

# Case Study of Hypertension Responding to Natural Progesterone Supplement

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## Abstract

A 35 year old, G4P4, suffering from poorly controlled hypertension since the birth of her last child four years prior, presented to the clinic to learn natural family planning. Her physicians had instructed her to avoid pregnancy due to her hypertension, her medications and her age. During her evaluation and follow up visits, she was found to have a considerably short or absent post ovulatory phase and was placed on a natural progesterone supplement for the post ovulatory period of days 18 through 28 using Prometrium™. Through the 3 months of treatment, her blood pressure was observed to decrease to normal levels with slow removal of all of her blood pressure medications. Following her third month of treatment with the progesterone, she was on no hypertensive medications and experienced blood pressure readings in the 120's/70-80's, down from levels that had reached into the 170's/110's while on medication. Following four years of unstable hypertension, this patient was able to stop antihypertensive medication within three months of initiation of natural progesterone supplement and maintain those normal blood pressure levels up to one year later.

## Introduction

Pregnancy induced hypertension potentially affects as many as 10% of all pregnancies.<sup>7</sup> This hypertension may appear as early as the second trimester or as late as 4 weeks postpartum, with average development by 1 week postpartum.<sup>7</sup> Incidence of no preexisting hypertensive condition is as high as 96% in one study.<sup>7</sup> With this large development of de novo hypertension, treatment modalities are still non-specific and non-curative. Treatment for pregnancy induced hypertension utilizes standard anti-hypertensives. In this case, Diovan, Toprol and Lasix. Diovan is a pregnancy category D, teratogenic drug, Toprol and Lasix are pregnancy category C, not recommended in pregnancy. All three are recovered in breast milk and not recommended for breast feeding. These drugs, essentially, prohibit women of childbearing years from conceiving or breastfeeding.

Preeclampsia and pregnancy induced hypertension have been shown to be associated with long term adverse cardiovascular changes.<sup>5,6</sup> Increased inflammatory and antiangiogenic cytokines remain in the circulatory system up to 8 years following delivery and have an adverse effect on endothelial function.<sup>6</sup> Because of these long-term adverse effects, forms of treatment that inhibit hypertensive development in pregnancy (postpartum) are of great interest in the obstetric world.

## Case Presentation

A 35 year old female presented to our clinic with a request to learn natural family planning. She stated her doctors advised her against pregnancy because of her hypertension, hypertensive medications and her age.

She stated her doctors had refused to prescribe oral contraceptives due to this history. The patient stated she developed this hypertension a few hours following the delivery of her last child and it has been difficult to control ever since. The patient also mentioned she would like to have another child before she is too old to conceive but is fearful of her blood pressure status with another pregnancy. She is learning natural family planning to avoid pregnancy for now.

*Prior Medical History:* The patient denied a hypertension diagnosis prior to birth of her last baby. She denied genetic disorders or diseases in her family.

*Prior Reproductive History:* The patient stated menarche was at the age of 13 and it was normal, regular 23-28 day cycles. More recently, she stated she has noticed heavy bleeding x3 days, moderate x4, light x3. The heavy bleeding had been worsening over the past 4 years, from one day per cycle to now 3 days per cycle and PMS had been developing over the past 6 months. She stated her primary doctor in unison with her obstetrician had run multiple tests, including ultrasound of heart and kidney, MRI of kidneys, 24 hour urine, and some kidney function test that she did not know the name, (this practitioner never received test results). All of these tests, she stated, returned revealing normal functioning of her kidneys and no disease process was identified.

*Prior Surgical History:* She stated she had a tonsillectomy with adenoidectomy in 1981.

She stated she has no known drug allergies.

*Family History:* Mom developed hypertension at age 45 and her paternal grandma developed breast cancer in her post-menopausal years.

*Social History:* The patient is married with four pregnancies and four deliveries; all normal, spontaneous, vaginal deliveries with the development of hypertension following only the last delivery. She stated she is a homemaker, home schools her children and walks daily for exercise. She smokes 4-5 cigarettes per day but stated she stopped smoking for each pregnancy. She mentioned that her weight had increased over her childbearing years from 155 lbs to now 194 lbs.

