

**Bon Secours Richmond
Pharmacy & Therapeutics Committees
Recommendation for Nifedipine use as a Tocolytic**

Recommendation: MEC Approved

- Nifedipine is recommended for addition to formulary restricted to treatment of preterm labor.
- Immediate release nifedipine will be added to the L&D Pyxis stations.
- Nifedipine, immediate release, will be added to the drug file for treatment of preterm labor, to be given by the oral route only (not for sublingual use) with a message "not to be used for blood pressure control".
- Nifedipine should not be given sublingual, as is absorption is minimal by this route. Oral dosing produces higher levels that are reached more quickly.

Findings:

- Nifedipine is not FDA approved to inhibit labor contractions.
- Nifedipine is pregnancy category C which means studies have shown that the drug exerts animal teratogenic or embryocidal effects, but there are no controlled studies in women, or no studies are available in either animals or women.
- Nifedipine crosses the placenta barrier; therefore, possibly increasing the risk for fetal distress.
- Absolute contraindications include: eclampsia, preeclampsia, abruptio placenta, chorioamnionitis, fetal death, fetal anomalies incompatible with life, cervical dilatation greater than 4 cm, or effacement of 80% or more at presentation (McCombs, 1995; Monga & Creasy, 1995).
- After an attempt with alternative treatments, and if there are no contraindications, nifedipine should only be used in patients between 24 and 32 completed weeks of gestation, with a goal to prolong pregnancy to or beyond 32 completed weeks (Higby et al, 1993).
- Adverse effects seen with nifedipine use comprise of peripheral edema, headache, dizziness, tachycardia, and flushing.
- Due to serious reported events of cerebrovascular ischemia, acute myocardial infarction, conduction disturbances, fetal distress, death, and especially excessive hypotension and stroke associated with the use of sublingual nifedipine it is strongly advised to only use the sustained release forms when used in the treatment of hypertension.
- Extended release is approximately 90% absorbed, and has an onset within twenty minutes. Substitution of extended-release tablets for immediate-release capsules may be done on an equal milligram dose basis, with subsequent titration to effect.
- There is a four-fold increase risk of mortality associated with the use of immediate release nifedipine for treatment of hypertension.

Studies

Numerous studies have compared nifedipine use for tocolysis compared to ritodrine, magnesium sulfate, diltiazem and terbutaline: efficacy results have been similar with possible fewer side effects for nifedipine.

A recent meta-analysis, 2001, of beta-adrenergic agonists versus nifedipine found pregnancy was prolonged more than 48 hours significantly more frequently in patients receiving nifedipine. Statistically significant lower rates of respiratory distress syndrome, NICU admission and side effects were found with nifedipine. Neonatal deaths appeared to be lower with nifedipine, but the statistical significance was not demonstrated.

Calcium channel blockers for inhibiting preterm labour; a systematic review of the evidence and a protocol for administration of nifedipine.

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OBJECTIVE: To assess the effects on maternal, fetal and neonatal outcomes of nifedipine (and other calcium channel blockers) administered as a tocolytic agent to women in preterm labour. **METHODS:** Standard methods of the Cochrane Collaboration and its Pregnancy and Childbirth Review Group were used. All published and unpublished randomised trials in which calcium channel blockers were used for tocolysis for women in preterm labour between 20 and 36 weeks' gestation, were considered. **MAIN RESULTS:** The systematic review includes 12 randomised controlled trials with a total of 1029 participating women. No trials were identified in which calcium channel blockers were compared with a placebo or no alternative tocolytic treatment. Calcium channel blockers appear to be more effective than betamimetic agents in prolonging pregnancy for 7 days or longer, are much less likely to cause maternal side-effects and are associated with reduced neonatal morbidity. **CONCLUSION:** Calcium channel blockers (especially nifedipine) can be considered safer and more effective tocolytic agents than betamimetics.

Publication Types:

- Meta-Analysis
- Review
- Review, Academic

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Effectiveness of nifedipine versus atosiban for tocolysis in preterm labour: a meta-analysis with an indirect comparison of randomised trials.

