Is Procardia XL 60 mg Q Daily Equivalent to 30 mg XL Given Twice Daily?

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NCT03595982

Document Date: 04-23-2018

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Lay Summary:

Antihypertensive therapy has been used in pregnant patients antepartum to improve blood pressure (BP) elevation in cases of chronic hypertension, and postpartum for persistent hypertension after delivery in cases of gestational hypertension and preeclampsia, as well as for management of chronic hypertension.

There is limited evidence regarding the precise BP level at which antihypertensive therapy is indicated during pregnancy for chronic hypertension. Treatment has been suggested in pregnant patients when systolic BP is ≥ 160 mmHg and at a lower diastolic BP threshold of 105 mm Hg, however some providers may initiate therapy at systolic BPs ≥ 150 mmHg.

Nifedipine is a peripheral arterial vasodilator and an ideal first line antihypertensive agent due to its low maternal side-effect profile. It has been proven to be safe in pregnancy. Conventional nifedipine can be started at 10 mg twice daily with a maximum dose of 120 mg/d, but frequently extended release tablets are preferred due to steady blood pressure control with once daily administration.

It is frequently used however as a twice daily dosing as many providers have noticed an increase in the BPs 12-24h from administration. Twice daily dosing might produce overlapping profiles that prevent elevation of BP at the time of the next administration and breakthrough elevations throughout the day in pregnant women.

The aim of this study is to investigate the mean plasma levels and standard deviations of Procardia at 24h after Procardia XL is administered as a 60 mg daily dose and the mean plasma levels after it is given as a 30 mg twice-daily dose. This will be a pilot study for a future randomized control trial that will allow us to determine whether 60 mg daily of Procardia XL is equivalent to 30 mg twice daily. Secondary outcome will be effective control of BP throughout the day (0h, 4h, 8h, 12h, 16h, 20h and 24h) defined as BPs below 160/105 as well as side effects of nifedipine as reported by patients

Objectives:

Determine the mean plasma levels and standard deviations of Procardia at 24h after Procardia XL is administered as a 60 mg daily dose and the mean plasma levels after it is given as a 30 mg twice daily dose. This pilot study will provide us with information to design a randomized controlled trial to test the hypothesis that pregnant patients taking 60 mg once daily of Procardia XL will have lower plasma levels and insufficient BP control towards the end of 24h compared to 30 mg of Procardia XL given twice daily.

Background:

Antihypertensive therapy has been used in pregnant patients antepartum to improve blood pressure (BP) elevation in cases of chronic hypertension, and postpartum for persistent hypertension after delivery in cases of gestational hypertension and preeclampsia, as well as for management of chronic hypertension.

There is limited evidence regarding the precise BP level at which antihypertensive therapy is indicated during pregnancy for chronic hypertension. Given the limitations of data as well as higher likelihood of outpatient therapy with less frequent blood pressure monitoring, treatment has been suggested in pregnant patients when systolic BP is ≥ 160 mmHg and at a lower diastolic BP threshold of 105 mm Hg [1], however some providers may initiate therapy at systolic BPs ≥ 150 mmHg.

Antihypertensive therapy has not been shown to improve fetal condition or to prevent preeclampsia. However, such therapy controls acceleration of BP, reduces antepartum hospitalization due to severe hypertension and should help prevent maternal complications from uncontrolled hypertension such as cardiovascular (congestive heart failure and myocardial ischemia), renal (renal injury or failure), or cerebrovascular (ischemic or hemorrhagic stroke) damage. [1]

Drugs such as methyldopa, labetalol, and nifedipine in many occasions are used as first line agents for control of hypertension in pregnancy.

