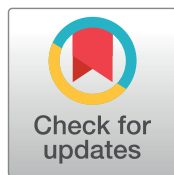




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ORIGINAL ARTICLE

Induction of labor with dinoprostone in hypertensive disorders of pregnancy: comparative analysis with normotensive pregnant women

Inducción del trabajo de parto con dinoprostona en trastornos hipertensivos del embarazo: análisis comparativo con gestantes normotensas

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Abstract

Objective:

To describe obstetric outcomes associated with the use of dinoprostone and its effectiveness in cervical ripening in pregnant women with hypertensive disorders of pregnancy compared to normotensive pregnant women.

Methods:

A retrospective cohort study was conducted at a tertiary-level hospital in Medellín, Colombia (March 2020 - October 2024). The study included pregnant women with singleton pregnancies, beyond 30 weeks of gestation, with a live fetus in cephalic presentation, and undergoing cervical ripening with dinoprostone vaginal insert. Women were excluded if they had used other ripening methods, had a favorable cervix at admission, or had an unclassified hypertensive disorder. Primary outcomes included successful cervical ripening, vaginal delivery, time to favorable Bishop score and to delivery, and indications for cesarean section. Adverse events considered were placental abruption, non-reassuring fetal status, tachysystole, and worsening of hypertensive condition.

Results:

A total of 400 patients were included (200 with hypertensive disorders, of whom 100 had severe preeclampsia). The success rate of cervical ripening was similar between patients with hypertensive disorders and healthy women (crude RR: 0.95, 95% CI: 0.88-1.03; adjusted RR for gestational age, maternal age, and parity 0.96, 95% CI: 0.88-1.04). The vaginal delivery rate was also similar (44% vs. 55%, $p = 0.16$). The median time to favorable Bishop score and to delivery was comparable between normotensive and hypertensive groups, even in severe cases. Cesarean delivery was mainly due to failed ripening and medical decision. Adverse events, except for tachysystole, were more frequent in the hypertensive group but did not reach statistical significance.

Conclusion:

Dinoprostone is effective in hypertensive pregnant women, including those receiving magnesium sulfate, with no significant differences compared to normotensive women.

Conflict of interest

The authors declare that they have no conflict of interest

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Resumen

Objetivo

Describir desenlaces obstétricos asociados al uso de dinoprostona y su efectividad en la maduración cervical en gestantes con trastornos hipertensivos asociados al embarazo frente a gestantes normotensas.

Métodos

Estudio de cohorte retrospectivo en hospital de tercer nivel en Medellín, Colombia (marzo 2020 - octubre 2024). Se incluyeron gestantes con embarazo único, mayores de 30 semanas, feto vivo en presentación cefálica y maduración cervical con óvulo de dinoprostona. Se excluyeron mujeres con uso de otros métodos de maduración, cérvix favorable al ingreso o trastorno hipertensivo no clasificado. Los desenlaces principales fueron maduración cervical exitosa, parto vaginal, tiempos hasta Bishop favorable y parto, e indicaciones de cesárea. Se consideraron eventos adversos como abrupcio placentario, estado fetal no tranquilizador, taquisistolia y empeoramiento hipertensivo.

Resultados

Se incluyeron 400 pacientes (200 hipertensas, de éstas, 100 con preeclampsia grave). La tasa de éxito en la maduración cervical fue similar en pacientes con trastornos hipertensivos y mujeres sanas RR crudo 0.95, IC 95%: 0.88-1.03, RR ajustado por edad gestacional, edad materna y paridad 0.96, IC 95%: 0.88-1.04. La tasa de parto vaginal fue similar 44 y 55% (p: 0.16). La mediana de tiempo a Bishop favorable y al parto fue comparable entre normotensas e hipertensas, incluso en casos graves. La cesárea se debió principalmente a maduración fallida y decisión médica. Los eventos adversos, excepto la taquisistolia, fueron más frecuentes en hipertensas, sin significación estadística.