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OBJECTIVE: To explore the effectiveness of nifedipine compared with atosiban for tocolysis in preterm labour. **DESIGN:** A systematic review of randomised controlled trials with meta-analysis using adjusted indirect comparison. **POPULATION:** Six hundred and seventy-nine women recruited in nine randomised trials evaluating the effectiveness of nifedipine versus beta-agonists, and 852 women recruited in four trials of atosiban versus beta-agonists. There were no trials comparing nifedipine directly with atosiban. **METHODS:** We performed meta-analysis with a technique involving an adjusted indirect comparison between nifedipine and atosiban using beta-agonists as the common comparator. This approach preserves the benefit accrued by randomisation in the original comparisons. **MAIN OUTCOME MEASURES:** Reduction in neonatal respiratory distress syndrome and delay in delivery by 48 hours. **RESULTS:** Nifedipine tocolysis was associated with a significant reduction in respiratory distress syndrome compared with atosiban (OR 0.55, 95% CI 0.32-0.97). It also increased the number of women whose delivery was delayed by 48 hours (OR 1.20, 95% CI 0.73-1.95), although this result was not statistically significant. **CONCLUSIONS:** When indirectly compared with atosiban, nifedipine tocolysis is more effective. In the absence of a direct comparison, our analysis provides a way to explore the potential benefits of nifedipine versus atosiban.

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3: *Obstet Gynecol.* 2001 May;97(5 Pt 2):840-7.

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Tocolysis with nifedipine or beta-adrenergic agonists: a meta-analysis.

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OBJECTIVE: To clarify the relative efficacy of nifedipine and beta-agonists for tocolysis. **DATA SOURCES:** The literature was searched in the following databases: MEDLINE 1965-1998, Embase 1988-1998, Current Contents 1997-1998, and the Cochrane Database for 1998. We also sought unpublished trials and abstracts submitted to major international congresses. Search terms were: "tocolysis," "nifedipine," "calcium channel blocker," "ritodrine," "terbutaline," and "salbutamol." **Methods of Study Selection:** Randomized controlled trials comparing tocolysis with nifedipine and beta-adrenergic agonists during preterm labor were reviewed. In cases with postrandomization exclusions, authors were contacted to obtain intent-to-treat results and to avoid analytical bias. We identified 11 published and two unpublished randomized trials. **TABULATION, INTEGRATION, AND RESULTS:** Data were extracted by two reviewers and analyzed by a blinded biostatistician with RevMan 3.1 software from the Cochrane Collaboration. We analyzed nine relevant randomized controlled trials that included 679 patients. Meta-analysis showed that nifedipine was more effective than the beta-agonists in delaying delivery at least 48 hours [odds ratio (OR) 1.52, 95% confidence interval (CI) 1.03, 2.24], or over 34 weeks (OR 1.87, 95% CI 1.11, 3.15). The agents did not differ as to the incidence of deliveries after 37 weeks (OR 1.29, 95% CI 0.85, 1.96) or the neonatal mortality rate (OR 1.51, 95% CI 0.63, 3.65). Treatment with nifedipine was interrupted significantly less often because of side effects (OR 0.12, 95% CI 0.05, 0.29) and led to better neonatal outcomes (fewer infants with respiratory distress syndrome: OR 0.57, 95% CI 0.37, 0.89) or transferred to neonatal intensive care units (OR 0.65, 95% CI 0.43, 0.97). **CONCLUSION:** With respect to neonatal outcome, nifedipine appears to be more effective than beta-agonists for tocolysis and should be considered for use as a first-line tocolytic agent.

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4: *Acta Obstet Gynecol Scand.* 1999 Oct;78(9):783-8.

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- [Acta Obstet Gynecol Scand. 2000 Jul;79\(7\):618-9.](#)

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Nifedipine versus ritodrine for suppression of preterm labor; a meta-analysis.

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BACKGROUND: Since large randomized clinical trials comparing the effectiveness of nifedipine and ritodrine in the suppression of preterm labor are lacking, we performed a meta-analysis on the subject. **METHODS:** We searched the databases Medline and EMBASE using the keywords 'nifedipine', 'ritodrine' and 'randomized' or 'randomised'. The studies were scored for blinding, method of randomization and type of analysis ('intention-to-treat' versus 'par protocol'). Subsequently, two by two tables were constructed using 'delay of labor by 48 hours or more', 'delay of labor beyond 36 weeks gestation', perinatal mortality, respiratory distress syndrome and admission to a

neonatal intensive care unit as end points. Homogeneity between the studies was tested with a Breslow-Day test. Pooled odds ratios were calculated in case homogeneity could not be rejected. RESULTS: We could detect ten studies that were published between 1986 and 1998, incorporating data of 681 patients. Nifedipine reduced the risk of delivery within 48 hours compared to ritodrine, but this difference was not statistically significant (odds ratio 0.85, 95% confidence interval 0.54 to 1.1). Nifedipine also reduced the risk of delivery before 36 weeks compared to ritodrine, and this difference was statistically significant (odds ratio 0.59, 95% confidence interval 0.39 to 0.90). We are not aware of studies reporting on long-term outcome. CONCLUSION: Since studies reporting on long-term neonatal outcomes are lacking, the choice between nifedipine and ritodrine can only be based on obstetrical and short-term neonatal outcomes. From that perspective, nifedipine should be the drug of first choice for the suppression of preterm labor.