Calcium channel blockers are a class of drugs that have not been extensively studied in pregnant women with chronic hypertension, however they are still considered standard of care for treatment of elevated BPs during pregnancy and after delivery. [1] Small amounts have been shown to cross the placenta [2], however to date no known association with birth defects have been found with reassuring long term follow-up of babies up to 1.5 years. [3] It is not associated with adverse perinatal outcomes and furthermore, nifedipine does not appear to adversely affect uterine or umbilical blood flow. [1]

Nifedipine is a peripheral arterial vasodilator and an ideal first line antihypertensive agent due to its low maternal side-effect profile. Conventional nifedipine can be started at 10 mg twice daily with a maximum dose of 120 mg/d, but frequently extended release tablets are preferred due to steady blood pressure control with once daily administration. The extended release tablet consists of a semipermeable membrane surrounding an osmotically active drug core and has been designed to provide nifedipine an approximately constant rate over 24h [4]. Recommended dosage in pregnancy range from 30-120 mg/d orally of slow release preparation [1].

Dosage adjustments usually occur at 7- to 14-day intervals , however, if clinically indicated, titration may be done more rapidly with appropriate monitoring. It is recommended to be consumed as a whole tablet, without crushing or chewing, once a day, however it is frequently used as a twice daily dosing in pregnancy and postpartum as many providers have noticed an increase in the BPs 12-24h from administration. Twice daily dosing might produce overlapping profiles that prevent elevation of BP at the time of the next administration and breakthrough elevations throughout the day.

Medications such as glargine, which has been FDA approved as a once daily dose medications, has been shown to have an actual duration of action that ranges from 10.8 to 24 h in some pregnant patients. [5]. This fairly wide range suggest that a second dose may be necessary to achieve optimal glycemic control, although this is considered off-label use. [6]

The aim of this pilot study is to investigate the distribution of plasma levels of Procardia at 24h after Procardia XL is administered as a 60 mg daily dose and the mean plasma levels after it is given as a 30 mg twice-daily dose. So far there are no studies providing this information which is essential to design a future randomized control trial that will allow us to determine whether 60 mg daily of Procardia XL is equivalent to 30 mg twice daily or if patients on 30 mg of Procardia XL twice daily have higher plasma levels of medication and improved BP control towards the end of 24h.

Studies from the FDA have determined plasma levels of Procardia XL at different doses. Plasma levels have been reported after administration of 30 mg and 90 mg of Procardia XL, however there is no information after 60 mg of Procardia XL is administered or after twice daily dosing is given. This information is however necessary to plan a larger scale randomized controlled trial to compare both regimens.

Secondary outcome will be effective control of BP throughout the day (0h, 4h, 8h, 12h, 16h, 20h and 24h) defined as BPs below 160/105 and frequency of side effects of nifedipine including peripheral edema (most common side effect, dose related), flushing, headache, dizziness, fatigue, constipation, nausea, and muscle cramps.

References

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Primary and secondary Study endpoints

The aim of this pilot study is to investigate the distribution of plasma levels of Procardia at 24h after Procardia XL is administered as a 60 mg daily dose and the mean plasma levels after it is given as a 30 mg twice-daily dose. So far there are no studies providing this information which is essential to design a future randomized control trial that will allow us to determine whether 60 mg daily of Procardia XL is equivalent to 30 mg twice daily or if patients on 30 mg of Procardia XL twice daily have higher plasma levels of medication and improved BP control towards the end of 24h.

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information after 60 mg of Procardia XL is administered or after twice daily dosing is given. This information is however necessary to plan a larger scale randomized controlled trial to compare both regimens.

Secondary outcome will be effective control of BP throughout the day (4h, 8h, 12h, 16h, 20h and 24h) defined as BPs below 160/105 and frequency of side effects of nifedipine including peripheral edema (most common side effect, dose related), flushing, headache, dizziness, fatigue, constipation, nausea, and muscle cramps.

Sites: Approved. Mount Sinai West Hospital.

Funding my Mount Sinai: Yes

Number of Subjects 20 Patients in total. 10 in each group.

Specify other setting of Human Research: Antepartum, Labor and Delivery and Postpartum at Mount Sinai West Hospital

Feasibility of Meeting Recruitment Goals: Feasible. We have at least one patient per week who requires antihypertensive medication in the antepartum, postpartum, or labor and delivery floor. The primary investigator or co-investigators will by notified by the providers taking care of these patients who meet criteria and are willing to participate in the study and we will approach them to discuss any further details and obtain consent.

