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EFFECTS OF VITAMIN A IN HYPERTENSIVE DISORDER OF PREGNANCY

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ABSTRACT

Objective: To evaluate effects of the serum level of vitamin A in hypertensive disorder of pregnancy, on maternal and newborn and their clinical outcomes. **Material and Methods:** A prospective cohort study. All total 958 pregnant women, admitted in obstetrics and gynecology department of first Affiliated Hospital of Dali University in Yunnan province from June 2017 to May 2018 included in study group who fulfilling the inclusion criteria. All the pregnant women selected randomly between the age 22 to 35 years and divided into four group. In the control group (normal pregnancy) 501 cases, 151 cases in GH Group, 126 cases in preeclampsia group, 180 cases of severe preeclampsia group. serum vitamin A detected by liquid chromatography-tandem mass spectrometry(LC-MS/MS). the data were statistically analyzed. the difference were Statistically significant at $p<0.05$. **Result:** There was no statistically significant difference in the results of all studies on maternal age, parity, BMI, and gestational weeks in the third trimester ($p>0.05$). There was no significant difference between the GH group and the control group ($p >0.5$). There is significant difference between preeclampsia group and severe preeclampsia group($p<0.05$). There is significant difference in vitamin A deficiency between the control group, the GH group, when vitamin A was severely deficient, the proportions of severe preeclampsia, preeclampsia, gestational hypertension and control group were 60.0%, 56.0%, 36.4%, and 0.4%, respectively, and the difference was statistically significant ($p<0.05$). There was no significant difference in cesarean section rate and spontaneous birth rate between gestational hypertension group and preeclampsia group ($p>0.05$). when the third trimester serum vitamin A<0.2mg/L vs. ≥ 0.2mg/L, the risk of preeclampsia group and severe preeclampsia group increased by 1 and 2 times respectively, the difference was statistically significant ($p<0.05$). the risk of severe preeclampsia was increased by 3 times, and the difference was statistically significant ($p<0.05$). risk of preeclampsia no increase, the difference was not statistically significant ($p>0.05$). **Conclusion:** The content of vitamin A is related to the occurrence of hypertensive disorders of pregnancy. The deficiency of vitamin A increase the risk of severe preeclampsia risk increased. Detection of serum levels of vitamin A during pregnancy can help predict Gestational hypertension.

KEYWORDS: vitamin A, gestational hypertension, preeclampsia.

INTRODUCTION

Hypertension is not unusual during pregnancy. Usually before delivery and pregnant women may have higher than normal blood pressure values. Preeclampsia, observed in 2%-8% of pregnancies, can be defined as hypertension accompanied by proteinuria, which usually occurs during the second half of pregnancy.[1]

The diagnosis of preeclampsia involves both proteinuria and pregnancy induced hypertension, according to the criteria of the American College of Obstetricians and Gynecologists.[2] Usually, preeclampsia starts after 20 weeks of gestation and is characterized by high blood pressure (140/90 mmHg) and proteinuria, that is, 300mg or more of protein in a 24-hour urine specimen collected from previously nonproteinuric, normotensive women.[3]

The pathophysiology of preeclampsia during pregnancy is not clear, but many pathophysiological elements may exist, such as inflammation, dyslipidemia, cytokine production.[4] oxidative stress[5] and elevated homocysteine. an imbalance between prostacyclin and thromboxane is involved in the etiology of preeclampsia[4] incomplete infiltration of trophoblasts of the uterine spiral artery that leads to placental ischemia, which finally releases inflammatory factors, immune cell activation and endothelial dysfunction.[6] It is also related to oxidative stress (OS)[7]; because pregnancy will increase OS, it results in large circulating reactive oxygen species (ROS) and reactive nitrogen species (RNS) increase.[8] Therefore, enhancing antioxidant capacity is the way to overcome OS during pregnancy. vitamin A is an essential fat-soluble micronutrient, which has the highest antioxidant potential among all

vitamins.[9,10] vitamins A is essential micronutrients, which play a vital role in maternal health and fetal development.[11] Some studies have shown that the levels of vitamin A low in PE.[12,13]

