

Influence of Vitamin D Supplementation in the Gestational Period in Patient with Multiple Sclerosis: A Case Report

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Abstract

Vitamin D is condensed by the complex human body from exposure to sunlight. However it can be absorbed through the consumption of foods such as fish liver oil, high fat fish such as (salmon), mushrooms, egg yolk and liver. The present study aimed to describe a case study of gestation with vitamin D supplementation in a patient with multiple sclerosis. The methodology used in this study was the case report. This study provided reports which may serve as evidence on the effect of vitamin D supplementation alone on the gestational process response.

Keywords: Vitamin D deficiency, Vitamin D insufficiency, Pregnancy, Multiple Sclerosis.

Introduction

Multiple sclerosis is a complex autoimmune disease (5), possibly due to a combination of genetic and environmental factors (27), with a demyelinating, neuroinflammatory and neurodegenerative characteristic of the system nervous central (SNC) (31). Although its occurrence is related to several factors combined (27), there is an understanding in relation that the disease (5) in the case of multiple sclerosis is characterized mainly by tissue lesions of the system nervous central which are associated with abnormal set of effector cells of the T lineage (31).

Yoshiyuki et al (27) reinforces in a randomized study that this vulnerability to complex diseases such as multiple sclerosis is determined by environmental and genetic factors and verified by human leukocyte antigen (HLA) genes which are not linked to human leukocyte antigen (25-27) because the CTLA-4 gene (27) has a genetic predisposition for multiple sclerosis and may occur (5) in other complex or serious diseases and is recognized by the human leukocyte antigen (HLA) specifically of class II which is localized on chromosome 6q21 and the CTLA-4 gene with localization on chromosome 2q33 (25-27), for example, in the Japanese complex diseases are associated with the polymorphism of the initiation codon of vitamin D receptor exon 2 (VDR fok-I) specifically on chromosome 12q12-12q14 (27). The vitamin D receptor belongs to a super family of nuclear hormone receptors (2) and modulates transcription of the target gene for response to 1,25-dihydroxyvitamin D₃ (1,25- (OH)₂ D₃) and some hormones have immunomodulatory potential (30). Vitamin D₃ is liposoluble (9), produced endogenously in the skin when there is sun exposure and is naturally found only in some foods (10).

There are two forms of Vitamin D which are considered physiologically active (2): colecalciferol or Vitamin D₃ (animal origin) and ergocalciferol or Vitamin D₂ (plant origin) (15) resulting in 10 to 20% of circulating Vitamin D in the organism (19).

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Vitamin D₃ supplementation can raise the serum vitamin D concentration and become three times more effective thus maintaining the level of this concentration for a longer time (15-19) since its average life is approximately 15 days (20). Vitamin D actions occur in the following locations in the human body (21): skin, intestine, bones, parathyroid glands, pancreas, small intestine and colon of the human fetus and brain (2).

Vitamin D serum concentration is usually altered by several factors that regulate its production in the skin (31), such as (21): skin pigmentation, latitude, season, aging, dressing, sunscreen use, air and obesity (22). The health professional who performs prenatal care in special populations as carriers of multiple sclerosis should correctly orient the sun exposure to ensure adequate concentrations of Vitamin D (18), which is usually 5 to 30 minutes for upper limbs and lower limbs (16), at a time between 10 and 15 hours (15), at least twice a week (15-16). However, this time of sun exposure will depend on the season (2), the latitude and the pigmentation of the skin (25), because sufficient sun exposure for absorption causes a minimal erythema and characterizes the intake of 20,000 IU of Vitamin D (19).

Some authors agree as reference of normal level of Vitamin D in relation to values ≥ 30 ng / mL or ≥ 75 nmol/L (20); when addressing the insufficiency values between 20 and < 30 ng / mL or between 50 nmol/L and < 75 nmol/L (16); and in relation to the deficiency the values < 20 ng / mL or < 50 nmol/L (10), according to criteria established by the Endocrine Society (19). The term hypovitaminosis D applies to either deficiency or insufficiency of Vitamin D (2), or also deficiency more insufficiency of Vitamin D (5-7). Vitamin D deficiency has been common in the world continents (14), particularly in the gestational period and has been identified as a public health problem (14-15), mainly in Brazil (9).