Facilities to be used for conducting research: We will be conducting our research on the antepartum ward, labor and delivery and postpartum ward as well as the MFM fellow office located at Mount Sinai West Hospital.

Inclusion:

Antepartum or postpartum patients between the age of 18-55 requiring 60 mg of Procardia XL to control elevated blood pressures secondary to preeclampsia, gestational hypertension, or chronic hypertension.

Exclusion:

- All patients receiving other antihypertensive medication

- All patients with a contraindication to nifedipine: Hypersensitivity to nifedipine or other calcium – channel blocker, cardiogenic shock, concomitant administration with strong CYP34A inducers (rifampim, rifabutin, phenobarbital, phenytoin, carbamazepine, St Johns Wort) → significantly reduces nifedipine efficacy, impaired liver function→ Patients with hepatic impairment (liver cirrhosis) have a longer disposition half-life and higher bioavailability of nifedipine than healthy volunteers

-Patients over the age of 55

Duration of an individual subjects participation in the study:

The individual subject will be participating in the study for approximately 24 hours from the time of randomization into one of the two groups: 60 mg Procardia XL daily vs 30 mg Procardia XL Q 12h until just prior to the 24h mark, when we will be obtaining the blood specimens to measure Procardia levels.

Other aspects that could increase subjects' vulnerability:

There are no further aspects that could increase subjects vulnerability

Safeguards to protect Subjects' rights and welfare:

In order to protect the subjects rights we will be consenting the patients after they have decided if they would like to participate in the study. Patients will be assured that their decision to participate in the study is completely optional and that their care will not be altered in the event that they do not wish to participate. Patients will be given time to decide if they would like to participate and all questions will be answered.

Duration of an individual subject's participation in the study:

The individual subject will be participating in the study for approximately 24 hours from the time of randomization into one of the two groups: 60 mg of Procardia XL daily vs 30 mg of Procardia XL Q 12h until just prior to the 24h mark, when we will be obtaining the blood specimens to measure Procardia levels.

Duration anticipated to enroll all study subjects: 24 months

Procedures for subjects to request withdrawal:

Patients can withdraw at anytime and will be aware of that option.
If the patient decides to withdraw we will then ask the patient if we can still collect their demographic and delivery data. If they allow this, then they will be included in the analysis and this will be stated in our results once the study is written. No identifiers will be included in the results. If they would like to withdraw completely we will not collect any further data and we will not include them in our analysis.

Procedures for Investigator to Withdraw subjects:

There is no circumstance that the patient will be withdrawn without their consent. There is no anticipated reason that a patient would need to be terminated from the study.

How participants will be identified:

Every patient that requires nifedipine starts at 30 mg XL daily.

If they break through (elevated BPs above 160/110) they will get extra nifedipine 10 mg(rapid acting). When a patient is noted to require a higher dose of medication, they will be asked by their physician if they are willing to participate in the study. If the patient agrees, a member of the research team will approach the patient and discuss the study with the patient. The next day patients will be randomized to be either in the 60 mg Procardia XL Q daily group vs the 30 XL Q 12h group.

Also if BPs are persistently above 150/105 (≥ 50% of the BPs over the first 24h after the first dose), the next day their dose will be increased to 60 mg and they will also be asked to participate in the study and consent will be obtained if they are agreeable to be randomized to receive either 60 XL daily or 30 XL Q 12h.

How research will be introduced to participants:

Once patient is noted to require a higher dose of medication either because they have severe range BPs despite their first dose of Procardia XL 30 mg or persistent elevated Bps ≥ 150/100 postpartum (or 160/100 for those with CHTN) the patient will be asked if
they are willing to participate in a study. This will initially be done by the physician taking care of the patient. If so, a member of the research team will be notified and then approach the patient. In a private setting, they will be introduced to the study and will be given as long as they need to decide whether they would like to participate in the study.
This is usually until the next dose is due (24h after the administration of the first dose of Procardia XL 30 mg).

