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Case report

Ozone in Preeclampsia of pregnancy. Case report.

Ozono en preclamsia del embarazo. Reporte de caso

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Keywords

preeclampsia, hypertension, ozone therapy, pregnancy, mayor autohemotherapy, gestosis, Diastolic blood pressure, systolic blood pressur.

Abstract

Preeclampsia is a common pregnancy disorder with important short-term complications for mother and baby. Evidence suggests preeclampsia also has implications for the mother beyond pregnancy, as well as long-term effects on offspring health. The objective of the present study is to determine the effect of ozone therapy administered in form of mayor autohemotherapy in hypertensive pregnant women at her 18th week gestation. Prescribed regular antihypertensive drugs were maintained. The application of ozone significantly ($p<0.05$) improved tensional figures and a significant dose reduction of the regular antihypertensive therapy was achieved. No side-effects were observed during the study. This study confirms and adds strong evidence that ozone therapy is an effective and safe method of treating hypertensive disorders during pregnancy preeclampsia...

Palabras clave

Preclampsia, hipertensión, ozonoterapia, embarazo, autohemoterapia mayor, gestosis, Presión arterial diastólica, Presión arterial sistólica.

Resumen

La preclampsia es un trastorno del embarazo frecuente con importantes complicaciones a corto plazo para la madre y el bebé. La evidencia sugiere que la preeclampsia también tiene implicaciones para la salud de la madre y no solo es un riesgo para el embarazo, así como los efectos a largo plazo en la salud de la descendencia. El objetivo del presente estudio es determinar el efecto de la ozonoterapia administrada en forma de autohemoterapia mayor en mujeres hipertensas embarazadas a las 18 semanas de gestación. Se mantuvieron medicamentos antihipertensivos regulares prescritos. La aplicación de ozono mejoró significativamente las cifras tensionales y se logró una reducción significativa ($p<0.05$) de la dosis de la terapia antihipertensiva regular. No se observaron efectos secundarios durante el estudio. Este estudio confirma y agrega una fuerte evidencia de que la ozonoterapia es un método efectivo y seguro para tratar los trastornos hipertensivos durante la preeclamsia durante el embarazo

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Introduction

Preeclampsia is a serious condition of pregnancy and can be particularly dangerous because many of the signs are silent and high blood pressure is one of an important sign of it. The disease is sometimes referred to as a silent killer because most people can't "feel" their blood pressure going up. As a result, patient awareness of the warning signs is one of the most important tools we have to successfully help women receive the care they need.

Ozone therapy in obstetrics has a beneficial influence on the clinical course of preeclampsia and hypertension diseases during pregnancy and fetoplacental insufficiency, reduces the risk of intrauterine fetal infection and a risk of pregnancy complications associated with fatness, improving the prognosis of these diseases.[1-3]

Preeclampsia is a multi-organ functional insufficiency syndrome. The abbreviation EPH reflect its fundamental symptoms, edema, proteinuria and hypertension. The gestosis develops because of the non-correspondence of the adaptive possibilities of the mother's organism to adequately supply the requirements of the developing fetus and is carried out through disorders of the perfusion capacity-diffusion of the placenta.[4,5]

One of the main hypotheses about the appearance of gestosis is the immunological, the hyper reaction of the mother to the antigens of the fetus that are incorporated into its bloodstream. The formation and deposition of autoimmune complexes in the placenta and in the kidneys leads to vascular spasm and the development of hypertension.[6,7]

Vascular spasm and hypertension enable the development of tissue ischemia, hypoxia, the accumulation of mucosaccharides, the strengthening of the permeability of capillary walls, the passage of proteins to tissues, disorders in osmotic pressure and the appearance of edemas. All this makes possible the damage to vital organs: the kidneys, the liver and the encephalon, and leads in severe cases to convulsions, coma and internal hemorrhages in the brain.[7]

In gestosis progressively worsens the uterine-placental blood circulation, ischemia and metabolic acidosis appear, which in turn causes intrauterine hypoxia that results in hypotrophy, life threatening and even death of the fetus.[8]