The need for adequate intake of Vitamin D is important to meet the constant demand for calcium (25), mainly for fetal growth and development (15), so pregnant women have been considered a high risk group (16), in which the risk oscillates with an increase of 20-40% in patients with Multiple Sclerosis (15-17). Vitamin D exerts a critical characteristic (15) on reproductive health and provides a multisystemic measure of functioning in pregnant women (17). This neurosteroid hormone (28), which is unique and regulates the development of placental function (15-17) and promotes fetal tolerance during gestation in the immune system (15), however the vitamin D deficiency during gestation is the risk factor for complications in certain pathologies (14), such as multiple sclerosis (8).

Vitamin D deficiency in the gestational period is associated with an increase in the complications of adverse perinatal outcomes (15), for example preeclampsia and preterm delivery (17). In fact, vitamin D supplementation in populations with multiple sclerosis may play a protective role in gestational etiology, according to some current epidemiological studies (14-17). Epidemiological studies (24), which addressed vitamin D exposure in the diet and through sunlight during the gestational period (17), mainly dietary intake of vitamin D reinforces a protective role in the etiology of multiple sclerosis during gestation (15).

Vitamin D has been recognized as an immunomodulatory role (15) and has emerged as an important potential determinant for the etiopathogenesis of immune-mediated disorders such as multiple sclerosis (14-17). However, the latent correlation between vitamin D in the womb and multiple sclerosis has clinical implications in a basic science (17). Firstly, we would have a biological connection with vitamin D deficiency in the recurrence of the outbreaks according to the stage of the development of multiple sclerosis (30), mainly in the gestational period (15), so it is important to consider both the immunological pathogenesis and the potentiality of the effect in relation to the biological development and lipid development of myelin (17).

In characterizing vitamin D supplementation and its importance in the prevention of gestational outbreaks in patients with multiple sclerosis (15), many children are deficient in fetal development (14), which leads to questions (17): Does vitamin D supplementation affect the gestational period in patients with multiple sclerosis? Although the effect of Vitamin D in the gestational period on Multiple Sclerosis has not been studied (18), mainly in adulthood (17), some epidemiological studies have evaluated the initial effects of Vitamin D on diets (19), in this case in other autoimmune diseases (25), such as type I diabetes (13), however, the results are not contradictory (14).

In view of the above, the present study in the case study model aimed to describe the supplementation of Vitamin D in the gestational period in a patient with Multiple Sclerosis.

Case Report

A 38-year-old female patient, a federal primate with a probable gestational age of 18 weeks and 03 days, sought the family health unit to perform prenatal care using corticosteroids for the treatment of an outbreak during pregnancy. Was evaluated by the family health team, did not present positivity for syphilis (rapid test) and HIV (rapid test). The patient had multiple sclerosis with onset of symptoms around 08 years ago, which showed loss of balance, paresthesia in the left lower limb, diplopia and deviation of the lip rhyme. Around four years ago, the diagnosis of Multiple Sclerosis was established, and the diagnosis was concluded with a neurologist. It was followed up by an interdisciplinary team. For the time being, natalizumab 300 mg, baclofen 10 mg and gabapentin 300 mg are in use.

The last crisis was reported about two years ago. It has no history of allergies. At the time of the prenatal visit, he had difficulty wandering due to the intense muscular weakness in both lower limbs, in order to finish the first consultation, routine prenatal exams were requested. In the first prenatal visit there were significant laboratory tests that showed a deficiency of Vitamin D (blood: 16 ng / ml) and anemia (Hb: 8.1 g/dl) (Table 01). Biochemical tests were requested for hypothetical diagnoses of infections presence of hydroelectrolytic disorders and nutritional changes in the gestational period related to vitamin D deficiency. Therefore, at the first prenatal visit, we performed a complete blood count, sodium, potassium, calcium, phosphorus, magnesium, urea and creatinine, glucose for the purpose of evaluating renal function and transaminase. Requested by the family health team in order to verify the liver function by the use of many medicines daily, whose result during the gestational period did not obtain alterations related to some disease.