How participants will be screened:

By looking at the antepartum and the postpartum patients that had insufficient response to 30 mg of Procardia XL (defined as those patients that received 30 mg of Procardia XL and required additional rapid acting nifedipine within the next 24h to improve control of BPs or whose BPs were persistently above 150/100 or 160/100 for CHTN in the postpartum period). Primary physicians taking care of these patients will be informed of this study and once they identify patients that meet criteria and are willing to participate in the study, they will notify one of the members of the research team. We will review clinical information from their medical records and if they do in fact meet all the requirements to participate in the study the patients will be approached to discuss the study in detail and obtain their consent.

Risks to subjects:

Overall there is minimal risk to subjects who participate in the study. In terms of the medication itself, calcium channel blockers are a class of drugs considered first line treatment by the American College of Obstetricians and Gynecologists to improve elevated BPs antepartum in cases of chronic hypertension and postpartum.

Small amount have been shown to cross the placenta, however to date no known association with birth defects have been found with reassuring long term follow-up of babies up to 1.5 years. It is not associated with adverse perinatal outcomes and furthermore, nifedipine does not appear to adversely affect uterine or umbilical blood flow.

It is a safe medication, however potential side effects include peripheral edema (most common side effect, dose related, 10-30%), flushing (23-27%), headache (10-23%), dizziness (23-27%), fatigue (6%), constipation (<2%), nausea (11%), and muscle cramps (8%). These are not life threatening, but in the case a patient can't tolerate the medication, they will be changed to another antihypertensive drug.

Risks associated with blood draw from a vein are uncommon but may include momentary discomfort at the site of the blood draw, possible bruising, redness, and swelling around the site, bleeding at the site, feeling of lightheadedness when the blood is drawn and rarely infection at the site of the blood draw.

Description of Procedures Taken to Lessen the Probability or Magnitude of Risks:

No special precautions will be taken due to the fact that this medication is routinely used for control of BPs in these patients.

As part of the routine management, BPs and vitals are monitored at regular intervals (every 4 to 8 h), together with monitoring of general well being and side effects.

Nurses will frequently assess symptoms and side effects will be documented and addressed by the physician taking care of the patient once the nurse notifies them.

In addition, standard safety measures for phlebotomy will be followed during blood draws for Procardia levels.

The primary investigator or co-investigator will follow these patients for at least 24h. During this time we will obtain data on side effects and vital signs from the patients medical record available to them.

Provisions for Research Related Harm/Injury

There is no anticipated research related harm for study subjects. There is a very small risk of adverse affects inherent to the medication but this is not due to participating in research. Medical personal will be readily available for any adverse outcome as is standard for all pregnant patients in such events.

Expected Direct Benefit to Subjects:

Each subject may be expected to directly benefit from participating in the study. Currently Procardia XL is a medication intended to be dosed every 24h, however we commonly see that towards the end of the 24h period there are elevations of patients' BPs, requiring sometimes additional doses of medication. We have been using Procardia XL off label in pregnancy as a twice daily medication with improved trends of BPs, however higher levels of medication at the end of the day with a twice daily dosing that would prevent these breakthrough elevated BPs has never been studied in a randomized controlled trial. Dividing high doses of medication might also potentially decrease discomfort from side effects such as peripheral edema, headache, dizziness, fatigue, constipation, nausea, and muscle cramps.

Benefits to society:

The purpose of this study is to investigate the mean plasma levels and standard deviations of Procardia at 24h after Procardia XL is administered as a 60 mg daily dose and the mean plasma levels after it is given as a 30 mg twice-daily dose. This will provide essential information to calculate an appropriate sample size for a future randomized control trial that will be appropriately powered to identify if different doses result in similar plasma levels or if twice daily medication achieves higher levels at 24h. We will then be able to determine if higher levels translate into improved control of BP in pregnant women and postpartum.

