INFORMATION BRIEF (RAPID REVIEW)

INTRAVENOUS NICARDIPINE IN HYPERTENSIVE EMERGENCY / CRISIS IN PREGNANCY

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
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TITLE: INTRAVENOUS NICARDIPINE IN HYPERTENSIVE EMERGENCY/CRISIS IN PREGNANCY

PURPOSE

To provide brief information on the effectiveness, safety and cost-effectiveness of Intravenous Nicardipine in Hypertensive Emergency/Crisis in Pregnancy. This assessment is initiated in response to a request from Maternal Fetal Medicine Specialist to support the potential expansion of off-label use of intravenous nicardipine in pregnant women, particularly in clinical scenarios where first-line agents such as intravenous labetalol are contraindicated, unavailable, or fail to achieve adequate blood pressure control.

BACKGROUND

Hypertensive disorders of pregnancy remain one of the leading causes of maternal and perinatal mortality, with an incidence of nearly 10%, posing short - and long - term risks for both mother and neonate. Sinkey RG et al (2020) reported, in pregnant women with hypertensive disorders, antihypertensive treatment is recommended when BP reaches ≥ 160 / 110 mm Hg to prevent serious complications. However, BP should not be lowered below 140 to150 mm Hg systolic or 90 to 100 mm Hg diastolic to ensure adequate uteroplacental perfusion.[1-6] When hypertension beyond 20 weeks of gestation and returns to normal levels postpartum, the National High Blood Pressure Education Program Working Group recommends that the term gestational hypertension be used. This group has categorised hypertensive disease of pregnancy into the following five groups (Table 1):

Table 1: Data adapted from the National High Blood Pressure Education Program: Working Group Report on High Blood Pressure in Pregnancy. [3]

Category	Definition
Gestational hypertension (Previously termed pregnancy-induced hypertension)	Hypertension develops during the pregnancy
	No proteinuria
	If the hypertension resolves by the 12th postpartum week, the diagnosis is changed to transient hypertension. (If preeclampsia does not develop and the elevated BP resolves postpartum, it is termed transient hypertension).
Chronic hypertension	Hypertension present before pregnancy or diagnosed before the 20th wk of gestation. (Hypertension is present at the time of conception).
	Hypertension that is diagnosed during the pregnancy and fails to resolve by 12 wk postpartum is retrospectively diagnosed as chronic hypertension.
Chronic hypertension with superimposed preeclampsia	Underlying diagnosis of hypertension
	Development of: • Worsening hypertension after 20 wk • New onset of proteinuria • Development of other signs and symptoms of preeclampsia
Preeclampsia	New onset hypertension. (Diagnosed when BP is elevated and proteinuria is present).

	More than 300 mg protein in a 24 - h urine collection
	The diagnosis is more certain if any one of the following is present: • Blood pressure > 160 mm Hg or > 110 mm Hg • Proteinuria > 2 g / 24 h or 21 by dipstick • Severe creatinine level > 1.2 mg / dL • Platelet count < 100,000 cells/mm^3 • Elevated liver enzymes • Persistent headache or other cerebral or visual disturbances • Persistent epigastric pain
Eclampsia	Tonic clonic seizure. (Tonic - clonic seizures due to preeclampsia or gestational hypertension).
	Any of the above hypertensive scenarios

Intravenous labetalol is internationally recognised as the preferred antihypertensive agent for severe hypertension in pregnancy due to its favorable safety profile and generally mild maternal side effects. However, neonatal complications such as bradycardia and hypoglycemia may occur, particularly at higher doses. Furthermore, beta - blockers should be administered with caution in patients with bronchospastic disease, reduced myocardial function, or baseline bradycardia. [4-16]

Nicardipine is a dihydropyridine calcium channel blocker that is usually given via an intravenous infusion that is titrated to response. Dihydropyridine calcium channel blockers lower blood pressure by acting peripherally and inhibiting calcium channels in the vasculature, lowering afterload. [17]

In Malaysia, intravenous nicardipine is registered under the brand name [redacted] manufactured b[redacted] [20] Intravenous nicardipine is listed in the Malaysian Ministry of Health (MOH) Drug Formulary as Nicardipine Hydrochloride 1mg/ml solution for infusion, and the specified indication is for the treatment of hypertensive crisis. [35]