Conclusiones

La dinoprostona es eficaz en pacientes hipertensas, incluso con uso de sulfato de magnesio, sin diferencias significativas frente a normotensas.

Remark

1) Why was this study conducted?

To evaluate the effectiveness and safety of labor induction with dinoprostone in pregnant women with hypertensive disorders associated with pregnancy compared to normotensive women. The rationale was that, although there are studies on labor induction with dinoprostone, there are gaps in the evidence regarding its effectiveness in women with hypertensive disorders associated with pregnancy, especially in those receiving magnesium sulfate. This is of relevance because clinical guidelines recommend vaginal termination of pregnancy to optimize maternal and neonatal outcomes. However, evidence on the success of cervical ripening and time to delivery in this subgroup is limited and often contradictory.

2) What were the most relevant results of the study?

1) Cervical ripening: The success rate of cervical ripening with dinoprostone was similar in hypertensive patients and normotensive patients (about 84-88%), with no significant statistical difference. 2) Vaginal delivery: The rate of vaginal delivery was comparable between both groups (44-55%), also without significant differences. 3) Time to cervical ripening and to delivery: Time measured in hours were similar between the groups, even in the subgroup which received magnesium sulfate. Furthermore, the decision to terminate a pregnancy by cesarean section was mainly influenced by medical criteria rather than by obstetric indication, especially in the most severe spectrums of pregnancy-associated hypertensive disease.

3) What do these results contribute?

Provide evidence that dinoprostone is an effective and safe method for cervical ripening in women with hypertensive disorders of pregnancy, including those with severe preeclampsia and magnesium sulfate use. This is clinically relevant because it supports the use of this method in a group of patients for whom there are fewer specific studies. Thus, it expands the evidence for medical decision making and contributes to reinforce the choice of vaginal delivery as the ideal route of gestational termination in these high-risk obstetric patients, in a safe and effective manner.

Introduction

Hypertensive disorders of pregnancy (HDP) are one of the most common complications of pregnancy and an important cause of maternal morbidity and mortality ¹. In Colombia, during the year 2023, HDPs were the leading cause of maternal mortality, accounting for approximately 20% of all deaths ². HDP include chronic hypertension, gestational hypertension, preeclampsia, severe preeclampsia, and eclampsia. To minimize complications, the American College of Obstetricians and Gynecologists recommends termination of pregnancy at established gestational ages according to the severity of the disorder. Thus, in chronic hypertension, gestational hypertension and preeclampsia without severity criteria, termination of pregnancy at 37 weeks is suggested, while in the case of severe preeclampsia, termination at 34 weeks is proposed ^{3,4}. Vaginal delivery is the preferred route of delivery because it provides better maternal and neonatal outcomes compared to cesarean section ⁵.

In the process of labor induction, pharmacological and mechanical methods are used to achieve cervical ripening ^{4,6}. Prostaglandin E2 (PGE2) preparations, such as misoprostol and dinoprostone, have gained wide acceptance for pharmacological induction of labor. In 1995, the U.S. Food and Drug Administration approved dinoprostone for vaginal insertion as a method of cervical ripening prior to labor induction ⁷.

Although several studies have evaluated the safety of labor induction in both uncomplicated term pregnancies and pregnancies with hypertensive disorders ^{8,9)} there are gaps in knowledge its effectiveness in pregnant women with HDP. Preliminary studies suggest that pregnant women with hypertension might require a lengthier time to reach cervical ripening compared with normotensive patients ^{10,11)} and hypertension has been identified as a risk factor for cesarean section due to failed induction ¹²⁻¹⁴.

In the case of severe preeclampsia, magnesium sulfate is required for the prevention of eclampsia, a treatment that some studies associate with tocolytic effects on the myometrium, which has been linked to a longer duration of labor induction and increased risk of failed induction ¹⁵⁻¹⁷. The frequent exclusion of severely hypertensive patients with preterm pregnancies and therefore receiving magnesium sulfate in induction studies significantly limits the available evidence for this high-risk subgroup and creates uncertainty about the influence of these factors on the efficacy of dinoprostone ¹⁸. Additionally, existing research is often limited by small sample sizes in patients with hypertensive disorders of pregnancy, which decreases the reliability of conclusions and makes it difficult to identify specific factors affecting ripening success at different grades of hypertension severity ^{10,11,19}. Based on this, the hypothesis proposed for this research is that patients with HDP have lower success in the rate of cervical ripening with dinoprostone, worsened by the use of magnesium sulfate, as well as longer time to delivery and a greater number of secondary adverse events.