Provisions to Protect the Privacy Interests of Subjects:

The patients will be approached by the primary physician to determine if they are willing to participate in the study. Once they agree, the physician will notify the investigator. The patient will then be approached by a member of the study team. All research related discussions will be held in the patient's private room. Any questions will be answered and fully discussed to maximize patient comfort. Patients will be allowed time to consider participation and we will explain to patients that we will follow up their information (Bps, side effects, Procardia Levels) but will not contact them directly. We will also assure the patient all the steps that will be taken to protect their privacy.

Economic impact on subjects:

We do not see any foreseeable additional costs to subjects for participating in this research study. The patient is going to take the same dose of medication either once daily or in divided doses.
Internal funding will be provided by Mount Sinai for testing of Procardia plasma Levels and the individuals will not be responsible for the cost of the blood test.

Data for Assessing Potential Risks to Pregnant Women and Fetuses:

Calcium channel blockers are a class of drugs that have not been extensively studied in pregnant women with chronic hypertension. With an ever-increasing body of evidence describing the safety efficacy and minimal side effects of the calcium channel blockers outside of pregnancy, a number of authors have investigated their use in pregnancy. The mode of action to reduce systemic vascular resistance and its ability to improve urine output by increasing renal blood flow and by inhibiting the release of antidiuretic hormone make it a highly appropriate drug for use in hypertension in pregnancy
Nifedipine has been compared with methyldopa for treatment of pregnancy induced hypertension and has shown to be comparable in its antihypertensive action. Ismail et al reaffirmed its antihypertensive efficacy in pregnancy without any adverse fetal outcome.
Sibai et al compared bed rest with oral nifedipine in 200 women with preeclampsia between 26-36 weeks of gestation. They showed a significant reduction in the systolic and diastolic blood pressure with nifedipine as well as a reduction in the number of deliveries for severe hypertension. No difference in fetal outcome was noted between the 2 groups.
Fenakel et al suggested nifedipine was superior to hydralazine in the treatment of preeclampsia remote from term. They also noted an increase in the urine output and associated decrease in peripheral edema in 12 of the 24 women on this drug. Perinatal outcome was similar between the drugs.
It appears that nifedipine is at least as good as hydralazine in its antihypertensive effect, but its onset of action is less likely to be precipitous. No adverse effect in the fetus has been shown.
Research in animals has confirmed its efficacy in pregnancy without any significant effect on placental blood flow or compromise to the fetus.
When nifedipine has been used in acute severe hypertension in pregnancy, Doppler measurements of velocity waveforms in the uterine artery have remained unchanged. Morettu et al have showed similar findings with chronic use of the drug in preeclampsia. Using radioisotopes, Lindow et al were also unable to show any significant change in uteroplacental blood flow after a single dose of nifedipine.
Small amount have been shown to cross the placenta, however to date no known association with birth defects have been found with reassuring long term follow-up of babies up to 1.5 years.
Studies have also shown no alteration of fetal cardiac output of fetal heart rate.
Maternal side effects with nifedipine seldom occur and there is rarely a need to stop the drug as a result of these.

Description of the study design

This is a Pilot Study for a Randomized controlled trial comparing two groups: Patients receiving 60 mg of Procardia once daily and those receiving the same dose divided as 30 mg of Procardia XL Q 12h. This study is expected to last 24 months and during this period of time we are planning to recruit 20 patients (10 in each group). Approximately 2cc of blood will be obtained from each patient at 24h from the administration of the 60 mg of Procardia XL or the first dose of 30 mg after randomization in the group receiving twice daily dosing. This will be send to the laboratory at Mount Sinai Hospital where the levels of Procardia will be calculated.
We plan to report demographics and clinical characteristics of patients enrolled in the study. The distribution, variability, and confidence intervals of plasma levels will be reported for those randomized into the twice daily 30 mg and once daily 60 mg Procardia XL groups. Additionally, the distribution of blood pressure levels collected every 4 hours, within 24 hours after treatment, for each group will be presented descriptively. Patient reported side effects during treatment will be reported as frequencies and proportions. The intention of these preliminary data would inform the feasibility of a larger efficacy randomized controlled trial.