Use in Pregnancy and Lactation:
Limited pharmacokinetic data indicate that intravenous nicardipine has low placental transfer and does not accumulate. Its use in the first two trimesters has not shown malformations or fetotoxicity. However, in the third trimester it may cause an undesirable tocolytic effect, and cases of acute pulmonary oedema have been reported, particularly in multiple pregnancies or with concomitant beta - 2 agonists. It should be avoided in such situations or in women with compromised cardiovascular conditions unless no alternatives exist. Nicardipine and its metabolites are excreted in breast milk at low levels, but due to insufficient safety data in infants, it is not recommended during breastfeeding. [19]

Pharmacokinetics:
Nicardipine is rapidly absorbed after intravenous administration with an onset of action in 5 to 15 minutes. Peak plasma levels are about 184 ng / ml, with steady - state concentrations (~ 157 ng / ml) achieved within 24 to 48 hours of continuous infusion. It is extensively protein bound, metabolised mainly by CYP3A4 into inactive glucuronide metabolites, and eliminated in a triphasic manner, distribution half - life approximately 6.4 hours, elimination half - life approximately 1.5 hours, and terminal half - life approximately 7.9 hours. Its clinical effects wear off within approximately 15 minutes after stopping infusion, and pharmacokinetics are not significantly altered in renal impairment. [20]

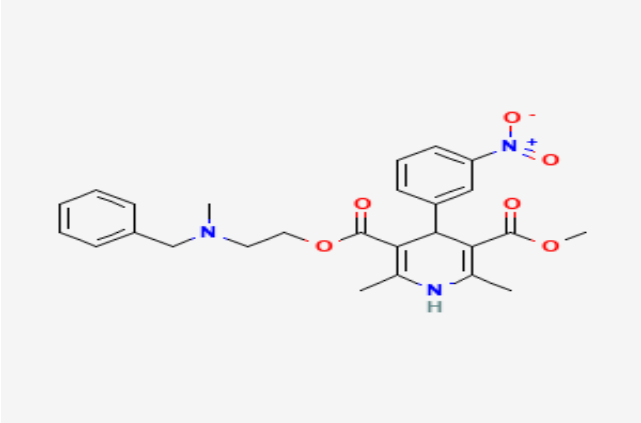

Figure 1: Chemical structure for Nicardipine. (Source: National Center for Biotechnology Information. PubChem Compound Summary for CID 4474, Nicardipine) [19]

Figure 2 : Nicardiin solution for infusion.
(Source : https://www.mims.com/malaysia/drug/info/ [redacted]

Based on Clinical Practice Guideline (CPG) for the Management of Hypertension (5th Edition, 2018), nicardipine is recommended as a parenteral agent for managing severe and acute hypertensive conditions, particularly Hypertensive Emergencies, but is not specifically listed as a primary drug for managing acute hypertensive crisis in pregnancy. For hypertension in pregnancy, the anti-hypertensive drugs of choice are methyldopa (first line) and labetalol (alternative first line), with nifedipine as the second line agent, while RAS blockers (ACEIs / ARBs) and thiazide diuretics are strictly contraindicated due to the risk of fetal anomalies. In the event of an acute hypertensive crisis (SBP ≥ 160 mmHg or DBP ≥ 110 mmHg), BP must be reduced within 30 to 60 minutes using acute agents like IV labetalol or oral nifedipine (10 mg stat dose) for rapid control, and parenteral magnesium sulphate is the drug of choice for preventing eclamptic fits. [22]

EVIDENCE SUMMARY

Two-hundred and twenty-two articles were retrieved from scientific databases of Ovid-Medline, Embase and reference list on intravenous nicardipine in hypertensive emergency / crisis in pregnancy using the following search terms "*hypertensive emergencies, pregnancy and intravenous nicardipine".* The last search was done on 23rd September 2025. Nine

studies were included in this review which consisted of two randomised controlled trial, five observational studies, one clinical study and one descriptive study.

EFFICACY/ EFFECTIVENESS

There were six studies retrieved on the effectiveness of intravenous nicardipine in hypertensive emergency / crisis in pregnancy.