In relation to routine exams such as; glucose and pressure, it was observed that in the gestational period the patient presented a blood pressure control (mean arterial pressure in the nine months of gestation: $100 \pm 10/90 \pm 10$ mmHg) and satisfactory glucose (82 ± 10 mg / dl). In order to evaluate fetal growth measures ultrasound examinations were performed, which were performed at 19.0 weeks of gestation; the first ultrasound was performed to establish the correct gestational age, which presented 19 weeks and one day. In the second and third trimesters, imaging tests were performed to verify possible changes and to confirm the fetal head circumference, abdominal circumference and femur length both sonograms were performed and fetal weight and length were normalized as estimated.

Table 01: Biochemical exams prior to the onset of prenatal care in the health of Family of Campo Grande/MS, 2017.

Gestational Period	Calcium (8.4-10.4 mg/ dl)	Parathyroid hormone (12.0 - 65.0 pg/mL)	Creatinine (0,6 – 1,2 mg/dL)	Hemoglobin (10 -11 g/dL)	Hematocrit (31% - 33%)	Vitamin D (30 – 40 ng/dL)
9 Weeks and 2 days	7,5	41,0	1,2	8,1	21,2%	16,0 ng/db
12 weeks 1 and day	8,0	52,0	1,0	8,0	29,2%	18,2 ng/db

The patient was asked to bring the medical prescription for the medication in use for the treatment of Multiple Sclerosis. The patient reported that about two years did not perform vitamin D supplementation and did not perform sun exposure for a fixed time during the week. At the end of the gestational period the patient progressed to normal delivery with no history of complications during delivery, and in the postpartum period she underwent the breastfeeding process in the fourteen-month period.

Table 02: Biochemical exams after the onset of prenatal care in the health of family in Campo Grande / MS, 2017.

Gestational Period	Calcium (8.4-10.4 mg/ dl)	Parathyroid hormone (12.0 - 65.0 pg/mL)	Creatinine (0,6 - 1,2 mg/dL)	Hemoglobin (10 -11 g/dL)	Hematocrit (31% - 33%)	Vitamin D (30 - 40 ng/dL)
19 Weeks and 05 days	7,5	41,0	1,2	8,1	21,2	16,0
20 weeks and 01 day	8,2	32,0	1,0	8,0	32,2	19,0
21 weeks and 2 days	9,1	21,0	0,6	12,7	31,0	35,6
22 weeks and 2 days	9,2	23,1	0,8	10,1	30,0	37,2
23 weeks and 4 days	9,1	18,7	0,7	10,1	31,0	21,2
24 weeks and 05 days	8,6	14,6	0,6	12,0	32,2	33,5
25 weeks and 01 day	8,5	13,2	0,6	12,2	32,1	34,5
27 weeks and 2 days	8,6	13,4	0,7	12,3	31,2	25,6
28 weeks and 1 day	8,4	13,2	0,6	12,1	31,0	37,2
29 weeks and 2 days	8,6	13,5	0,7	11,2	31,1	39,3
30 weeks and 4 days	8,4	13,1	0,6	10,1	30,0	31,2
31 weeks and 2 days	8,5	13,2	0,8	10,3	30,5	33,2
32 weeks and 1 day	8,4	13,1	0,6	10,5	32,2	35,1
33 weeks and 01 day	9,3	15,6	1,0	10,9	31,2	38,2
34 weeks and 2 days	8,6	14,3	0,9	11,1	30,2	39,4
35 weeks and 4 days	9,1	11,6	0,7	12,4	31,0	39,7
36 weeks and 2 days	8,6	11,5	0,6	11,2	31,2	39,8
37 weeks and 1 day	8,5	13,2	0,6	11,9	31,6	37,6
38 weeks and 2 days	8,4	12,2	0,7	12,1	31,2	38,9
39 weeks and 01 day	8,9	13,1	0,6	12,2	32,0	39,0

Discussion

Multiple sclerosis is an autoimmune and demyelinating disease (23), a degenerative disease of the central nervous system (23). It is considered to be an inflammatory disease which is one of the most prevalent causes in women of childbearing age (14). Pregnancy is characterized by physiological and metabolic changes in response to fetal growth (14), which requires the need for specific nutrition for this period (15). Whereas the nutritional status of pregnant women is a particular concern in regions where nutritional deficiency is a public health problem (17).