Considering the limited previous research and inconclusive data, this study aimed to evaluate the effect of HDPs and its treatment on cervical ripening with dinoprostone.

Materials and Methods

Type of study and population

An observational, analytical, retrospective cohort study was conducted, comprising the analysis of information from medical records at the Hospital San Vicente Fundación (HUSVF), between March 2020 and October 2024. The San Vicente Fundación Hospital is a private institution that offers high complexity medical services in the city of Medellín to the population of the contributory and subsidized regime of the General System of Social Security in Health. At the time of this study, the HUSVF assisted an average of 1,400 deliveries in a year, had an Intensive Care Unit (ICU) for adults and neonates, and a Special Care Unit for pregnant women considered to be at high obstetrical risk.

The research was implemented with the approval of the research ethics committees of the HUSVF and the Faculty of Medicine of the Universidad de Antioquia and was exempt from obtaining informed consent according to the classification as non-risk research, as per resolution 8430 of 1993 of Colombia.

Inclusion and exclusion criteria

Patients with singleton pregnancy, gestational age greater than 30 weeks, live fetus, in cephalic presentation, with cervical ripening requirement conducted with a single ovum of dinoprostone 10 mg extended release were included. The decision on cervical ripening requirements was made by the treating obstetrician after evaluation of the characteristics of the cervix. Patients with concomitant use of other pharmacological or mechanical methods for cervical ripening, women with hypertensive disorder not correctly classified due to insufficient data, Bishop's index greater than 5 or favorable cervical status at admission were excluded.

Exposure. Patients with hypertensive disorders classified according to the criteria established by ACOG ⁴⁾ and requiring dinoprostone for cervical ripening.

No exposure. Patients without any chronic or pregnancy-associated hypertensive disorder requiring dinoprostone for cervical ripening.

Outcomes. Delivery route (vaginal delivery or cesarean section), successful cervical ripening defined as a Bishop's score equal to or greater than 6 after vaginal dinoprostone administration, following evidence reported in randomized studies and clinical guidelines on labor induction^{20,21}. Cervical ripening time and time to delivery, measured in minutes from dinoprostone insertion, adverse effects such as abruptio placentae, unsatisfactory fetal status, tachysystole or worsening of maternal hypertensive disease.

Collection of information

The list of patients who received dinoprostone was received and the medical records were reviewed consecutively to include those who met the criteria described until the pre-established sample size was reached. Two authors reviewed the medical records, with double review in cases when there were concerns about the quality or clarity of the information.

Study variables

Age (number of years completed), vaginal deliveries, gestational age (number of weeks of pregnancy at the beginning of labor induction), anthropometric classification of nutritional status according to the body mass index (BMI) recorded in the clinical history at admission and according to the WHO classification²²) normal weight, underweight, overweight, obesity grades 1, 2 and 3), baseline maternal morbidity (including autoimmune and hematological diseases, thyroid disorders, heart disease, arrhythmias, mental disorders, pregestational and gestational diabetes, chronic hypertension and neoplasms), prenatal controls, diagnosis with which induction of labor was indicated (including the maternal morbidities already described, term and post-term pregnancy, hepatobiliary disease), hypertensive disorders associated with pregnancy, fetal growth restriction, isoimmunization, prolonged rupture of membranes, fetal infections), type of hypertensive disorder (including chronic hypertension, gestational hypertension, non-severe preeclampsia and severe preeclampsia), Bishop's score according to the vaginal examination performed by the specialist prior to dinoprostone insertion, in some cases there was an objective numerical measurement of it, but in the majority it was classified as "favorable" or "unfavorable", route of delivery, cervical ripening time (from the insertion of dinoprostone until reaching favorable Bishop), indications for cesarean section, use of nifedipine, time of administration of magnesium sulfate (in minutes and concomitantly with dinoprostone). According to institutional protocol, if 24 hours after the insertion of dinoprostone there were no favorable cervical changes, it was considered failed ripening and the medication was removed to define the subsequent action and this was considered failure in ripening for this research, therefore, successful ripening was the one that obtained a cervix considered favorable by the obstetrician within the first 24 hours. Worsening of hypertensive disease was defined as the report in the clinical history of abnormal endothelial damage paraclinics, appearance of HELLP syndrome, eclampsia.