Preeclampsia can cause fetal growth restriction, preterm delivery, and maternal and infant morbidity and mortality[14], as well as an increased risk of having infants who are born prematurely with a risk of complications.[15] In a preeclamptic mother, the chances of cardiovascular diseases such as ischemic heart disease, chronic hypertension, and stroke increase later in life[16], while children born from preeclamptic pregnancies have an increased risk of metabolic syndrome, coronary heart disease, and stroke in the adult life.[17] Further, they are at a higher risk for a variety of disorders such as endocrine and nutritional disorders throughout adolescence.[18]

Disparate studies have investigated the association between the risk of preeclampsia and maternal oxidative stress. In preeclampsia, there is an imbalance between antioxidant defenses and pro-oxidant production[14], but it remains unknown whether an imbalance between antioxidants and pro-oxidants leads to preeclampsia or occurs after preeclampsia.[4] It has been reported that an imbalance between the antioxidants defense system and free radical production may plays a major role in the pathogenesis of preeclampsia.[4,5] Furthermore several experimental studies have reported an association between the high intake of dietary antioxidants (e.g. vitamin E, copper and selenium) and low levels of oxidant stress.[4] Many studies have approved that the maternal diet is significantly associated with the development of preeclampsia.

A meta-analysis showed that oral supplementation with antioxidants did not show effects in the prevention of preeclampsia.[19] Therefore, this study was designed to evaluate whether low intake of dietary antioxidants (vitamin A) is a risk factor of preeclampsia In pregnant women. we aimed to identify whether the daily intake of dietary factors such as macronutrients and micronutrients could contribute to the development of preeclampsia to design an effective educational program, in corporation with concerned stake holders who target women at risk of preeclampsia before conception. We hypothesized that low intake of antioxidants and high intake of saturated fats are associated with preeclampsia in pregnant women.

METHOD AND MATERIAL

Procedure

Sample were collected randomly from JUNE 2017 to MAY 2018 in the first affiliated Hospital of Dali University, Yunnan province. all total of 958 hospitalized pregnant women, age < 35 years old and 32 to 38 weeks of gestation. previously normotensive and nonproteinuric, were included in the study as controls**.** Women who had certain medical conditions including type 1 diabetes, type 2 diabetes, dyslipidemia, cardiovascular disease, thyroid dis ease, and celiac disease, and those who were previously diagnosed with preeclampsia were excluded from the study. A total of 958 pregnant women, admitted in obstetrics and gynecology department were taken. Study group(457) - Gestational Hypertensive Group(151), preeclampsia group(126), severe preeclampsia group(180). The control group comprised of pregnant women without hypertension (501). Cases were selected after high blood pressure was confirmed by systolic blood pressure measurements >140 mmHg or diastolic blood pressure >90 mmHg on two different occasions with an interval of 4 or more hours accompanied by a protein concentration of +1. Approxi mately all preeclamptic women were admitted to the department of obstetrics in the hospital and remained in the hospital under good medical management. Pre eclamptic pregnant women, in their last weeks of preg nancy, were referred to the delivery department. The blood pressure for all women was measured in the sitting position after a ten-minute rest period using a wall mounted blood pressure device. The blood pressure for all women was measured in the sitting position after a ten-minute rest period using a wall mounted blood pressure devic. Two ml of venous blood was used to estimate serum vitamin A levels. Vitamin A level in each group was detected by liquid chromatography-tandem mass spectrometry(LC-MS/MS) with high performance liquid chromatography (HPLC). Patients were categorised according to level of serum vitamin A and severity of Gestational hypertension.

Diagnostic Criteria

Vitamin A
Normal: 0.3-0.7mg/L
Elevated: >0.7mg/L
Deficiency: 0.3mg/L

Ethical considerations

All participants were informed about the study and asked to participate. The objectives, benefits, and the protocol of the study were briefly explained by the main researcher. After agreement, they were asked to sign a consent form. This protocol met the criteria set by the clinical trial & scientific research committee. The approval was also taken to facilitate the researcher's tasks such as filling out the questionnaire and interviewing the participants.