Bij de Weg JM et al (2024) conducted a randomised controlled trial to evaluate whether intravenous nicardipine improves neonatal outcome, due to a quicker blood pressure regulation with minimal side effects compared to labetalol. This study was conducted from August 2018 to April 2022 in two Dutch hospitals, enrolling women ≥ 24 weeks with a singleton pregnancy and a first episode of severe hypertension (systolic ≥ 160 mmHg and / or diastolic ≥ 110 mmHg) requiring intravenous antihypertensive treatment. Participants (30 women (14 receiving labetalol and 16 receiving nicardipine)) were randomised (1:1) to intravenous labetalol or nicardipine, stratified by gestational age (< 34 / ≥ 34 weeks) and for participating center. Labetalol started at 20 mg / hr with 20 mg / hr increments every 30 minutes (maximum 2400 mg / day), and nicardipine at 1 mg / hr with 1 mg / hr increments every 15 minutes (maximum 10 mg / hr). Inadequate response led to crossover. Blood pressure targets were 130 to 155 / 85 to 105 mmHg, monitored frequently, with fetal monitoring until stabilisation. The primary outcome was a composite of adverse fetal or neonatal outcomes (severe Respiratory Distress Syndrome (RDS), Bronchopulmonary Dysplasia (BPD), Intraventricular Hemorrhage (IVH) IIB or worse, Necrotizing Enterocolitis (NEC) or perinatal death). Secondary outcomes included maternal complications (eclampsia, cerebral hemorrhage, liver rupture, pulmonary edema, ICU admission, death), treatment resistance, time/dosage to achieve BP control, delivery outcomes, and neonatal outcomes (preterm birth, bradycardia, asphyxia, hypoglycemia, NICU admission/duration). Data were analysed by intention-to-treat using appropriate parametric or nonparametric tests, with $p < 0.05$ considered significant.

The study found that overall, baseline characteristics were comparable in the two arms, except for occurrence of chronic hypertension (44 % in the nicardipine group versus 28.6 % in the labetalol group. The composite of adverse fetal or neonatal outcomes was not significantly different between the labetalol group (43%, n = 6) and the nicardipine group (25%, n = 4), yielding an Odds Ratio (OR) of 0.28 (95% CI 0.05 to 1.43, p = 0.12). Respiratory Distress Syndrome occurred 3.5 times more often in the labetalol group (42.9%) compared to the nicardipine group (12.5%, p = 0.04). For secondary outcome, the median time until blood pressure control was significantly faster with nicardipine (45 [15 – 150] minutes) compared to labetalol (120 [60 – 127.5] minutes, p = 0.05). Neonatal hypoglycemia occurred more frequently in the nicardipine group (31.3%, n = 5) versus the labetalol group (7.1%, n = 1), although the OR of 4.50 (95% CI 0.44 to 46.17) was not statistically significant. The median number of days admitted on NICU level 3 was higher in neonates born after maternal treatment with labetalol (26.0 [9.0 – 48.0]) compared to treatment with nicardipine (8.0 [4.0 – 13.5]). The author also reported that during the study, one fetal death occurred in the labetalol group due to severe growth restriction with poor prognosis, and one neonatal death in the nicardipine group at 29 weeks from multi - organ failure with NEC. One woman on labetalol required crossover to nicardipine for therapy resistance, achieving blood pressure (BP) control within 15 minutes at the lowest dose. Another developed severe

hypotension and CTG abnormalities that resolved after dose reduction. In the nicardipine group, mild side effects (gastrointestinal discomfort, headaches, reflex tachycardia) were reported without need for intervention. Overall, BP control was achieved faster with nicardipine than labetalol. Due to the small sample size, the authors concluded that definitive evidence regarding the optimal treatment choice could not be provided, noting that observed differences in RDS and neonatal hypoglycemia might be coincidental findings. [23]