No reassuring fetal status (NRFS) defined as a circumstance during labor in which it was inferred that the fetus might be at risk of hypoxia or acidosis based on fetal monitoring or intermittent fetal cardiac auscultation.

Statistical analysis

Sample size. To have 95% confidence with 90% power, assuming a difference of 4 hours between the groups with and without pregnancy-associated hypertensive disorders in the time to obtain a mature cervix and assuming equal variances with standard deviation of 10 hours, 85 women per group were required. To have 95% confidence with a power of 80%, assuming that the group of women without hypertensive disorder would have a 75% and the group with hypertensive disorder a 60% chance of obtaining a mature cervix, 166 patients per group were required. To control for possible uncertainties in these assumptions and, to compensate for

possible exclusions, the sample size was increased to 200 patients per group. To evaluate the effect of magnesium sulfate on success and time to maturity, it was decided to divide the group of women with hypertensive disorder in half between those who did and did not receive the drug.

Management variables. Qualitative variables are presented with absolute number and proportion in terms of percentage. Discrete quantitative variables are presented as median and 25th and 75th percentiles or mean and standard deviation. To define the appropriate test for comparison of qualitative variables, compliance with the normality assumption was evaluated according to the Shapiro Wilk test. To respect the cohort design and to be able to have adjusted relative risks, Poisson regressions were used with the inclusion of the Huber/White/Sandwich robust estimator with cervical ripening as the outcome. Relative risks are presented with their respective 95% confidence intervals. In the adjusted analysis, variables that had previously been considered as confounders according to the literature review were included, although they did not show statistical significance in the univariate analysis. Given that the magnesium sulfate variable does not act in the dinoprostone-success relationship as a confounding variable but as a mediator, it was decided *a priori* to present the results of the HDP group discriminated according to its use²³. A significant absence of data was found in the BMI variable, a potential confounding variable, therefore, regression models were generated that exclude all cases with missing data and the stability of the risk estimate was assessed using multiple imputation. The Mann-Whitney U test was used to evaluate differences in times, because the data did not have a normal distribution. The level of statistical significance was set at 0.05. The analyses were performed with SPSS 29 software.

Results

Two hundred pregnant women without hypertensive disease and 200 hypertensive patients were included, of whom 100 received magnesium sulfate. The participant recruitment flowchart can be seen in Figure 1 and the demographic and obstetric characterization in Table 1. Gestational age was lower in the group of patients with severe preeclampsia, because these