Statistical analysis

Using Excel 2014 to collect statistics on all data to establish a database, SPSs21.0 software used for statistical analysis and processing. The independent-t test, pearson chi-square test is used. The rate of counting data (%) indicates that the $p<0.05$ is statistically significant in the use of the chi-square test. Use multi-factor logistic regression analysis.

RESULT

1. General Information

Total of 958 pregnant women were included in the study, the basic information of the research object was expressed by $\bar{x}\pm s$, and the difference between the groups was compared by variance analysis.

Table 1: Demographic characteristics of pregnant women.

Group	Number of patients(n)	Age(y)	Parity	BMI(kg/m2)	Blood Collection Pregnancy Week(w)
Control	501	35.89 ±2	2.07±0.88	21.55±1.37	34.13±1.02
Gestational hypertension	151	34.76 ±2	1.90±0.86	21.63±1.38	34.03±1.10
preeclampsia	126	32.60 ±2	1.98±0.78	20.78±1.39	34.20±1.03
Severe preeclampsia	180	34.88 ±2	2.05±0.92	22.65±1.40	34.39±1.14
F		2.49	0.25	0.98	0.69
P		>0.05	>0.05	>0.05	>0.05

The results showed no significant difference in the age, parity, body mass index (BMI) and pregnancy week average of pregnant women (P>0.05) between the groups (see table 1.)

Table 2: Analysis of Vit.A and hypertensive disorder of pregnancy.

Group	N	VitAmg /L
Control	501	0.4016 ± 0.1670
Gestational hypertension	151	0.3706 ±0.1787
preeclampsia	126	0.2170 ±0.1037
Severe preeclampsia	180	0.1130 ± 0.0105

The VitA contents of control group, Gestational Hypertensive group, preeclampsia group and severe preeclampsia were 0.4016±0.1670, 0.3706±0.1787, 0.2170±0.1037 and 0.1130±0.0105 respectively: There was a continuous decline in VitA content in hypertensive diseases during pregnancy, and comparisons found that there was no statistically significant difference in the content of the Gestational hypertensive group during pregnancy compared with that in the control group (t=1.9615, P=0.0502) (P>0.05). while the content of VitA was significantly decreased among the preeclampsia, and severe preeclampsia. There was a statistically significant difference between preeclampsia and severe preeclampsia group (t=13.3665, P=0.000) (P<0.05) (table2).

Table 3: Relation of Vit A content during pregnancy and gestational hypertension.

Group	N	Normal N %	Mild deficiency N %	Severe deficiency N %
Control	501	496 99.0	3 0.6	2 0.4
Gestational hypertension	151	10 7.0	86 57.0	55 36.4
preeclampsia	126	10 8.0	45 36.0	71 56.0
Severe preeclampsia	180	5 2.8	67 37.2	108 60.0

serum vit A levels were classified according to literature standards.vit A was normal (0.3< vit A <0.7mg/L). There was a statistically significant difference in the deficiency rate of VitA in the mild deficiency (0.2<vitA< 0.3mg) and severe deficiency (vitA<0.2mg/L). control group, the Gestational hypertensive group, the preeclampsia group and the severe preeclampsia group (x2=840.717, P= 0.000) P<0.05., and the difference of VitA deficiency rate between the preeclampsia group and the severe preeclampsia group was statistically significant (X2=4.302, P=0.038) P<0.05; When VitA was severely deficient, the proportion of severe preeclampsia was 60.0%, the preeclampsia group was 56%, the gestational hypertension group was 36.4%, and the control group was the smallest (0.4%). and the control group accounted for the largest proportion of 99%, while the Gestational hypertension group was 7%, the preeclampsia group was 8%, and the proportion of severe preeclampsia group was the smallest 2.8%. (table 3.)

Table 4: Incidence risk assessment for serum vitA <0.2mg/L compared with ≥0.2mg/L.