Another randomised controlled trial was conducted by Elatrous S et al (2002) evaluated whether nicardipine is more effective than labetalol in the initial management of acute hypertensive emergencies in pregnancy. The study was conducted in the obstetric ward of the teaching hospital of Monastir, Tunisia enrolled 60 pregnant women over 18 with severe hypertension (systolic BP ≥ 170 mmHg or diastolic BP ≥ 110 mmHg) beyond 24 weeks gestation. Patients, after informed consent and ethical approval, were randomized to receive either intravenous labetalol or nicardipine. All participants also received magnesium sulfate for seizure prophylaxis. The primary objective for both groups was a sustained 20% reduction in systolic or diastolic blood pressure within a one - hour study period. Labetalol was administered as an initial 1 mg / kg bolus, followed by a 1.5 mg / kg bolus if needed, then a maintenance infusion. Nicardipine started with a 10 mg bolus over 5 minutes, with subsequent infusions at increasing rates if necessary, followed by a maintenance infusion. Blood pressure and heart rate were monitored at set intervals, and maternal and fetal side effects were recorded. Statistical analysis involved t - tests, χ^2 tests, and ANOVA, with a sample size of 30 per group determined to detect a 25% difference in success rates. The study found that the efficacy rates for achieving a 20% blood pressure reduction did not significantly differ between labetalol (63%) and nicardipine (70%), as indicated by an absolute difference of 7% (95% CI –16 to 30; p = 0.58). The time taken to reach this goal was also comparable (labetalol: 12.38 ± 6.25 min; nicardipine: 11.09 ± 3.68 min, not significant), implying similar speed of onset for the therapeutic effect. However, nicardipine required significantly more dose modifications (1.4 ± 0.4 times) compared to labetalol (0.5 ± 0.2 times, p = 0.05). While both drugs significantly lowered blood pressure within the first five minutes, nicardipine led to an overall significantly greater decrease in both systolic and diastolic BP ($p < 0.05$). Nicardipine was associated with a slight but significant increase in maternal heart rate ($p < 0.01$). Other maternal side effects were minor, and fetal tolerance was generally good, with only one transient deceleration noted in the labetalol group. [24]

A retrospective cohort study was conducted by Kim MK et al (2022) at Seoul National University Bundang Hospital from January 2018 to December 2020, investigated the management of hypertensive disorders of pregnancy (including chronic hypertension, gestational hypertension, pre - eclampsia (PE), superimposed PE, and eclampsia) in consecutive pregnant women delivering after 24 weeks gestation due to maternal hypertensive indications. Among 309 patients, 209 (68%) presented with uncontrolled blood pressure (systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg) on the day of delivery. Patients were divided into two groups : those receiving continuous intravenous nicardipine infusion (0.5 mcg / kg / minutes) for severe or PE-related hypertension, and those managed by intermittent intravenous boluses of labetalol or hydralazine for high BP spikes (systolic BP > 160 mmHg or diastolic BP > 110 mmHg). All patients also received magnesium sulfate for seizure prophylaxis. Maternal characteristics, all the measured BP data, other vital signs, the types and numbers of administered medications, and the cumulative doses were evaluated through electronic medical chart review. All BP data for 28 hours (from 4 hours before delivery to 24 hours after delivery) were analysed at 4 - hour intervals. The highest

BP data and the proportion of uncontrolled BP defined as a systolic BP of ≥ 160 mm Hg or a diastolic BP of ≥ 110 mm Hg in each time interval were extracted from each patient. Side effects were also monitored. The study comprised 135 patients with PE, 44 with gestational hypertension, 10 with chronic hypertension, 18 with superimposed PE, and two with eclampsia, with 53 out of 209 (25.4%) patients with uncontrolled BP receiving continuous nicardipine infusion. The nicardipine group had a significantly earlier mean gestational age at delivery (34.5 vs 35.1 weeks, p = 0.046) and a higher rate of eclampsia (4% vs 0%, p = 0.015). Patients in the control group required higher proportions of additional labetalol (14.1% vs 9.4%) and hydralazine (13.5% vs 5.7%) and larger median total dosages of these medications compared to the nicardipine group. Immediately before delivery, the nicardipine group had significantly higher mean diastolic BP (116 vs 111 mmHg, p = 0.043). However, between 16 and 20 hours postpartum, both systolic (137 / 80 vs 141 / 84 mmHg, p = 0.031) and diastolic BP (p = 0.035) were significantly lower in the nicardipine group. This trend of lower BP in the nicardipine group extended to the subgroup on oral anti-hypertensives, with significantly lower systolic and diastolic BP between 20 and 24 hours postpartum (132 / 80 vs 146 / 89 mmHg). While the nicardipine group initially showed a higher proportion of uncontrolled BP before delivery (38% vs 32%, p = 0.032), they exhibited lower, though not statistically significant, rates of uncontrolled BP detection during all postpartum intervals from eight hours onward. [25]