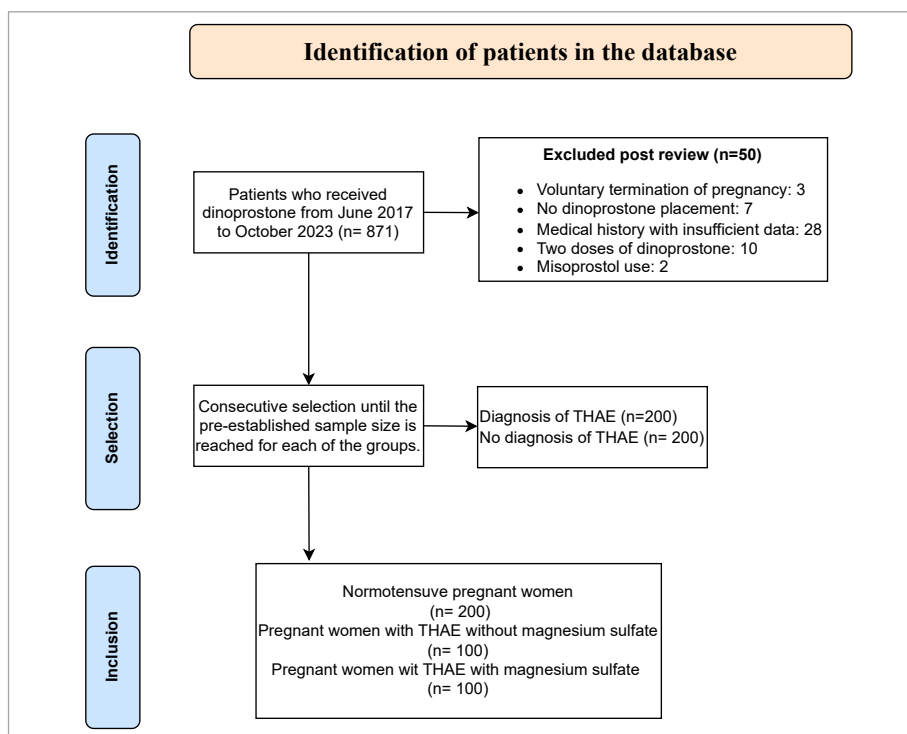


Figure 1. Recruitment flowchart. Flow chart for identification, selection and inclusion of participants and inclusion of participants

Table 1. Clinical characteristics of patients receiving dinoprostone for cervical ripening.

| | Normotensive pregnant women N = 200 | Pregnant women with pregnancy-associated hypertensive disorders | |
|-------------------------------------|--|---|---|
| | | THAE without magnesium sulfate N= 100 | Severe preeclampsia with use of magnesium sulfate N= 100 |
| Maternal age (mean (SD)) | 26.9 ± 6.2 | 28.5 ± 6.8 | 27.7 ± 7.3 |
| Gestational age (Mean (SD)) | 38 ± 1.4 | 37 ± 1.6 | 35.8 ± 1.9 |
| CPN (Median (Q1-Q3)) | 7 (6-9) | 7 (6-8) | 6 (5-7) |
| n (%) | n (%) | n (%) | |
| Nifedipine requirement | Not applicable | 48 (48) | 81 (81) |
| Active phase oxytocin requirement | 68 (34.0) | 39 (39) | 40 (40) |
| Parity | | | |
| Nulliparous | 137 (68.5) | 53 (53) | 56 (56) |
| Delivery =1 | 38 (19.0) | 31 (31) | 18 (18) |
| Delivery >1 | 25 (12.5) | 16 (16) | 26 (26) |
| Anthropometric classification (BMI) | | | |
| Normal | 29 (14.5) | 6 (6) | 5 (5) |
| Overweight | 68 (34.0) | 21 (21) | 25 (25) |
| Obesity grade 1 | 49 (24.5) | 24 (24) | 18 (18) |
| Obesity grade 2 | 9 (4.5) | 23 (23) | 13 (13) |
| Obesity grade 3 | 5 (2.5) | 9 (9) | 8 (8) |
| Underweight | 1 (0.5) | - | - |
| No Data | 39 (19.5) | 17 (17) | 31 (31) |
| Maternal comorbidity | | | |
| None | 74 (37.0) | 49 (49) | 70 (70) |
| Maternal congenital heart disease | 43 (21.5) | 5 (5) | 3 (3) |
| Other diseases | 28 (14.0) | 7 (7) | 4 (4) |
| Gestational diabetes | 21 (10.5) | 8 (8) | 5 (5) |
| Arrhythmias | 15 (7.5) | 2 (2) | 2 (2) |
| Chronic hypertension | - | 19 (19) | 11 (11) |
| Thyroid disease | 9 (4.5) | 7 (7) | 3 (3) |
| Pregestational diabetes mellitus | 3 (1.5) | 1 (1) | 1 (1) |
| Maternal anemia | 3 (1.5) | - | - |
| Systemic lupus erythematosus | 1 (0.5) | - | 1 (1) |
| Depressive disorder | 1 (0.5) | 1 (1) | - |
| Chronic hepatitis | - | 1 (1) | - |
| Rheumatoid arthritis | 1 (0.5) | - | - |
| Gestational thrombocytopenia | 1 (0.5) | - | - |