The placenta is the primary site of exchange between the mother and her fetus. Its major function is to provide diffusion of foodstuffs and oxygen from the mother's blood into the fetus blood and diffusion of excretory products from the fetus back into the mother.[2,3,8]

The administration of ozone therapy at minimal therapeutic concentrations of ozone to patients with preeclampsia, enables the dynamic balance of the LOP and the processes that occur in the antioxidant system, increases the capacity for the deformation of erythrocytes, improves microcirculation and exchange capillary. Optimization of oxygen metabolism and exchange processes, normalization of tissue metabolism is observed.[9]

The objective of the present study is to determine the effect of ozone therapy administered in form of mayor autohemotherapy in hypertensive pregnant women at her 18th week gestation.

Description of Case

A 33-year-old pregnant woman, gravid 2 para 2, presented with hypertension and proteinuria at 18 weeks of gestation. She had a history of preeclampsia in her first pregnancy six years ago. During that pregnancy, at 20th weeks of gestation, she developed high blood pressure and proteinuria. She was hospitalized since week 28th and eventually delivered by emergency caesarean section at week 34th. Blood pressure returned to normal post-partum and she received no further medical follow-up. She had thyroid cancer at age 8. Family history was remarkable for her mother's side diagnosis of hypertension in her fifth decade. Her father is battling with colon cancer and sister has had history of preeclampsia. She did not smoke nor drink any alcohol. She was not taking any regular medications, health products, or herbs. Symptomatology: Severe headaches, upper and lower abdominal pain, nausea, vomiting and dizziness, oliguria, sudden weight gain, edema in lower extremities.

At 18 weeks of gestation, blood pressure was found to be elevated at 140/100 mm. Hg. during a routine antenatal clinic visit. She reported severe headaches, upper and lower abdominal pain, nausea, vomiting and dizziness, decreased urine output, sudden weight gain and edema in lower extremities. On physical examination: pulse 89/min, regular, normal volume, all peripheral pulses felt. Body mass index was 34.9 kg/m2 obesity III, B/L pedal edema +. Heart sounds were normal, and there were no signs suggestive of congestive heart failure. Radial-femoral pulses were congruent, and there were no audible renal bruits.

Baseline laboratory investigations showed normal renal and liver function with normal serum urate concentration. Random glucose was 109 [70-100] mg/dL & Hgb1ac 4.6% [4.5%-6.3%]. Complete blood count revealed hemoglobin level 14.7 g/dL (normal range 12.3 g/dL–15.3 g/dL) and a slightly raised platelet count of 306 × 109/L (normal range 140 109·L–500 · 109/L). Quantitation of urine in a stick +.

Differential diagnosis

Chronic hypertension is estimated to be present in ≈3% to 5% of pregnancies[8] and is increasingly more commonly encountered. Factors contributing to the increase in prevalence include 2 major risk factors for hypertension, obesity and older age, which are of increasing prevalence in pregnancy. These shifts in risk and childbearing have resulted in an increased number of women who will require counseling on the risks of chronic hypertension in pregnancy and management of their antihypertensive medications both in anticipation of and during pregnancy.5 Because many pregnancies are unplanned,[10] all women with chronic hypertension should receive regular counseling so that they can anticipate any issues that may arise if they become pregnant and optimize their health and care to temper risk.

The complications by hypertension during pregnancy could involve both mother and fetus. Hypertensive disorders of pregnancy imply: chronic hypertension, gestational hypertension, preeclampsia, and preeclampsia superimposed on chronic hypertension.

