become the main mode of delivery. Regardless of the choice of delivery mode, if the preeclampsia, the more serious the disease, the worse the prognosis. higher the rate of birth

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of non-viable infants. Therefore, according to the situation of the pregnant women, the choice is based on the situation of the pregnant and themselves [17,19,21].

Prognosis of Severe Pre-Eclampsia- Vitamin D during pregnancy manifests significant changes, to meet optimal embryonic developmental and immune regulation of the ongoing pregnancy. Specifically, significant increases in maternal serum calcitriol without changes in serum 25(OH) D or calcium concentrations are evident in conjunction with the dependence of neonatal vitamin D stores [22,23]. On that basis, any adverse pregnancy outcomes associated with hypovitaminosis D should be accessed through the perspective of immune dysregulation both at the systemic and placental levels. it signifies the supplementation of vitamin D in pregnancy have the role for the improvement of maternal hypertensive complication and improving the fetal outcome [23,24].

CONCLUSIONS

This review has successfully evaluated the association between low maternal vitamin D status and increased risk of hypertensive disorders. It has concluded that pregnant women in severe prenatal period should be strictly observed, such as interval time of prenatal examination, whether high salt diet, high fat diet, high sugar diet, weight change, oedema change, blood pressure fluctuation and self-change of urine and eggs; if pregnant women with severe preeclampsia find oedema, excessive weight gain, pre-hypertension change and low protein. Haemorrhage and lack of Vit A and D are warning signs of early onset severe pre-eclampsia. Early Warning Information Should be Strengthened through Systematic Monitoring. The review discussed the Indications for the termination of pregnancy effectively and also concluded Vitamin D therapy during pregnancy manifests significant changes, to meet optimal embryonic developmental and immune regulation of the ongoing pregnancy.

CONTRIBUTION OF AUTHORS

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