Nij Bijvank SW et al (2022) conducted an open access multicenter retrospective case series in two tertiary care hospitals in the Netherlands, the Isala Women's and Children's Hospital and the Erasmus Medical Center (MC). The study aimed to confirm the effectiveness and safety of using the intravenous calcium antagonist, nicardipine, for treating severe antepartum hypertension (SBP) of 160 mm Hg or more and / or diastolic blood pressure (DBP) of 110 mm Hg or more, measured at two separate times, 30 min apart, with a standard sphygmomanometer, based on phase V Korotkoff sounds in women beyond 20 weeks gestation. This study included 830 pregnant women. The study found that nicardipine achieved 100% treatment success in lowering blood pressure, with 77.4% (621 / 802) reaching target levels (SBP < 160 mmHg, DBP < 100 mmHg) within two hours; the median time to success was 76.5 minutes (5 to 3175). After one hour, blood pressure significantly decreased (all p < 0.001): median SBP from 170 to 152 mmHg, DBP from 105 to 91 mmHg, and Mean Arterial Pressure (MAP) from 127 to 112 mmHg; SBP < 160 mmHg was achieved in 63.4% (507 / 800) and MAP < 120 mmHg in 75.8% (608 / 800). Temporary DBP < 70 mmHg occurred in 42.7% (349 / 818), more often at Erasmus MC (46.8%) than Isala Hospital (36.3%, p = 0.001), resolving without clinical consequences. Nicardipine was discontinued in 21.5% due to adverse effects, including hypotension in 10.8% (90 / 830). Heart rate rose from 81 to 90 bpm (p < 0.001); reflex tachycardia (> 20 bpm) occurred in 11.5% (92 / 800), heart rate decreased in 20.6% (117 / 569), and severe bradycardia (< 40 bpm) occurred in 1.0% (8 / 830), leading to discontinuation in one case. Symptom incidence decreased significantly, headaches from 42.7% to 15.2% (p < 0.001) and nausea or vomiting from 27% to 5.3% (p < 0.001). Pulmonary edema increased from 0.5% to 1.7% (p = 0.027). Fetal outcomes included one case (0.1%) of distress due to maternal hypotension (DBP < 70 mmHg) during treatment requiring emergency cesarean, and fetal demise in 5.6% (46 / 815), mostly due to pregnancy termination or non - intervention policy. [26]

A retrospective study from Lan L et al (2024) evaluated the effect of intravenous infusion of nicardipine for the treatment of severe peripartum hypertension and to established the effects of oral labetalol combined with nifedipine controlled - release tablets (NCRT) after the

target blood pressure was achieved by intravenous nicardipine treatment in the management of severe peripartum hypertension in maternal intensive care units (ICUs). This study was conducted at Chongqing Health Center for Women and Children, China on December 2016 to August 2022, enrolling all maternal ICU patients treated with intravenous nicardipine for severe peripartum hypertension (SBP ≥ 160 and/or DBP ≥ 110 mmHg), excluding those below than 18 years. Blood pressure and heart rate were continuously monitored via arterial catheter, with target BP determined by oscillometry. Nicardipine infusion started at 2 mg / h (SBP 160 to 179) or 4 mg / h (SBP ≥180), adjusted by 0.5 to 1 mg / h to a maximum of 6 mg / h, aiming for BP < 140 / 90 mmHg. After stabilisation for 5 to 6 hours, oral labetalol (200 to 300 mg, up to 3 times / day) was introduced, with possible addition of nifedipine controlled - release tablets (NCRT, 30 mg bid) if BP rose again, nicardipine taper overlapped 2 to 4 hours. Treatment efficacy was defined as achieving target BP within 60 min for nicardipine and maintaining it under labetalol or labetalol + NCRT and failure was SBP ≥ 160 mmHg requiring multidisciplinary treatment (MDT) or resumption of nicardipine. Safety outcomes included hypotension (SBP < 90 or DBP < 70), tachycardia (> 100 bpm), bradycardia (< 60 bpm), pulmonary edema, and postpartum hemorrhage (> 500 mL). The included participants were 131 patients. This study demonstrated that initial stabilisation with intravenous nicardipine was highly effective, achieving the target BP (< 140 / 90 mmHg) in all patients (100%) within 60 minutes. The time required to reach this target was significantly shorter ($p < 0.05$) for those with initial SBP 160 to 179 mmHg (15.23 ± 10.10 minutes) compared to those with SBP ≥ 180 mmHg (28.75 ± 17.75 minutes). Regarding subsequent oral maintenance therapy, labetalol alone failed to maintain the target BP in the vast majority, succeeding in only 6.9% (9 / 131) of patients, which meant that 79.4% (104 / 131) required the combination protocol (oral labetalol + nifedipine controlled - release tablet (NCRT)) due to re - elevation to SBP 140 to 159 mmHg, and 13.74% (18 / 131) required restarting nicardipine due to SBP ≥ 160 mmHg. The labetalol + NCRT protocol proved highly successful, maintaining the target BP in 92.31% (96 / 104) of those who transitioned to it. While initial nicardipine showed minor, tolerable side effects like flushing (6.25% vs. 16.87%) and headache (8.33% vs. 18.07%), the introduction of the labetalol + NCRT combination significantly increased minor adverse maternal outcomes, including flushing ($p = 0.004$) and headache ($p = 0.003$) compared to labetalol alone. [27]