Description of the procedures being performed:

This is a Pilot study for a Randomized controlled trial comparing two groups: Patients receiving 60 mg of Procardia once daily and those receiving the same dose divided as 30 mg XL Q 12h.
This study will include all pregnant patients and patients up to 6 weeks postpartum who are between the ages of 18-55.
Exclusion criteria include
- All patients receiving other antihypertensive medication
- All patients with a contraindication to nifedipine: Hypersensitivity to nifedipine or other calcium – channel blocker, cardiogenic shock, concomitant administration with strong CYP34A inducers (rifampim, rifabutin, phenobarbital, phenytoin, carbamazepine, St Johns Wort) → significantly reduces nifedipine efficacy, impaired liver function→ Patients with hepatic impairment (liver cirrhosis) have a longer disposition half-life and higher bioavailability of nifedipine than healthy volunteers.
This study will be conducted on the labor floor, antepartum or postpartum floor at Mount Sinai West Hospital. When a patient's BP is persistently elevated after a dose of 30 mg of Procardia XL (requiring at least an extra dose of short acting nifedipine) the dose is increased to 60 mg Procardia XL.
Also if BPs are persistently above 150/105 (≥ 50% of the BPs over the first 24h after the first dose), the next day their dose will be increased to 60 mg and they will also be asked to participate in the study.
Patients will be randomly assigned to receive 60 mg of Procardia XL either once daily or divided in 2 doses of 30 mg given 12h apart.
Depending on the group the person gets randomized into they will receive 60 mg of nifedipine at 0h vs 30 mg of nifedipine at 0h followed by 30 mg extra at 12h, These medications will be administered by a nurse or physician on the floor.
At the end of the 24h (plus or minus 30 min) a blood sample (2cc) with be obtained and sent to Mount Sinai Hospital to determine serum Procardia levels. This blood samples will be stored until this research study is finished and will be disposed after. A total of 2 cc of blood will be obtained from each patient.
Also the patient will take a survey of side effects of the BP medication. BPs will be measured Q 4h and documented at 0h, 4h, 8h, 12h, 16h, 20h and 24h (plus or minus 30 min)

Description of the source records that will be used to collect data about subjects:

In order to collect data about the side effects, a member of the research team will provide a questionnaire to the patient at the end of the 24 h and all questionnaires will be placed in a locked cabinet in the PI's office in Mount Sinai West. All other data about demographics, pregnancy, as well as all BPs documented throughout the 24h period will be collected using labor and delivery electronic medical record system (Epic). Levels of medication will be obtained from the laboratory section.

Description of Data that will be collected including Long term follow up:

Protected Health Information (PHI) will be collected and used in the study. No PHI will be disclosed. Only study personnel will have access to subject information. The study investigators will collect medical information about the subject over the course of the study. Study data will be entered into a de-identified research secure password protected database, using a unique code numbering system. A code number linked to subject identity will be used instead of names. The code number will not be derived from any patient identifiers, such as patient name or medical record number. The record linking the subjects' name with their assigned codes will be kept on a password protected file on a secure departmental drive. Only the PI will have access to this file. All study forms will be kept private and stored in a locked file cabinet in a secure location in the office of the PI. The secure computerized research database will be on a password-protected file within the OB/GYN department at Mount Sinai West. The linked code and dates of service are the only patient identifiers to be collected onto the computerized database spreadsheet along with the subject's medical information needed for the purposes of the study. Once data collection and analysis is completed, the linked code and data will be deleted.

When and Where Consent will be obtained:

Anyone requiring 60 mg of procardia Xl will be approached to participate in the study.
A member of the research team will then review the consent with them. The investigator will give the potential subject the opportunity to ask any questions and have them answered. They will be given the opportunity to think about the study (only those investigators listed as study personnel and authorized to obtain consent, will obtain informed consent). Once a patient wishes to join the study and informed consent is obtained, the subject can participate. Each subject will receive a signed copy of the consent form. The subject can withdraw from the study at any time without any retribution.