On initial exam: HT: 5'11", WT: 194 lbs, BP: 158/84 (on meds)

Physical exam was normal with the exception of:

Her thyroid gland was slightly enlarged bilaterally but soft and without masses. Her heart exhibited a regular rate and rhythm w/split S2. The uterus was not enlarged and there were no masses palpable upon pelvic exam.

Blood draw was performed and the lab results are listed on Table 2.

At this visit, she was instructed in the methods of monitoring fertility and charting her observed symptoms. An appointment was made for her to return in two weeks and successive visits would be scheduled 14-16 days apart. She was advised to lose weight and instructed on weight loss methods and exercise routines. She was also instructed to take her blood pressure at home using her home monitor, twice daily: once upon first

arising and again in mid-day. She was instructed to stop smoking immediately. She was given Ampicillin for her bacteriuria once C&S returned.

2nd Visit:

This visit was sixteen days later and she had charted 11 days of her cycle and was on day 2 of menses. Her charts were reviewed. Her BP: 170/90 and she had lost 2 lbs. with weight at 192 lbs. We discussed her symptoms of observing mucus during her fertile period and determined that the end of mucus observations occurred 3 days before menses began. Looking at the entire cycle, she had recorded only 23 days from onset of menses the prior month to the onset this month. With this information, we discussed the potential use of natural progesterone to supplement the second half of her cycle with the hopes of elongating the post ovulatory phase of her cycle (from her possible 3 days in this cycle to a more normal 14 days). She was given a prescription for Prometrium™ to begin on day 17 of her cycle and take for 10 days at bedtime. She was in agreement with this plan. She had succeeded in her smoking cessation by this visit.

3rd Visit:

14 days later she returned for another follow up to her charting. She remained in her pre-ovulatory phase according to her observations, so had not yet started her progesterone.

4th Visit:

14 days later, was timed to occur following the onset of her next menstrual cycle and following her first 10 day dose of progesterone. At this visit, she states she stopped her Diovan and Lasix on her own due to the fact that her blood pressure had dropped shortly after beginning the progesterone, according to her home monitor. She states at this visit, that she is now taking previously prescribed Toprol and hydrochlorothiazide. Her cycle had elongated to 27 days with 10 days of dry observations following her presumed ovulatory time.

5th Visit:

21 days later, she was just starting her second cycle of progesterone, being on day 18 of her current cycle. She was still taking her Toprol and hydrochlorothiazide. She was instructed to stop her Toprol if her blood pressure throughout the day remained below 130/80.

6th Visit:

Seven days later, she announced that she had stopped the Toprol at the last visit and was now only taking 25 mg of hydrochlorothiazide once daily. By this visit, she had completed 2 full cycles of charting with supplemental natural progesterone in the last 10 days of each cycle. She stated that all home BP readings had been in the 120's/70's since her last visit with us and she felt good. She was instructed to stop the hydrochlorothiazide, continue on her regimen of progesterone on days 18-27; continue with weight loss efforts, daily exercise and daily blood pressure monitoring. She was not scheduled for a follow up visit until 1 month from this date.

At her next visit, which was approximately 30 days from the prior visit, she announced she had a positive pregnancy test.

We performed an ultrasound to verify implantation without bleeding and this was verified. She had no complaints at this visit and was continuing her progesterone supplement. Our office advised her to continue this supplement until 12 weeks pregnant minimally. She will be given requisitions for serum progesterone

levels every 3 months to determine if supplement remains necessary. Due to her prior development of hypertension in her postpartum period, we recommended she return to progesterone use in her third trimester if she stops it at 12 weeks. But absolutely, she is to restart her progesterone in her postpartum period. Because our clinic did not have an obstetrician on staff, she was referred to a high risk Maternal Fetal Medicine specialist in a near-by city and was temporarily lost to follow up.