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CALCIUM ANTAGONIST THERAPY OF PREMATURE LABOR

•PATIENT DATA/BACKGROUND:

•Preterm labor refers to spontaneous, regular, rhythmic uterine contractions with progressive cervical dilatation and/or effacement, with or without intact membranes prior to the 37th week of gestation (McCombs, 1995). Despite concerted efforts towards detection, prevention, and treatment of preterm labor, during the decade of the 1980s its incidence increased from 9.3% to 10.7% in 1989 (Monga & Creasy, 1995). A significant amount of perinatal morbidity and mortality is reported in infants under 28 to 30 weeks gestation. Including only non-anomalous infants, 8% of births are responsible for 75% of perinatal deaths (Leonardi et al, 1992); the survival rate for gestations of 24 weeks is 17%, increasing to 51% at 26 weeks, and 95% at 32 weeks Higby et al (1993). Amongst major morbidity findings, the incidence of intraventricular hemorrhage, necrotizing enterocolitis, and patent ductus decline significantly after 32 weeks, and respiratory distress is highest before week 36 (Monga & Creasy, 1995). Increasing gestation by even one week between 24 and 32 weeks is of significant benefit to the fetus (Higby et al, 1993).

•Tocolytic therapy is not indicated in every case of preterm labor, however, with one estimate suggesting as few as 9% of preterm deliveries would be acceptable candidates for either maternal or fetal reasons (Monga & Creasy, 1995). Eclampsia, preeclampsia, abruptio placenta, chorioamnionitis, fetal death, fetal anomalies incompatible with life, cervical dilatation greater than 4 cm, or effacement of 80% or more at presentation are among the contraindications to treatment (McCombs, 1995; Monga & Creasy, 1995). In the absence of any contraindication, tocolytic therapy should be reserved for pregnancies between 24 and 32 completed weeks of gestation, with a goal to prolong pregnancy to or beyond 32 completed weeks (Higby et al, 1993).

•Among the many clinical difficulties in assessing the effectiveness of any agent used as a tocolytic is the difficulty of accurately diagnosing preterm labor which will progress spontaneously to preterm delivery; in meta-analysis of 12 studies, 72% of "control" patients diagnosed with preterm labor in fact delivered at term without pharmacologic intervention (Monga & Creasy, 1995).

•RESPONSE:

•IN VITRO FINDINGS

•Substantial evidence shows that uterine muscle activity is dependent on extracellular calcium (Read & Wellby, 1986). Various calcium antagonists (nifedipine, nicardipine, isradipine, diltiazem) which block the slow voltage-dependent calcium channels, inhibit release of intracellular calcium from sarcolemmal stores, and increase efflux of calcium from the cell (Monga & Creasy, 1995), have all shown an ability to inhibit either spontaneous or induced contraction in isolated uterine tissue taken either at hysterectomy or cesarean section delivery. Onset of action within 10 minutes following diltiazem was demonstrated (Lechner et al, 1989), with complete inhibition of transducer-induced contraction apparent after 60 minutes. Nifedipine produced a concentration-dependent inhibition of potassium, oxytocin, and vasopressin-induced contractions (Ulmstem et al, 1978; Fiorman et al, 1979; Morizak et al, 1988). In a comparative study of nifedipine and nicardipine, time to onset of maximal inhibition was longer for nicardipine than for nifedipine, suggesting a difference in the site of action of the drugs. Nicardipine, which was found to be of greater potency, may also affect additional intracellular sites, while nifedipine's action is mainly at membrane receptors (Margaard et al, 1983).