The following are the 3 common types of gestational hypertension:
Chronic Hypertension– Women who have high blood pressure (over 140/90) before pregnancy, early in pregnancy (before 20 weeks), or continue to have it after delivery.[7]
Gestational Hypertension– High blood pressure that develops after week 20 in pregnancy and goes away after delivery.[8]
Preeclampsia – Both chronic hypertension and gestational hypertension can lead to this severe condition after week 20 of pregnancy. Symptoms include high blood pressure and protein in the urine. This can lead to serious complications for both mom and baby if not treated quickly.[7,8]

All forms of hypertension can constrict the blood vessels in the uterus that supply the fetus with oxygen and nutrients. The fetal consequences of hypertension include low birth weight, intra-uterine growth restriction, prematurity, still birth and increased risk of cardiovascular diseases in adult life.[1,11] Premature and low-birth weight newborn face an increased risk of health problems during the newborn period and lasting disabilities, such as learning problems and cerebral palsy are the complications.[11]

An important cause of hypertension that occurs during pregnancy is preeclampsia. It is a condition unique to the gravid state and is characterized by the onset of raised blood pressure and proteinuria in late pregnancy, at or after 20 weeks of gestation.[12] Preeclampsia may be associated with hyperuricaemia, deranged liver function, and signs of neurologic irritability such as headaches, hyperreflexia, and seizures. In our patient, hypertension developed at a relatively early stage of pregnancy than is customarily observed in preeclampsia. Although she had proteinuria, it should be remembered that this could also reflect underlying renal damage due to chronic untreated hypertension. Additionally, her electrocardiogram showed left ventricular hypertrophy, which was another indicator of chronicity.

Based on high blood pressure 140 / 100 mmHg or higher, on 3 test within a one week period, proteinuria (the urine stick with one (+) positive) and edema of lower limbs plus history of developing the same condition in a previous pregnancy we the condition can be classify as preeclampsia.

Management

At week 17 patient started with 1 g of Alpha-methyl Dopa every 12 hours, use of steroids for 48 hours if fetus < 34 weeks, Folic acid 5 mg tab daily, prenatal multivitamin daily and dietary measures. At week 18 patient kept high blood pressure taking maximum doses of alpha-methyl-dopa. Then, it was proceeded to implement the ozone protocol under the previous signature of the informed consent by the patient.

Protocol:

Generator used, Ozonobaric P, Sedecal-Spain. A digital arm wall sphygmomanometer was used to measure the blood pressures.
As a reference point it was taken the Madrid Declaration 2015.
Major autohemotherapy 100 mL of blood, 100 mL of ozone.
AHTM twice a week
Dose:
1st & 2nd week: 1.2 mg
3th & 6th week: 1.5 mg
7th & 10th week: 2.0 mg
10th & 13th week: 2.5 mg; one session per week
GSH 600 mg/week + 1g Vit C till the end of pregnancy.

Expectation

Hypertension during pregnancy can be the cause of placental insufficiency which may be due to:

Decreased production of vasodilator substances e.g. prostacyclin and nitric oxide. Diffuse placental micro thrombosis or inflammatory placental decidual vasculopathy or abnormal trophoblastic invasion of endometrium.[13] Decreased vascular endothelial growth factor (VEGF). Decreased placental growth factor (PLGF).[13] On the other hand, the potential advantages deriving from ozone therapy (ATHM) in hypertension are supported in the following facts:

1) Decreasing blood viscosity.[1]

2) Stimulating growth and differentiation of terminal villi.[14]

3) Inducing a spasmolytic effect and reduction of micro vessel permeability.[15]

4) Increasing tissue oxygenation and enhancement of endogenous angiogenic procedures.[14,15]

5) Increasing cardiac output and reducing peripheral vascular resistance.[15,16]

6) Releasing growth factors like PDGF (platelet derived growth factor), TGF-beta (transforming growth factor) and VEGF.[17]

7) Synthesizing and releasing vasodilatation factors such as prostacyclin, nitric oxide and endothelium derived hyperpolarizing factor (EDHF).[18]

Statistical analysis: Values Systolic blood pressure (SBP) and Diastolic blood pressure (DBP). Were expressed as mean ± standard error of the mean (SEM). Statistical analysis was performed with SPSS 12.0 software. For the analysis of normality, Kolmogorov-Smirnov, Shapiro-Wilk was used, followed by Wilcoxon test to compare the behavior of the variable after and before the treatment. Values of $p < 0.05$ were considered statistically significant.