SD: standard deviations.

patients usually have induction of labor indicated when they meet severity criteria, once fetal viability has been achieved. Overweight and grade 1 obesity predominated in the groups of normotensive and preeclampsia patients, while in the group of non-severe hypertensive pregnant women, grade 1 and 2 obesity prevailed.

Maternal heart disease, comprising valvular disease and aortic coarctation, was the main concomitant disease in normotensive patients, whereas chronic hypertension predominated in non-severe hypertensive patients. The group called “other diseases” circumscribes diseases that occurred in only 1 or 2 patients, such as migraine, asthma, epilepsy, renal lithiasis, among others.

The main indication for cervical ripening in patients without hypertensive disorders was maternal heart disease, followed by fetal growth restriction and prolonged pregnancy. In patients with pregnancy-associated hypertension, this condition was the main indication for inducing cervical ripening (Table 2).

The success rate in cervical ripening was similar in patients with hypertensive disorders and healthy women (Table 3) (RR: 0.95, 95% CI: 0.88-1.03), and this was not affected when adjusting for the variables established *a priori*, gestational age, maternal age and parity (RR: 0.96, 95% CI: 0.88-1.04). No information was available on the presence of obesity, an important confounding variable, in 87 women, of whom only 9 had cervical ripening failure, 3 were normotensive, 2 were hypertensive without magnesium sulfate requirements, and 4 were

Table 2. Indications for cervical ripening with dinoprostone in normotensive and hypertensive pregnant women.

| | Normotensive pregnant women N = 200 | Pregnant women with hypertensive disorders associated with pregnancy | |
|---|-------------------------------------|--|--|
| | | THAE without magnesium sulfate N= 100 | Severe preeclampsia with use of magnesium sulfate N= 100 |
| THAE | - | 94 (94%) | 100 (100%) |
| Maternal heart disease | 37 (18.5%) | - | - |
| Fetal growth restriction | 35 (17.5%) | - | - |
| Term and late term pregnancy | 33 (16.5%) | - | - |
| Gestational and pregestational diabetes | 20 (10%) | 4 (4%) | - |
| Prolonged rupture of membranes | 16 (8%) | 2 (2%) | - |
| Arrhythmia | 12 (6%) | - | - |
| Cholecystopathies | 11 (5.5%) | - | - |
| Fetal malformation | 10 (5%) | - | - |
| Other maternal morbidity | 26 (13%) | - | - |

hypertensive with magnesium sulfate requirements. The model that includes obesity, which therefore excludes from the analysis all women without it, estimated a similar risk (RR: 0.97, 95% CI: 0.87-1.1) and the models with complete data from multiple imputation also did not modify the association found.

In the group of patients with hypertensive disorders, those who received magnesium sulfate had a frequency of successful cervical ripening identical to the group of patients who did not receive this drug (Table 3).

Oxytocin was used in the active phase of labor in 34% (68) of normotensive patients, 39% (39) of hypertensive patients, and 40% (40) of those receiving magnesium sulfate.

The time to maturation was similar among the three groups (Table 3), with no statistically significant differences between the group of women with HDP (Median 14.3, IQR: 9.4-24.0) and normotensive women (Median 13.3, IQR: 9.1-20.5) (p : 0.146).

Vaginal delivery was the predominant route of birth in the normotensive and non-severe hypertensive groups; however, in patients with severe preeclampsia, cesarean section was the most common route of delivery. There were no statistically significant differences between the normotensive and HDP groups (p = 0.16).

The time from the onset of maturation to the time of vaginal delivery was similar in the three subgroups (Table 3). No statistically significant differences were found between the normotensive and HDP groups with and without the use of magnesium sulfate (p = 0.49).