•CLINICAL INVESTIGATIONS

•POST PARTUM EFFECTS

•The effects of the calcium antagonists nifedipine and isradipine on the intact uterus were investigated during the post-partum period following both therapeutic abortion and normal delivery (Ingemarsson et al, 1989). Five healthy women undergoing therapeutic abortions in the 16th and 22nd week of pregnancy were treated with prostaglandin (PGF_{2a}) 25 to 40 milligrams. Uterine activity was monitored by microtransducer throughout. After 3 to 5 hours of PGF_{2a} instillation, labor-like contractions were recorded for 30 minutes. At this time, patients received 30 milligrams of NIFEDIPINE orally, with decreased uterine activity recorded within 10 to 20 minutes (372 montevideo units versus 203 montevideo units) (Anderson et al, 1979). ISRADIPINE 0.5 milligram as an IV bolus injection was administered to 7 post-partum women who experienced spontaneous uterine activity, and as 1 milligram IV infusion over 15 minutes to another 8 women with oxytocin-stimulated uterine activity. The effect of isradipine in these women was compared with those in matched controls, and in women who received 0.25 milligram terbutaline by IV bolus injection. Uterine inhibition was seen within 1 to 2 minutes after isradipine injection and was sustained for 2 hours. A transient decrease in blood pressure was seen but hypotension was not recorded.

•COMPARATIVE THERAPEUTIC USE

•RITODRINE

•Nifedipine has been reported superior to ritodrine in the suppression of preterm labor in one study (Read & Wellby, 1986). Nifedipine was given in doses of 30 mg orally initially, followed by 20 mg orally every 8 hours for 3 days, with ritodrine being given by IV infusion initially at a rate of 50 mcg/minute, and increasing by 50 mcg increments every 10 minutes to 300 mcg/minute or until contractions ceased, or maternal tachycardia (140 beats per minute) or fetal tachycardia (180 beats/minute) occurred. Following 12 hours of intravenous ritodrine, the infusion was gradually reduced unless contractions recurred, and oral ritodrine 10 mg every 4 hours for 48 hours was administered. Nifedipine

was effective in suppressing uterine activity in 15 of 20 patients, compared to 9 of 20 receiving ritodrine; 7 of 20 patients given no treatment experienced suppression of uterine activity. Side effects occurred in 13 women receiving ritodrine (palpitations, anxiety), whereas flushing of the face, neck and chest occurred in 90% of patients given nifedipine.

- Nifedipine was comparable, but not superior, to ritodrine for delaying delivery for either 48 hours, 7 days, or until the 36th week of gestation. Fetal and neonatal outcomes were similar for both treatments. Maternal side effects were less frequent with nifedipine. Regimens compared sublingual nifedipine (10 mg) repeated at 20 minute intervals until contractions ceased, to a maximum of 40 mg within 1 hour (26 of 33 received 9 doses), then 20 mg nifedipine orally every 4 to 6 hours. Ritodrine was initiated at 50 mcg/minute infused intravenously, increased by 50 mcg/minute until a maximum of 350 mcg/minute was administered, uterine contractions stopped, or unacceptable side effects occurred. Tocolysis was successful (greater than 48 hours) in 6 of 8 patients with premature rupture of membranes treated with nifedipine and 6 of 6 treated with ritodrine. Treatment failures occurred in 15 patients begun on nifedipine and 16 begun on ritodrine. In each case, 5 patients were switched to the alternative regimen with successful tocolysis achieved in 3 patients each. Side effects were noted in 18 of 38 patients receiving ritodrine with EKG abnormalities or chest pain requiring discontinuation in 3. Only 5 of 38 nifedipine patients experienced side effects with none discontinued (Ferguson et al, 1990).

- In a prospective, randomized comparison of standard ritodrine IV/oral regimens (19 patients) vs oral nifedipine (30 mg initially, then 20 mg every 6 hours for 24 hours, then every 8 hours for 24 hours, then every 8 to 12 hours in 23 patients), no difference in suppression of preterm labor was noted. Patients had fewer subjective and objective complaints on nifedipine; infants born to the nifedipine group were statistically larger in birth weight and had fewer and shorter hospital admissions particularly in the ICU. No differences in umbilical blood gases were noted between the treatment groups (Bracero et al, 1991).

- TERBUTALINE

- Oral nifedipine and subcutaneous terbutaline were shown to be similarly effective in the initial treatment of premature labor (Smith & Woodland, 1993). In this trial, 52 women were randomized to either nifedipine 30 milligrams orally as a single dose or terbutaline 0.25 milligrams subcutaneously every 20 minutes until contractions stopped. Both nifedipine and terbutaline were effective, with success rates of 68% and 71%, respectively. Nifedipine-treated patients experienced fewer side effects; the majority of which were hypotension, flushing and dizziness. More than half of the patients given terbutaline noted side effects, predominantly irritability, fetal and maternal tachycardia.