Results

Patient has had an excellent response. She was more energetic and happy, hasn't gotten sick not even with the common cold. Her edema lower considerably between the first 3 sessions. She lost 7kg in 5 sessions. Readjust 500 mg of Alpha-methyl Dopa every 12 h (sometimes she forgets to drink it). No more headaches. Urine analysis without any alterations nor infections. She has enjoy this pregnancy and less complications. Last pregnancy she was hospitalize in 28 weeks of gestation and an emergency C section at 34 weeks.

Emergency C section ILA at 4. Baby at 34.5 weeks of gestation. She had a speedy recovery after her C section, they discharge her from the hospital the second day after delivery. She had no complications. The baby had and Apgar of 8/9, Weight 2.5 kg exclusively.

DATE	SBP/DBP mm. Hg	DATE	SBP/DBP mm. Hg
10-24-2017	140/100	12/15/2017	110/70
10-27-2017	120/80	12/19/2017	108/70
10-31-2017	110/70	12/22/2017	110/70
11-03-2017	110/70	12/26/2017	110/70
11/07/2017	110/70	01/02/2018	115/70
11/10/2017	110/70	01/05/2018	118/70
11/14/2017	120/70	01/09/2018	116/70
11/17/2017	110/70	01/12/2018	110/70
11/21/2017	110/70	01/15/2018	114/70
11/24/2017	110/70	01/22/2018	114/70
11/28/2017	110/70	01/29/2018	116/70
12/01/2017	110/60	02/02/2018	115/70
12/05/2017	110/70	02/06/2018	112/70
12/08/2017	110/70	02/08/2018	114/70
12/12/2017	110/70		

Figure 1. Blood pressure evolution during the follow-up of the patient. Represents the tensional values express in mmHg. Systolic blood pressure (SBP); Diastolic blood pressure (DBP).

Ozone therapy in obstetrics exerts a beneficial influence on the clinical course of threatened abortion, gestosis, pregnancy anemia, fetoplacental insufficiency, reduces a risk of intrauterine fetus infection and a risk of fatness-associated pregnancy complications, improves a prognosis of these diseases.[1,3] Ozone therapy reduces stationary treatment time, like it shows in figure 1, reduces the use of medicinal agents. Ozone therapy significantly ($p<0.05$) reduces a risk of such complications as delivery weakness, postnatal and early postnatal bleedings.[1] The use of ozone as a component of treatment complex improves perinatal adaptation of newborn children.[16]

The immunomodulation effect of ozone is based on its ability to activate the phagocytosis through the formation of peroxides and stimulation of the production of cytokines by lymphocytes and monocytes.[17] Modification of blood corpuscle membranes and fine-structure of vascular bed as well as a decrease in the viscosity properties of blood leads to an improvement of the blood micro-flow and respiratory metabolism at the tissue level.[16] Ozone also stimulates production of superoxide dismutase, catalase, and glutathione peroxidase, which are the enzymes in the cell wall which protect the cell from free radical damage, so ozone actually helps prevent free radical damage.[17]

Improvement of macro- and microcirculation that results in the normalization of placenta hormonogenic function. Decrease in the activity of lipid peroxidation processes and simultaneous stimulation of the antioxidant defense system of human body.[1] Decrease (if available) in the hyper coagulation activity of blood.[16] Immunomodulation action develops particularly through a decrease in blood level of circulating immune complexes, IgM, group and Rh antibodies, increase in the phagocytic activity of neutrophils.[16]

Conclusion

This study confirmed and added strong evidence that MAHT is an effective and safe method in treating hypertensive disorders during pregnancy. MAHT and methyldopa could decrease the harmful effects of hypertensive disorders during pregnancy through the positive effects of significant decreasing ($p<0.05$) maternal high blood pressure (SBP and DBP) and improving fetoplacental blood flow in hypertensive pregnant women.

The addition of medical ozone to the multimodality therapy exerts a positive influence providing a detoxication, analgesic and sedative effect that allows considerably reducing the use of appropriate traditional medicaments. This improves immediate results, particularly reduces residuals of complication. A decrease in relapse percentage after the use of ozone as a component of pathogenetic therapy speaks in favor of optimization of remote results.

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