Waiting period for obtaining consent

The patient will be given as much time as they need to consider consenting for the study.
The patient will be given as much time as they need to consider consenting for the study. Each patient that requires additional procardia during the first 24h after the initial dose of Procadia 30 mg XL is administered with be approached to participate in the study. They will be given time until administration of the second dose of Procardia is due (24h from the initial dose). At this time they will be given either 60 mg once or 30 mg followed by 30 mg at 12h.

What languages other than english will be used

Any language can be used as long as an approved interpreter is available for that language at the time of consent.

The primary investigator's primary language is spanish. This will also facility explanation of the study to the participating spanish speaking population.

Description of Health Information that will be viewed, recorded or generated:

See appendix for variables.

How PHI Will Be Protected from Improper Use or Disclosure

Primary outcome data to be collected includes: Serum Procardia level at 12h and 24h. Other information that will be recorded includes BP at 0h, 8h, 16 h and 24h and side effects such as peripheral edema (not present prior to initiation of treatment), headache, dizziness, fatigue, constipation, nausea, muscle cramps. Demographic data will also be collected such as age, race, BMI, gravity, parity. We will collect information regarding previous use of antihypertensive (before pregnancy or during pregnancy), reason for BP control (preeclampsia, CHTN, postpartum hypertension), timing of inclusion: Antepartum (gestational age), postpartum.

Description of Non-Health information that will be viewed or recorded:

Patients demographics including age, race, BMI, gravity and parity will be viewed and recorded.

Explanation why research could not be practicably conducted w/o access to and use of PHI:

In order to conduct this study we must look at the PHI in order to obtain information from the clinic, office and antepartum floor that will allow us to answer our research question.

Explanation why research could not be practicably conducted w/o a waiver or alteration of authorization:

We will be consenting patients under our care. As such, HIPPA authorization will be provided

How PI will be protected from improper use or disclosure:

Protected Health Information (PHI) will be collected and used in the study. No PHI will be disclosed. Only study personnel will have access to subject information. The study investigators will collect medical information about the subject over the course of the study. Study data will be entered into a de-identified research database, using a unique code numbering system. A code number linked to subject identity will be used instead of names. The code number will not be derived from any patient identifiers, such as patient name or medical record number. The record linking the subjects' name with their assigned codes will be kept on a password protected file on a secure departmental drive. Only the PI will have access to this file. All study forms will be kept private and stored in a locked file cabinet in a secure location in the office of the PI. The computerized research database will be on a password-protected file within the OB/GYN department at Mount Sinai West. The linked code and dates of service are the only patient identifiers to be collected onto the computerized database spreadsheet along with the subject's medical information needed for the purposes of the study. Once data collection and analysis is completed, the linked code and data will be deleted.

When and How PHI Will Be Destroyed:

The files containing the data and linking files (containing PHI) will be deleted once all data has been analyzed. This will likely be approximately within 1 year of study completion.
Location Where Data Will Be Stored

The research data file is stored on a secure "departmental" network drive and the file will be password protected.

Duration Data will be stored

Data will be stored until the data is analyzed, within 1 year from study completion.

Location where date will be stored:

The research data file is stored on a secure "departmental" network drive and the file will be password protected.

Steps That Will Be Taken to Secure the Data during Storage, Use, and Transmission

The study investigators will collect medical information about the subject over the course of the study. Study data will be entered into a de-identified research database, using a unique code numbering system. A code number linked to subject identity will be used instead of names. The code number will not be derived from any patient identifiers, such as patient name or medical record number. The record linking the subjects' name with their assigned codes will be kept on the computer in a separate secure folder. All files are password protected on a secure server.

Data Analysis Plan Including Any Statistical Procedures:

We plan to report patient demographics and clinical characteristics enrolled in the study. The distribution, variability, and confidence intervals of plasma levels will be reported for those randomized into the twice daily 30 mg and once daily 60 mg Procardia XL groups. Additionally, the distribution of blood pressure levels collected every 4 hours, within 24 hours after treatment, for each group will be presented descriptively. Patient reported side effects during treatment will be reported as frequencies and proportions. The intention of these preliminary data would inform the feasibility of a larger efficacy randomized controlled trial.