Group	When less(<0.2mg/L) B P OR 95%CI	When more (≥ 0.2mg/L) B P OR 95%CI
Control	Reference	Reference
preeclampsia	1.27 0.009 1.46 1.14-7.42	1.82 0.103 1.45 0.20-21.53
Severe preeclampsia	1.49 0.010 2.14 1.44-10.22	1.75 0.021 3.18 1.34-20.09

When serum Vit A < 0.2mg/L in the third trimester of pregnancy is relative to ≥0.2mg/L, preeclampsia group and severe preeclampsia group. The risk of preeclampsia group increased by 1 and 2 times respectively, and the difference was statistically significant (OR value was 1.46,95% CI 1.14-7.42; OR 2. 14,95% CI 1.44 10.22; The risk of severe preeclampsia increased three times after Multivariate Logistic Regression Analysis to Control Pregnant Women age, gestational age, BMI and gestational week (P < 0.05) (OR value 3.18, 95% CI 1.34-20.09), but the risk of preeclampsia did not increase (P > 0.05) (OR value 1.45, 95% CI 0.20-21.53) (see Table 4.)

DISCUSSION

1. Relationship between Vitamin A and hypertensive disorder of pregnancy:

VitaminA is transformed from all trans retinol in normal physiology, and Vitamin A affects physiological processes such as bone growth, regeneration and embryonic formation.

The relationship between Vitamin A and the occurrence and development of hypertension in pregnancy has been paid more attention, and a number of studies have confirmed the correlation between them. Kolusaril[20] study of 250 patients with hypertension in pregnancy found that the control group (normal pregnancy) serum Vitamin A and its precursor beta-carotene value in pregnancy during the starting period were significantly higher than the disease group. In this experiment, it was found that Vitamin A content showed a continuous decline in hypertensive diseases during pregnancy, and the comparison found that there was no statistically significant difference in the content of the GH group compared with that in the control group (P>0.05), while the content of Vitamin A was significantly decreased among the rest of the groups. There was a statistically significant difference between the preeclampsia group and the severe preeclampsia group, and the results suggested that Vitamin A content may be related to the occurrence of hypertensive diseases during pregnancy. This experiment further studied the changes of hypertension and Vitamin A content in pregnancy, and found that there were significant differences in the deficiency rate of Vitamin A in the control group, GH group, preeclampsia group and severe preeclampsia group (P<0.05). The proportion of Vitamin A deficiency in patients with hypertension was different in different degrees. When serum Vitamin A was ≤ 0.2mg/l (severe deficiency), the proportion of severe preeclampsia group > preeclampsia Group > gestational hypertension group, considering the severity of hypertension in pregnancy may be closely related to the deficiency of Vitamin A. it is speculated that serious deficiency can increase the risk of severe preeclampsia. The results of this experiment show that Vitamin A content may be correlated with the occurrence and progression of hypertension in pregnancy, which is one of the most important pathogenic factors in hypertensive disorder pregnancy.[21,20]

Currently, the WHO recommends routine vitamin A supplementation during pregnancy or at any time during lactation in areas with endemic vitamin A deficiency (where night blindness occurs) (WHO 1998). The principal forms used as nutritional supplements are vitamin A palmitate (retinyl palmitate) and vitamin A acetate (retinyl acetate), but carotenoids (most commonly betacarotene) and retinoids (retinol, retinal, retinoic acid) can also be used as nutritional supplements (DRI 2001).[22]

In future role of vitamin A may more useful, to manage normal pregnancy to reduce multiple complications in patients with hypertensive disorder of pregnancy like anemia, postpartum hemorrhage, cesarean section, etc. and neonatal complications like intrauterine fetal distress, growth restriction, gestational weight, etc.) The incidence of both has positive and significant.

CONCLUSION

1. The contents of vitamin A is related to the occurrence of hypertensive disorder of pregnancy.
2. The deficiency of vitamin A have correlation with occurrence and progression of hypertensive disorder of pregnancy but severe deficiency of vitA increase the risk of severe preeclampsia. the vitA level of blood serum in third trimester of pregnancy <0.2mg/L, increased risk for both preeclampsia and severe preeclampsia.
3. serum level of vitA during pregnancy can help in predicting pregnancy induced hypertension.

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