- COMBINATION THERAPY

- VERAPAMIL PLUS RITODRINE

- VERAPAMIL was added to ritodrine in an attempt to both prolong pregnancy and reduce the maternal cardiac side effects induced by the beta sympathomimetic. Women experiencing preterm labor were randomly assigned either ritodrine alone or both ritodrine plus verapamil. Patients treated with ritodrine showed an average 28 day prolongation of pregnancy, compared to the 37 day prolongation with combination therapy (Rodriguez-Escudero et al, 1981).

- Earlier investigations with verapamil in the early 1970s could not show benefit because of dose-limiting cardiovascular side effects. No later studies with verapamil are cited in major reviews (Higby et al, 1993; Monga & Creasy, 1995; Leonardi & Hankins, 1992).

- NIFEDIPINE PLUS TERBUTALINE

- Combined use of nifedipine and terbutaline was successful in producing prolonged inhibition of preterm labor in a 31-year-old patient with complicated obstetrical problems. Oral nifedipine 20 mg 3 times daily in combination with oral terbutaline 5 mg every 4 hours prolonged gestation time for 55 days. No adverse effects to the infant were reported. (Kaul et al, 1985).

- In a randomized study of 80 patients with single pregnancies of less than 34 weeks gestation, sublingual nifedipine was as effective as IV magnesium sulfate followed by terbutaline in arresting and preventing idiopathic preterm labor. Nifedipine was dosed as 10 mg every 20 minutes to a maximum of 40 mg within the first hour of excessive uterine activity, followed by 20 mg orally every 4 hours for 48 hours, then 10 mg every 8 hours till 34 weeks gestation (Glock et al, 1993).

- FETAL EFFECTS

- The absence of Doppler waveform changes during nifedipine use in 11 pregnancies suggests that nifedipine does not adversely affect uteroplacental and human fetal blood flow. Doppler waveforms were reported from various arteries of the fetus such as renal arteries, umbilical arteries, ductus arteriosus and aortic valve. The uterine arteries were also studied. The results showed no significant difference in the pulsatility index in any of the vessels studied. Each mother had received 30 milligrams of nifedipine orally, followed by a 20 milligram oral dose 4 hours later. Fetal status was assessed by Doppler technique 5 hours after loading and 1 hour after the second dose of nifedipine (Mari et al, 1989). Nifedipine did not cause an increase in fetal bilirubin production when it is used as a tocolytic agent (Ferguson et al, 1989).

- CONCLUSION:

- With their potential efficacy for inhibiting contractility in myometrial tissue, calcium channel blockers may lower uterine contractility and aid prolonging preterm labor, although their use in this area should still be considered inconclusive and investigational. Current data also support that this is achieved with minimal adverse effects to the mother and fetus.

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NIFEDIPINE SUBLINGUAL ADMINISTRATION

•PATIENT DATA/BACKGROUND:

•Does sublingual nifedipine provide a shorter onset of action than orally administered nifedipine?

•RESPONSE:

•Nifedipine is a potent coronary and peripheral vasodilator, and is used in the treatment of congestive heart failure, acute pulmonary edema, angina pectoris, chronic hypertension and hypertensive emergencies or urgencies. Due to the desirability of a fast onset of action in these applications, particularly accelerated hypertension, sublingual administration has become common (Anon, 1991) although the US FDA has rejected official approval of the sublingual route for indication as lacking both safety and efficacy data (Messerli et al, 1991; Grossman et al, 1996). The usual sublingual method of administration is to have the patient chew the gelatin capsule then hold the contents sublingually for a few minutes (Brown et al, 1986; Eide et al, 1989; McAllister, 1986). However, the absorption of sublingual nifedipine appears to be minimal, and it has been recommended that for the shortest onset of therapeutic activity the capsule should be bitten and then swallowed with water (McAllister, 1986; van Harten et al, 1987). Attempting to pierce the capsule and transfer the contents to a syringe for subsequent sublingual administration (Bloomfield & Carter, 1996) is unreliable and not usually recommended. The liquid volume of the 10 mg nifedipine capsule is only 0.34 ml. As much as 67% of this volume can be lost using a syringe extraction-extrusion technique, reducing the delivered dose to less than 4 mg (Schumann, 1991). A sublingual spray dosage form of nifedipine is being tested in Europe (Kurkciyan et al, 1994).