The most frequently reported maternal and fetal adverse effects are shown in Table 4.

Discussion

In our study, we found that the success rate in cervical ripening and vaginal deliveries, as well as the time to achieve them in the management with dinoprostone were similar between normotensive and hypertensive patients, including those who required magnesium sulfate.

In the literature, we only found one study that describes a success rate specifically up to the time to achieve cervical ripening like ours, with 44.6%, in a population that included a small sample of patients with HDP²⁴; however, they do not present specific values for this population. Most of the studies that evaluate the success of induction have as outcome the rate of vaginal delivery. From the data presented in Figure 3, on a meta-analysis of 2024 comparing oxytocin with vaginal dinoprostone, a success rate was calculated for dinoprostone that ranged from 75% to 98%, with a weighted average of 84.2%²⁵, these percentages are higher than those

Table 3. Clinical results of normotensive and hypertensive pregnant women who received dinoprostone for cervical ripening.

| | Normotensive pregnant women N = 200 | Pregnant women with pregnancy-associated hypertensive disorders | |
|---|-------------------------------------|---|--|
| | | THAE without magnesium sulfate N= 100 | Severe preeclampsia with use of magnesium sulfate N= 100 |
| Successful cervical ripening | 177 (88.5%) | 84 (84%) | 84 (84%) |
| Vaginal delivery | 111 (55.5%) | 53 (53%) | 44 (44%) |
| Time in hours to favorable cervix. Median (Q1-Q3) | 13.3 (9.1-20.5) | 13.6 (8.9-22.8) | 16.8 (10.4-24) |
| Time in hours to delivery Median (Q1-Q3) | 16.5 (11.4-26.1) | 15.6 (11.2-25.9) | 16.9 (12.8-28.7) |

*Q1 quartile 1 or 25th percentile, Q2 quartile 3 or 75th percentile.

Table 4. Adverse outcomes in normotensive and hypertensive pregnant women who received dinoprostone for cervical ripening.

| | Normotensive pregnant women N = 200 | Pregnant women with hypertensive disorders associated with pregnancy | |
|------------------------------------|-------------------------------------|--|--|
| | | THAE without magnesium sulfate N= 100 | Severe preeclampsia with use of magnesium sulfate N= 100 |
| Total, adverse outcomes | 25 (12.5%) | 14 (14%) | 23 (23%) |
| Non-reassuring fetal status | 11 (5.5%) | 7 (7%) | 11 (11%) |
| Tachysystole | 14 (7%) | 2 (2%) | 3 (3%) |
| Worsening of hypertensive disorder | NA | 2 (2%) | 8 (8%) |
| Abruptio | - | 3 (3%) | 1 (1%) |

achieved in our study (44%-55%). The differences may be explained by a bigger proportion of hypertensive patients in our study, a medical condition that leads more frequently to cesarean section, while the meta-analysis does not differentiate the indications for termination of pregnancy, specifically those related to hypertensive disorders.

In patients with HDP, including the subgroup that received magnesium sulfate, the time to reach a mature cervix was comparable to that of normotensive patients (13.6 h vs. 13.3 h, respectively), similar to those of Cañadas *et al.*²⁶, who reported an average time of 12.91 hours, but approximately 4 hours longer than that reported by Yan *et al.*²⁷, who strictly described the duration of cervical ripening in a population with small-for-gestational-age fetuses. However, these studies did not discriminate comorbidities or specific maternal indications, such as HDP.

The time from dinoprostone insertion to delivery was almost identical among normotensive, hypertensive and hypertensive patients treated with magnesium sulfate, but less than reported in the literature, where it ranged from 20 hours²⁷⁻²⁹ to 50.3 hours³⁰. This wide fluctuation could possibly be explained by the fact that these studies included patients with multiple indications for termination of pregnancy, the use of different dinoprostone protocols, with previous (12 hours) or later (>24 hours) withdrawals, concomitant use of oxytocin in unfavorable cervix and exclusion of patients with severe preeclampsia. The protocol presented here was more uniform in that no pregnant women received concomitant oxytocin, withdrawal of dinoprostone was up to 24 hours of insertion, and specific groups were made to measure the response to dinoprostone. In addition, we highlight that the administration of oxytocin as an adjuvant in labor was similar between groups, regardless of the use of magnesium sulfate, whereas previous studies do not detail the distribution of oxytocin use.