Table 1: Summary of Weight and Blood Pressure

Visit	Weight in pounds	Blood pressure
2-(prior to onset of meds)	192	170/90
3-(30 days from initial)	192	158/110
4-(first visit 2 weeks after initiation of medication)	193	130/84
5-(just initiated 2 <sup>nd</sup> cycle of progesterone)	193	122/72
6-(just completed second cycle of progesterone)	193	114/74

One year later, she returned to our clinic with this tale: Instead of seeing the maternal- fetal medicine specialist through her pregnancy, she went to a local obstetrician who instructed her to stop the progesterone at 6 weeks of pregnancy. She states she developed contractions and vaginal bleeding at 33 weeks gestation and was placed on bed rest with medication to stop contractions (she did not know the name of this medication). She states the medication and bed rest controlled her labor and she continued her pregnancy until her 37th week. At this time she delivered, via vaginal delivery, an 8 lb. 3 oz. male infant. She stated that following delivery, she began hemorrhaging. Utilizing medication and massage this was controlled. She stated that her blood pressure had remained within normal limits during this pregnancy and as of today, had continued within normal ranges.

She returned to our clinic to restart her charting and refill her progesterone. At this time she complained of vaginal discharge with odor and exam revealed bacterial vaginosis. She was treated with Cleocin™ vaginal cream. Appointment was not scheduled, she was to return as needed for follow up. WT: 189lbs, BP: 124/82

She returned two months later with complaints of dizziness, fainting, tiredness and depression. She stated she had been to her primary physician for these symptoms and he had started her on Labetolol for prior history of hypertension and instructed her to lose weight and begin exercise. Since initiating the Labetolol, the dizziness, fainting and depression have worsened. She denied any other symptoms. WT: unchanged BP: 110/60

She was instructed to stop the once daily Labetolol and was sent for blood work which revealed Hashimoto’s thyroiditis and she was referred to an endocrinologist for chronic care. She was instructed to continue with her natural progesterone for the last 10 days of each cycle and to return for problems and annual exams.

## Discussion

This case study suggests that natural progesterone may have a positive effect on blood pressure in pregnancy induced hypertension as her weight did not change appreciably through the course of this study. Little concrete information is known about the effects of naturally produced progesterone in early through late pregnancy complications. What is known regarding progesterone's effects on the pregnancy comes from studies performed in early trimester implantation. Here, progesterone may act as the nuclear transcription factor inducing the remodeling of the uterine decidual spiral arterioles to a straightened, low pressure, high volume arteriole that feeds a growing fetus through increased VEGF and IGF-1 activity.<sup>2</sup> When a placenta's microvasculature exhibits poor development, adverse effects on pregnancy occur, including, decreased oxygenation and nutrition to the fetus. With decreased flow, renin-angiotensin- aldosterone system is initiated and vasoconstriction increases thereby complicating the decreased flow of blood to the fetus resulting in adverse outcomes.<sup>6</sup> One side effect of this dysfunction may be a blunting of the baroreflex function resulting in postpartum hypertension.<sup>6</sup> If natural progesterone can be used as a treatment for pregnancy induced hypertension, it is a medication that is safe for pregnancy and lactation. Obviously, more research needs to be done on both the positive effects of natural progesterone on arteriole development in early pregnancy and the correlation of natural progesterone on subsequent damage to the endothelium and juxtaglomerular cells, as well as its effects on antiangiogenic and inflammatory cytokines.

## References

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Table 2: Summary of Lab Values

Urine culture	was positive for Alpha Streptococcus	
FSH LH	18.8 MIU/ml 34.6 MIU/ml	
LABS:	Final Results	N O R M A L VALUES:
Thyroid Peroxidase:	226.4 U/ml	0-60 U/ml
Thyroglobin Antibody:	96.7 U/ml	0-30 U/ml
T3-reverse:	374 pg/ml	90-350 pg/ml
TSH:	0.931 MIU/ml	0.350-4.50 MIU/ml
T3 total:	145 ng/dl	60-181 ng/dl
T4 free:	1.19 ng/dl	0.89-1.76 ng/dl
FSH:	3.0 MIU/ml	<20 MIU/ml
LH:	4.5 MIU/ml	<16
C B C : all WNL		
C M P : all WNL		
Ferritin:	10 ng/ml	10-291 ng/ml
Testosterone:	22 ng/dl	14-76 ng/dl
DHEAS:	81 mcg/dl	35-430 mcg/dl
Vit B12:	283 pg/ml	211-911 pg/ml
Folate:	13.5 ng/ml	>5 ng/ml
HBA1C:	5.3mg/dl	nondiabetic <5.8
ANA:	negative	negative