Nooij LS et al (2014) conducted retrospective chart review on 2006 to 2010 at Medical Center Haaglanden, The Netherlands to evaluate maternal and neonatal adverse effects in women with severe gestational hypertension (BP ≥ 140 / 90 mmHg without proteinuria) or preeclampsia (per International Society for the Study of Hypertension in Pregnancy (ISSHP) criteria) treated with intravenous labetalol or nicardipine. The primary outcome was successful BP control without needing additional or alternative antihypertensives, with treatment failure defined as BP > 160 / 110 mmHg despite maximum dosage. Secondary outcomes were maternal and neonatal side effects. Neonatal dysmaturity is defined as a birthweight less than 2.3rd percentile in comparison to the average birth weights in the Netherlands for that gestational age. For further research on the knowledge about nicardipine in comparison to labetalol, a meta - analysis was executed. This study, comparing 99 women treated with intravenous nicardipine to 76 women treated with labetalol for severe gestational hypertension or preeclampsia, found that nicardipine achieved adequate blood pressure control with a success rate of 97%, which was higher than the 84.2% success rate observed for labetalol. Analysis of maternal side effects showed that women treated with nicardipine reported headaches more often (39% vs. 28%), along with nausea (15% vs. 5%) and tachycardia (7% vs. 1%). Conversely, labetalol

treatment resulted more often in sudden hypotension leading to fetal distress (5.3% vs. 2% for nicardipine). Regarding neonatal outcomes specific to the retrospective study, neonates born from women treated with labetalol suffered more often from respiratory symptoms (28% vs. 10%), and neonatal hypotension needing treatment occurred more often in the labetalol group (5% vs. 3%), although these neonatal side effect results were not statistically significant. The subsequent meta-analysis combining this retrospective study with Elatrous S et al., showed that intravenous nicardipine had a significantly higher treatment success rate than labetalol. Maternal adverse effects were more frequent with nicardipine, particularly headache and tachycardia, while nausea was reported more often but not significantly. In contrast, labetalol was associated with more cases of hypotension leading to fetal distress. Neonatal side effects (hypotension, hypoglycemia, respiratory symptoms) were assessed only in the Nooij LS et al study, with neonatal hypotension slightly more common in the labetalol group, though not statistically significant. [28]

SAFETY

Adverse events

Ye F et al (2022) conducted a clinical trial to evaluate the effect of two concentrations of intravenous administration of nicardipine hydrochloride on nicardipine - related phlebitis in patients with preeclampsia. The study found that intravenous infusion of nicardipine hydrochloride at a constant dose but low concentration (LC group : 30 mg in 500 ml) is significantly superior to the high concentration (HC group : 30 mg in 250 ml) regimen in reducing nicardipine - related phlebitis in preeclampsia patients. Specifically, the LC group showed a significantly lower overall incidence rate of phlebitis (20.00% vs. 42.00%; $p < 0.05$), substantially lower severity of phlebitis, and a significantly longer time until phlebitis onset (42.08 h vs. 30.14 h; $p = 0.000$). Furthermore, the low - concentration administration resulted in reduced symptoms of inflammation and pain, indicated by a lower visual analogue scale (VAS) score (4.31 vs. 7.16; $p = 0.000$), a smaller indurated area (14.38 cm^2 vs. 22.21 cm^2; $p = 0.000$), and a higher average skin temperature (37.11 °C vs. 36.60 °C; $p = 0.000$). Crucially, the sources confirmed that neither concentration provoked any systemic adverse reactions in the gastrointestinal tract, cardiovascular system, or nervous system throughout the treatment. [29]