When addressing gestation in patients with Multiple Sclerosis, which has been under study since 1950 and there are controversies, some prospective and observational studies have shown that there is a significant decline in outbreaks during pregnancy (17), especially in the third trimester of gestation and followed by a worsening in the first trimester postpartum (15-18). Thus, the need for vitamin D supplementation in patients with multiple sclerosis in the gestational period is reinforced (18), which is already being performed in women of higher fertile age (17), since it favors the absorption of calcium in the body and reduces the risk of diseases such as rickets (25), osteoporosis, autoimmune diseases and constant outbreaks in neurodegenerative diseases (23), such as multiple sclerosis (8).

The patient in the study who received vitamin D supplementation in the gestational period showed a reinforcement in the regulation of the CD4 + T cells response (26), visualized in the laboratory tests by the increase of blood cells, which favored the promotion of the immunoprotective cells (21), such as T helper 2 (Th2) cells which can suppress T helper 1 (Th1) cells (26) and this process may limit Th1 mediated inflammatory responses mainly reflecting tissue damage while enhancement and mediation anti-Th2 as an inflammatory response thus having a response to the decrease in recurrent and recurrent outbreaks which were confirmed by improvement in the muscle weakness symptom (23-26).

In this case study with a patient with multiple sclerosis and pregnant women, the prenatal consultation was predetermined in relation to the patient making an adequate intake of Vitamin D during the gestation period (17) as was done in previous studies regarding Vitamin D supplementation in multiple sclerosis (11), for example, a multi-center study in progress in the USA reports that the dose should be a moderate dose around 5000 IU of vitamin D3 orally (12), thus the multidisciplinary team of prenatal health has addressed the continued demand for vitamin D supplementation which will influence calcium absorption for balanced fetal development (25).

The alert to health professionals who performed the prenatal care in relation to the probable Vitamin D deficiency and, in parallel, that of Calcium increased when the patient reported that she did not receive vitamin D supplementation and sun exposure in the gestational period (14). It is worth remembering that in the absence of regular exposure to the sun (15), only food sources are not sufficient to maintain adequate levels (16). Thus, drug supplementation is necessary (14). The Brazilian society of endocrinology recommends that the dose range be around 800 to 5000 IU for day according to age (18).

Some randomized studies have demonstrated that supplementation with 5,000 IU/day of vitamin D during the gestational period leads to a reduction in the risk of morbidities such as maternal infections (22) in cesarean section and preterm delivery (14). From such cited evidence (14, 22), this was at the dosage established daily for supplementation in this case study conducted in primary care. On the other hand, the toxic dose of Vitamin D should be considered higher than 10,000 IU daily over a period of at least 30 days (20).

As a result of the laboratory examination presented in Table 2, the patient did not present during the gestational period a diagnosis of acute renal failure secondary to hypercalcemia (25), since parathyroid hormone remained in the normal patterns associated with the vitamin D rates, which did not present severe changes in blood levels (28). Hypovitaminosis was not observed during gestational follow-up (14), as there was no increase in Paratomium secretion (28).

In the gestational period, as previously reported, there is no influence of pregnancy on the progression of the disease (14), however, the fact that the pregnant woman, especially with multiple sclerosis, may present difficulties in mobilization (17). Therefore, the patient reported difficulty in walking due to the intense muscular weakness in both lower limbs (29) and soon could present aggravation and an increase of the spasticity as the pregnancy happens, therefore, the patient would present relative weight increase and displacement of the center of gravity (14). When discussing the increase in blood pressure during gestation and relating to vitamin D deficiency in pregnant women with multiple sclerosis, an increase in blood pressure reported in previous studies (30) is generally associated with a condition related to increased maternal morbidity and mortality, fetal and perinatal (18).

Hypertension presents a risk of convulsion and complications during delivery, and during the gestational period of the patient in this case study, a blood pressure control was observed (mean arterial pressure in the nine months of gestation: $100 \pm 10/90 \pm 10$ mmHg) (18). Some randomized studies have pointed out that vitamin D supplementation reduces the risk of preeclampsia, which has been proven in the evaluation in this case study, noting that the patient showed low urinary calcium excretion, associated with low level of ionized calcium and maintained control in levels of parathyroid hormone and normal levels of vitamin D (16-18).

Research results have emphasized the importance of non-classical Vitamin D function in gestation (14) and placenta which is related to hypovitaminosis D disorders in preeclampsia pregnancy (18), for example, previous studies in women (25), these low levels of ionized calcium with high levels of parathyroid hormone associated with low levels of vitamin D $1,25(\text{OH})_2\text{D}_3$ increases the risk of gestational diabetes (28).