In the literature review based on current diagnostic criteria for HDP, indications for termination of pregnancy and for the use of magnesium sulfate, we found that Lapaire *et al.*³⁰, reported, similar to our findings, that magnesium sulfate does not prolong delivery time. On the other hand, Mei *et al.*¹⁷, in a recent multicenter cohort study, described an average labor time of 22 hours in the group treated with magnesium sulfate, 4 hours longer than in the group without this treatment. This contrasts with our results, where we found no significant differences in these subgroups. One possible explanation is that, in our study, a quarter of the indications for the cesarean section were the choice of the practitioner, without documentation in the medical record of an accepted indication, which could have reduced the number of

patients who would have achieved vaginal delivery in longer times. This also explains that in the group treated with magnesium sulfate, the cesarean section outnumbered delivery by a narrow margin of difference; compared to the group without the connotation of greater severity (normotensive and hypertensive without magnesium sulfate) where the dominant route of delivery was vaginal delivery.

The medical decision of the attending physician regarding the route of gestational termination in relation to the spectrum of disease severity is an important factor in our study, where the cesarean section rates were 44.5% in normotensives and 43.0% in hypertensives without severe compromise, values comparable to those of Huang *et al.*³¹, but higher than other studies in large populations with HDP (26% to 39%)^{13,14}. In patients with severe preeclampsia who received magnesium sulfate, the prevalence of cesarean section is consistent with previous studies suggesting this same trend, although with lower percentages^{17,18}.

Most of the patients in our study had BMI in the overweight or obese grade I range. Some studies suggest that an elevated BMI reduces uterine contractility and sensitivity to oxytocin¹⁵, other studies have identified significant differences in the success of labor induction^{32,33}, we found that the success rate of cervical ripening in our study was not affected in obese patients, although we did not have the BMI value for all our patients.

A strength of the present study is its focus on cervical ripening as the primary outcome, rather than successful induction defined as vaginal delivery within 24 hours, which allows us to specifically analyze the response to dinoprostone treatment without interference from additional intrapartum factors²⁴. In addition, we highlight the protocolized use of dinoprostone in a single center, which contributes to the homogeneity of the data and allows us to explore its effectiveness in patients with HDP, a subject little studied due to the predominance of misoprostol in literature, given its lower cost and greater thermal stability^{34,35}.

The main limitation of the study lies in its retrospective observational design, where the assessment of cervical ripening may be subject to inter-rater variability, in addition to the difficulty in determining the exact time at which cervical ripening is achieved. However, we consider that this possibly does not generate a differential bias, because normotensive patients presented clinical conditions that required strict monitoring of labor and therefore, it could be assumed that errors in the definition of the time at which delivery is achieved are randomly distributed between the groups, additionally the specific focus on cervical ripening allowed direct evaluation of the response to treatment, excluding intrapartum factors that could bias the results. There was an important loss of data in the obesity variable, however, the association remained stable in the model generated by multiple imputation. Finally, the low frequency of adverse events does not allow statistical testing, in addition to the fact that preeclampsia is a significant independent risk factor for a higher rate of maternal and fetal complications^{36,37}.

Conclusion

The use of dinoprostone for cervical ripening in patients with hypertensive disorders of pregnancy proved to be an effective strategy, with results like those obtained in normotensive patients, even in those who required magnesium sulfate.

The findings reported in this study are consistent with those reported in recent literature and reinforce the usefulness of dinoprostone as a viable tool in the induction of labor in THAE patients with and without magnesium sulfate requirements, contributing to the knowledge of safe and effective therapeutic options in a population at increased obstetric risk.

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