Gineco.eu [14] 49-51 [2018]
DOI: 10.18643/gieu.2018.49

Nifedipine side effects during the first 48 hours of premature labour treatment and their treatment impact in the maternal foetal outcome

Anila Karameta

University Hospital for Obstetrics & Gynaecology "Koco Gliozheni", Tirania, Albania

Correspondence:
Anila Karameta
E-mail: karametaanila@gmail.com

Abstract

Nifedipine is the first line tocolytic agent used in tocolytic protocols of University Hospital for Obstetrics & Gynaecology "Koco Gliozheni" from Albania for 9 years. It has a good tocolytic effect, fewer adverse and side effects compared to other tocolyticagents, easy way of administration and low cost. During our study period we randomly created groups from 480 total patients: the 1st group (n=280) applied nifedipine tocolysis; the 2nd group (n=200), patients pre-advised about nifedipine side effects and the 3rd group (n= 45) included patients of the 1st group that interrupted nifedipine tocolysis because of its side effects, but reentered in therapy after being advised about the importance of premature labour treatment and the ways to treat nifedipine side effects. About 7 patients who discontinuated nifedipine tocolysis for its side effects, after being supported psychologically, treated with fluid regimen and medicaments to relief the simptoms, underwent successfully to the nifedipine tocolysis. In the present study, all the patients who were psychologically prepeared to experience the nifedipine side effects and used fluid diet regimen, experienced less and lighter side effects. Vital signs profile monitoring is very important for a safe treatment. Nifedipine side effects detection/observation and treatment is very important for the successful treatment of premature labour, especially for a better outcome of both mother and foetus.

Keywords: *nifedipine, premature labour, side effects, treatment*

Introduction

Nifedipine was first found to have tocolytic effects in 1980[1]. Nifedipine is the tocolytic agent of choice in the everyday practice of our hospital for about nine years[2]. Nifedipine as a tocolytic agent is effective (i.e. it has less side and adverse effects than other tocolytic agents, it has an easy way of administration and have a low cost)[3].

Methods

In 480 cases, preterm labour was suppressed for more than 48 hours. All women presenting in preterm labour 22 to 34 weeks of gestation, between June 2012 and June 2017 from University Hospital for Obstetrics & Gynaecology "Koco Gliozheni" from Albania were included. Preterm labour was defined as regular painful uterine contractions, at a frequency of 2 or more per 10 minutes, regardless of whether there had been cervical changes. To improve homogeneity of the study population, only women for whom tocolysis with nifedipine was not contra-indicated were included. The informed consent was taken from all the patients.

Exclusion criteria for nifedpinetocolytic therapy were signs of abruption placentae, intrauterine infection, foetaldistress, or cervical dilatation of more than 5 cm.

During our study period we randomly created groups of patients:

- the 1st group (n=280) applied nifedipine tocolysis;
- the 2nd group (n=200), patients pre-advised about nifedipine side effects. They were recommended to applicate fluid therapy;
- the 3rd group (n= 45) included patients of the 1st group that interrupted nifedipine tocolysis because of its side effects, but reentered in therapy after being advised about the importance of premature labour treatment and the ways to treat nifedipine side effects (liquids; when necessary paracetamol 0.5 g; atenolol 0.025g).

Some patients who experienced severe hypotension (<80/50mmHg) or severe headache reentered successfully in nifedipinetocolysis this way.

We have monitored: demographic details, any risk factors for preterm labour, assessment of the preterm labour on admission, maternal arterial tension (SBP= systolic blood pressure and DBP=diastolic blood pressure), maternal heart rate (MHR), foetal heart rate (FHR), nifedipine side effects and every 15 minutes for the first hour, than after 2, 3, and 4 hours.