The patient in this case study on presenting satisfactory glucose (82 ± 10 mg / dl) in routine laboratory tests and according to previous studies can say that Vitamin D is known to define the patterns in insulin secretion (13), Vitamin D regulates insulin secretion by pancreatic β cells (19), as it affects circulating glucose levels (23). Thus, low Vitamin D concentration is a risk factor for insulin resistance in pregnant women (23), glucose intolerance and especially metabolic syndrome characteristics in normoglycemic women (13).

If there is an increase in vitamin D deficiency at the beginning of gestation, it will lead to a significant increase in the risk of gestational diabetes at the end of the gestational period (23). According to Gauree et al (31) and as in the reference (19), it was found that low levels of Vitamin D increased the risk of gestational diabetes by around 49% (14). Another 24 meta-analysis studies corroborate the results of the reference (19), that is, there is an increased risk of gestational diabetes around 54% (16). This is because inadequate glycemic control of pregnant women with gestational diabetic disease in early pregnancy may be associated with maternal hypovitaminosis D and the low bone mineral content of the newborn (17).

The low levels of hemoglobin and hematocrit at the beginning of the gestational follow-up of the patient in the health of the family reinforces what previous research shows in relation to the association of the presence of anemia with vitamin D deficiency (19), an earlier study done with adolescents between 14 and 18 years of age showed that their Vitamin D and hemoglobin levels measured by blood test related the anemic association to vitamin D deficiency (31).

When the blood test was performed on the patient with multiple sclerosis and pregnant women participating in this case study, it was concluded that the higher the blood level of Vitamin D found (31), the lower the risk of developing anemia (9). With low stocks of Vitamin D mainly in patients with diseases such as multiple sclerosis (12), the mother can change the condition of the newborn's Vitamin D levels so it is important to note that rickets can be prevented in breastfed newborns by the use of vitamin D supplementation in the mother during the gestational period. Keeping the normal percentage of vitamin D in pregnant women with multiple sclerosis in the gestational period (10) favors the development of balanced fetal weight at birth and normal neonatal length, which was found in the imaging studies performed during the gestational period of the pregnant woman participating in the study of case (10-11).

The pregnant woman with multiple sclerosis who participated in this case study did not present complications related to the aggravation of multiple sclerosis in the gestational period. Recently an experimental study related the use of Vitamin D as a protective effect against multiple sclerosis in pregnant women (24). A randomized observational study has shown that vitamin D supplementation in women with multiple sclerosis during pregnancy decreases the likelihood that the child will develop multiple sclerosis later in life (25), as Andrzej et al. (24) in a previous study direct gene connections between Vitamin D and the variable genes that are involved in multiple sclerosis decreases with Vitamin D supplementation and thus has a decreased risk of developing the disease in the future.

In laboratory routine in the Brazilian pregnant woman, we do not require tests to evaluate the serum concentration of Vitamin D (19). However, there are regions where there is a prevalence of vitamin D insufficiency in the general population, including pregnant women (4), so it would be safe to include in the routine laboratory tests the serum vitamin D score (16), since in previous experimental studies which were carried out in the city of Curitiba, Brazil, which included pregnant women obtained a statistical result that during winter there is an increase in the vitamin D deficiency in the pregnant population (19). Thus, it would be ideal for a woman with multiple sclerosis who intends to have a close follow-up on the health of the family in relation to the serum level of Vitamin D and sufficient in the before the gestational period (17) and especially during the gestational period, requiring evaluation and monitoring of the serum concentration of vitamin D to prevent or treat hypovitaminosis D (14). Soon the Family Health Professionals who performed the prenatal in the program of the ministry of health, such as; doctor and nurse performed a vitamin D supplementation in the patient with the objective of avoiding maternal-fetal complications (14), neonatal and especially in early childhood and adulthood of the developing fetus (17).

Conclusion

This study provided reports which may serve as evidence on the effect of vitamin D supplementation alone on the gestational process response. Providing pregnant women with vitamin D supplementation reduces the risk of pre-eclampsia, preterm delivery and low birth weight. However, further clinical studies are needed, such as case studies conducted with methodological rigor to confirm these effects.

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