•Onset of measurable response is within 5 to 10 minutes following sublingual dosing of nifedipine, somewhat slower than nitroglycerin, but sooner than with sublingual captopril (Anon, 1991; Angeli et al, 1991; Pastorelli et al, 1991; Bussmann et al, 1992; Grossman et al, 1996). Peak effects can be expected within 1 hour. First dose response is adequate in approximately 70% to 75%; repeat doses given 15 to 30 minutes later in nonresponders will result in adequate control in another 25% (Hirschl, 1995; Kurkciyan et al, 1994)

•Both cardiac and non-cardiac adverse effects can be encountered. Hemodynamic events such as flushing, tachycardia, and headache are usually not significant, but can be of concern particularly in hypovolemic patients or those with underlying coronary or cerebral artery disease. Use in hypertensive crisis associated with acute myocardial infarction or stroke may not be warranted due to potentially large or unpredictable changes in blood pressure, and other agents such as nitroglycerin or sublingual captopril have been recommended in these situations (Hirschl, 1995; Bussmann et al, 1992; Gifford, 1991; Pastorelli et al, 1991; Messerli et al, 1991). Serious adverse events associated with sublingual nifedipine include reports of aphasia with hemiparesis, electrocardiogram changes consistent with ischemia (T-wave depression or inversion) or frank myocardial infarction, sinus arrest, and fetal distress when used in eclampsia (Grossman et al, 1996). Non-cardiac complaints are associated with the strong mint taste of the liquid nifedipine and can include burning paresthesia of the mouth and throat (Schumann, 1991).

•Recent studies indicate that the absorption of nifedipine through the buccal mucosa is poor. Intubated patients incapable of swallowing have demonstrated only negligible absorption; when nasogastric tubes sealing the esophagogastric junction were deflated, rapid rises in serum concentration were apparent, suggesting gastric absorption (Schumann, 1991). Similar findings were noted following sublingual administration of a 10 milligram capsule in healthy volunteers. Subjects bit a nifedipine 10 milligram capsule without swallowing; this produced median maximal plasma levels of 10 ng/mL at 45 minutes with most of the dose recovered in the mouth (89%). However, when the capsule was bitten and then swallowed (with 150 mL water), mean maximal plasma levels of 71 ng/mL were observed at 30 minutes (van Harten et al, 1987). Following nifedipine 10 milligrams sublingually in 6 healthy subjects, peak serum concentrations averaged 42 ng/mL with a mean time to peak of 74 minutes, as compared to 100 ng/mL at 40 minutes following an oral dose. However, sublingual nifedipine achieved a measurable concentration more rapidly than orally administered nifedipine (Brown et al, 1986).

•CLINICAL STUDIES

•SUBLINGUAL NIFEDIPINE 10 to 20 milligrams was safe and effective in the emergency management of moderate to severe hypertension in 43 patients. Both 10 and 20 milligram doses produced significant reduction in blood pressure when compared to placebo. Effects were seen in one to five minutes and reached a maximum in 20 to 30 minutes. Only the 20 milligram dose of nifedipine significantly increased heart rate. Side effects were minimal in both treatment groups (Beer et al, 1981). In one series of over 100 patients, satisfactory responses were noted in all following single doses of either 10 or 20 milligrams, although patients with hypertensive encephalopathy, renal disease, or angina were slower to respond. No worsening of either cerebral or coronary symptoms were noted in this study. One death due to cerebral hemorrhage was not attributed to nifedipine therapy (Gonzalez-Carmona et al, 1991).

•Sublingual nifedipine (0.25 to 0.5 milligram/kilogram) was safe and effective in lowering blood pressure in 21 children (aged 8 to 16 years) with hypertensive emergencies. Results obtained were similar to those found in adults. Blood pressure was reduced within 30 minutes and remained decreased for over 6 hours (Dilmen et al, 1983).

•CONCLUSION:

•Although several studies have demonstrated the effectiveness of sublingually administered nifedipine in the treatment of acute cardiovascular disorders, there appears to be no pharmacokinetic advantage to this route of administration. Furthermore, it seems that the therapeutic effectiveness of sublingually administered nifedipine is due to oral

absorption. One study reported that 89% of a sublingually administered dose was recovered in the mouth, indicating poor buccal absorption. However, in another study, a measurable nifedipine level was obtained more rapidly with sublingual nifedipine than with orally administered nifedipine. Nonetheless, it has been recommended that the capsule should be bitten and then swallowed with water for the shortest onset of action.

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