Maternal tachycardia was defined as a MHR of >140 beats per minute. Hypotension was measured as a blood

Received: *March 23, 2018*
Revised: *April 21, 2018*
Accepted: *May 03, 2018*

pressure of <90/60mm Hg and foetal tachycardia as a FHR of >180 beats per minute

A four-point Likert scale multiple-choice questionnaire [ranging from: 0 (no symptoms) to 3 (severe symptoms)], was used to assess the perceived degree of nifedipine side effects (flushing, headache, nausea, dizziness, shortness of breath).

All assessments were performed at predefined intervals from the onset of treatment.

Repeated measures analysis of variance was performed to identify any time-dependent association with nifedipine treatment.

Nifedipine has for sure vasoactive properties. Its usage can be accompained by some side effects for example: hypotension (various intensity), headache (at various intensity), maternal tachycardia (MHR>140 beats/minute), foetal tachycardia (FHR>180 beats/minute), dizziness, shortness of breath, palpitations, pulmonary-oedema, sleepingdisoders, dermatitis.

Nifedipine taken orally reaches the peak plasmatic levels 30-60 minutes after oral administration. Its biological half-life is two hours.

Statistical analysis

All the data were entered prospectively in a predefined data information sheet. The Statistical Package (Windows version 14.0; SPSS Inc, Chicago [IL], US) was used for analysis of all data.

Differences in categorical and continuous data were assessed using the Chi squared test and Student's t test, respectively. Maternal and foetal vital signs were analyze during repeated measures analysis of variance (ANOVA) with time of measurement as the within-subject factor to test whether any time dependent relationship existed. A P value of 0.05 or lower was considered statistically significant

Results

Maternal arterial tension (systolic and diastolic) usually has the lowest values 2-3 hours after the treatment onset, followed by plateau values after 12 hours.

About 12 patients experienced arterial hypotension (<90/60 mm Hg). Three of them experienced profound arterial hypotension (<80/50 mmHg). Two of them reenetered in nifedipinetocolysis, treating them with intravenous liquids.

MHR usually reaches the peak values1-2 hours after treatment onset. Seventeen patients experienced tachycardia (>140 beats/minute). Seven of them suffered of mitral regurgitation. Maternal tachycardia was treated with atenolol (25 mg every 12 hours).

FHR usually reaches the peak values 0.75-1-2 hours after treatment onset, returning than by baseline values. In five cases foetal tachycardia was encountered (>180 beats/minute).

Headache (at various intensity) usually happens 1-2 hours after treatment onset. It persists usually 12-24 hours. Patients who are recommended to use fluid therapy, usually experience headache at lower intensity.

Moderate headache was experienced in 389 cases (76%). Only 10 women interrupted therapy because of severe headache. 5 of them reentered in therapy treating them with liquids and Paracetamol (0.5 g every 8 hours).

We had two cases with dermatitis. It appeared 5-6 hours after the onset of the treatment and persisted till the end of tocolytic therapy.

Shortness of breath was generally found when MHR>105 beats/minute.

Nifedipine is accused less than other tocolytic agents about pulmonary oedema. We did not find any case of pulmonary oedema caused by niedipine,

We have studied foetal growth and foetal fluximetric parametres at the onset of treatment, during therapy and to the end of tocolysis.

We did not find any adverse nifedipine effect to the fetus. In 94 % of cases we treated premature labour with nifedipine for more than 48 hours. During the course of time we noticed that psychological support, fluid therapy and some symptomatic relief agents had a very good impact to the successful treatment of premature labor.

Treatment was discontinued in 12 women (2%) because of profound hypotension (<90/60 mmHg), 10 women (1.96%) because of severe headache and 1 woman (0.196%) because of severe flushing.

Only seventeen patients (3.33%) developed maternal tachycardia (≥140 beats per minute), and in 5 patients (0.98%) foetal tachycardia (≥180 beats per minute) was encountered.

Moderate headache was experienced in389 women (76%), flushing in 347 women (68%), dizziness in 14 women (2.7%), nausea in 10 women (1.96%) and shortness of breath in 12 women (2.35%).

Repeated measures analysis of variance with time ofmeasurement revealed asignificant reduction in maternal blood pressure and increase in maternal heart rate that plateau 12 hours after the therapy onset.