Matsumura H et al (2014) conducted a cross sectional study to investigate the placental transfer of nicardipine, intravenously administered to mothers with preeclampsia to manage severe hypertension, and postpartum disposition in breast milk. A total of 18 mothers with severe preeclampsia and treated with intravenous nicardipine to control the hypertension were enrolled, including 15 with singleton and 3 with twin pregnancies, including 2 with monochorinic diamniotic twins and 1 with dichorionic diamniotic twins. This study reported that intravenous nicardipine infusion is safe for the fetus and neonate due to its low levels of placental transfer and disposition into breast milk, while simultaneously being safe for the mother due to its dose adjustable controllability of maternal hypertension. Nicardipine dose and maternal plasma (MP) concentration were found to be linearly correlated, and significant linear correlations were also observed between MP concentrations and concentrations found in umbilical cord arterial plasma (UaP) and umbilical cord venous plasma (UvP). The mean placental transfer ratios were low: the UvP / MPd ratio was 0.12, and the UaP / MPd ratio was 0.12. Furthermore, nicardipine concentrations in postpartum maternal plasma and

breast milk (BrM) were significantly correlated, and the BrM / MP ratio ranged from 0.06 to 0.30. The mean relative infant dose (RID) was calculated to be very low at 0.082%, falling well below the 10% threshold generally considered safe for infants. No perinatal deaths occurred, and none of the 21 neonates had low Apgar scores. [30]

The European Medicines Agency (EMA) and its Pharmacovigilance Risk Assessment Committee (PRAC) recommended updating the product characteristics (SPCs) for nicardipine to reflect the risk of acute pulmonary oedema (APO) when used as a tocolytic, and reaffirmed that nicardipine use in indications other than acute, life - threatening high blood pressure (including severe pre - eclampsia) is no longer recommended. [31]

Regulatory approval

Several intravenous (IV) formulations of nicardipine have been approved by the United States Food and Drug Administration (FDA), including injectable nicardipine hydrochloride manufactured by [redacted] (New Drug Application [NDA] : 022276), [redacted] (NDA : 090664), and [redacted] (NDA : 211121). These formulations are indicated in the United States for the short - term management of hypertension in situations where oral therapy is not feasible or desirable. In Malaysia, an intravenous nicardipine formulation is approved by the National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia, under the brand name [redacted] (manufactured by [redacted]) with the registration number MAL22016011ACZ. According to Ministry of Health Medicines Formulary (MOHMF), intravenous nicardipine registered in Malaysia is indicated for the treatment of hypertensive crisis with caution of congestive heart failure, pulmonary oedema, suspected coronary ischemia, pregnancy, history of hepatic dysfunction or impaired hepatic function, portal hypertension, pre-existing elevated intracranial pressure, stroke, infants and children. [32,33.35]

COST-EFFECTIVENESS

There was no evidence retrieved on cost-effectiveness of the intravenous nicardipine hypertensive emergency / crisis in pregnancy.

According to the Malaysia Medicines Price Guide (MyPrime), the prices for intravenous nicardipine are listed in the table below: [34]

Table 2: Malaysia Medicines Price Guide (MyPriMe) for Nicardipine Hydrochloride. [34]

Product Registration Number	Generic Name	Brand Name	Packaging Description (Per Pack)	Unit (SKU)	Quantity (SKU)	Retail Price per Unit (RM)	Retail Price per Pack (RM)	Price Updated Year
MAL22016011ACZ	Nicardipine Hydrochloride 1 mg/ml Solution for Infusion	[redacted] 1MG/ML SOLUTION FOR INFUSION	10 pre-filled syringes of 10 ml	Pre-filled syringe	10	[redacted]		2024

CONCLUSION

Based on the above review, evidence demonstrated that intravenous (IV) nicardipine appeared to be effective and fast - acting antihypertensive agent for the management of hypertensive emergency / crisis in pregnancy. It achieves better blood pressure control and faster-acting compared to labetalol. Its safety profile is generally favorable, with most maternal side effects being minor such as headache and nausea. Fetal and neonatal exposure is minimal due to low placental transfer. While some studies suggest a potential for increased neonatal hypoglycemia and maternal pulmonary edema, these findings require further investigation with larger sample sizes. The risk of injection site phlebitis can be mitigated by using a lower concentration formulation. In Malaysia, intravenous nicardipine is approved for treating hypertensive crisis, but it must be used with caution in patients with specific conditions particularly in pregnant women, children, and individuals with pre-existing cardiac, pulmonary, hepatic, or neurological conditions. Its use as a tocolytic is strongly discouraged due to the risk of pulmonary edema. There was no study retrieved on cost - effectiveness of the intravenous nicardipine hypertensive emergency/crisis in pregnancy.

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