The FHR returned to baseline values 3 hours after commencing therapy. Repeated measures revealed that the main effect of time of measurement was significant for all four vital signs.

[MHR: F (3.9.561)=21.1, P<0.0001; SBP: F (7.6,1116)=18.5, P<0.0001; DBP: F(8.02.1179) =22.5, P<0.0001; FHR: F(5.8.813)=11.8, P<0.0001]. Maternal SBP and DBP both decreased linearly during the first 45 minutes of treatment [SBP: F (2.7.462)=46.9, P<0.0001;

DBP: F (8.02.1179) =22.5, P<0.0001] and subsequently remained at a low level without any significant change.

SBP: F (5.2.776) =1.5, P=0.19; DBP: F(5.5.810)=1.7, P=0.13 throughout the next 12 hours of monitoring. MHR and FHR followed a similar overall trend in that both increased for the first 60 minutes of treatment [MHR: F (3.3.565) =108.7, P<0.0001; FHR: F(3.3.531)=12.6, P<0.001].

Discussion

In the present study, all the patients who were psychologically prepared to experience the nifedipine side effects and used fluid diet regimen, experienced less and lighter side effects.

About 7 patients who did not take nifedipine continuously for its side effects, after being supported psychologically, treated with fluid regimen and medicaments to relief the simptoms, underwent successfully to the nifedipine tocolysis.

We examined fetal growth, fluximetric parametres and biophysical foetal profile, before the treatment, during the treatment and to the end of treatment. We did not find any adverse nifedipine influence to the foetus.

Nifedipine side effects good management increases the chances of a successful premature labour treatment and of a better outcome of both mother and foetus[4-9].

Conclusions

In general, the use of nifedipine as the first-line tocolytic was safe.

However close monitoring of vital signs is very important for a safe treatment.

The good management (i.e. prevention/detection/observation/treatment) of nifedipine side effects has a positive impact to the successful premature labour treatment and to the outcome of both mother and foetus. ■

Conflict of interests: The author declares no conflict of interests.

References

1. 1. Braunwald E. Mechanism of action of calcium-channel blocking agents. *N Engl J Med* 1982, 307, 1618-27.
2. 2. Ulmsten U, Andersson KE, Forman A. Relaxing effects of Nifedipine on the nonpregnant human uterus in vitro and *in vivo*. *Obstet Gynecol* 1978, 52, 436-41.
3. 3. Ulmsten U, Andersson KE, Wingerup L. Treatment of premature labor with the calcium antagonist nifedipine. *Arch Gynecol* 1980, 229, 1-5.
4. 4. Clinical Guideline No. 1(B). Tocolytic drugs for women inpreterm labour. London: Royal College of Obstetricians and Gynaecologists, 2002.
5. 5. King JF, Flenady VJ, Papatsonis DN, Dekker GA, Carbonne B. Calcium channel blockers for inhibiting preterm labour. *Cochrane Database Syst Rev* 2003, (1), CD002255.
6. 6. Oei SG. Calcium channel blockers for tocolysis: a reviewof their role and safety following reports of serious adverseevents. *Eur J Obstet Gynecol Reprod Biol* 2006, 126, 13745.
7. 7. Papatsonis DN, Van Geijn HP, Adèr HJ, Lange FM, Bleker OP, Dekker GA. Nifedipine and ritodrine in the managementof preterm labor: a randomized multicenter trial. *Obstet-Gynecol* 1997, 90, 230-4.
8. 8. Ferguson JE, Schutz T, Pershe R, Stevenson DK, Blaschke T. Nifedipine pharmacokinetics during preterm labortocolysis. *Am J Obstet Gynecol* 1989, 161, 1485-90.
9. 9. Manninen AK, Juhakoski A. Nifedipine concentrations in maternal and umbilical serum, amniotic fluid, breast milk and urine of mothers and offspring. *Int J Pharmacol Res* 1991, 11(5), 231-6.