AIM OF THE WORK

The aim of this study is to assess the efficacy of the nitric oxide donor isosorbide mononitrate on cervical ripening at 41 weeks'gestation.

PATIENTS

This study was conducted on 100 pregnant women recruited from February to October 2014 at the outpatient clinic of El Shatby Maternity University -Hospital .

Cases will be divided into 2 groups(50 cases in each group):

- **Group A:** 40 mg isosorbide mononitrate will be applied intravaginally in posterior fornix once at 41 weeks gestational age as an outpatient procedure.
- **Group B:** placebo will be applied intravaginally in posterior fornix once at 41 weeks gestational age as an outpatient procedure.

All patients must fulfill the following critria:

- Patients age are 18-35 years old.
- Uncomplicated singleton pregnancy.
- Pregnant women at gestational age of 41weeks.

Gestational age is considered reliable if patient had a reliable last menstrual period (LMP) defined by date, with history of regular menstruation and no oral contraceptives or lactation for at least 3 months prior to conception.

Exclusion criteria

- Pregnancy associated diseases as preeclampsia, diabetes, placenta previa or unexplained vaginal bleeding during pregnancy.
- Medical diseases as cardiac, pulmonary, renal or hepatic disease.
- Hypotensive conditions (blood pressure less than 90/60).
- History of severe persistent headache.
- Major cephalopelvic disproportion or fetal malpresentation.
- Fetal distress.
- Ruptured fetal membranes.
- History of cesarean delivery or major uterine scar surgery.
- Intolerance to isosorbide mononitrae.

The drug used:

Nitric oxide donor isosorbide mononitrate 40 mg tablet (Effox^{R}- Minapharm company).

METHODS

After approval of the local ethics committee an informed consent will be taken from every woman included in the study. Each patient will be subjected to:

- Complete history taking including medical history and relevant surgery.
- Complete obstetric history with special attention to last menstrual period.
- Routine investigations: complete blood picture, fasting blood sugar and complete urine analysis.
- General examination to exclude any systemic disease.
- Obstetric examination to assess gestational age, presentation and previous scars.
- Vaginal examination to assess the pelvis, Bishop score and the presenting part.
- Obstetric ultrasonography to assess the gestational age, presentation, fetal weight and the amniotic fluid index.
- Biophysical profile and Doppler to assess fetal condition.
- Cases will be divided into 2 groups (50 cases in each group):
  - Group A :40 mg isosorbide mononitrate (Effox^{R}- Minapharm company) tablet will be applied intravaginally in posterior fornix once at 41 gestational age as an outpatient procedure.
  - Group B : placebo will be applied intravaginally in posterior fornix once at 41 gestational age as an outpatient procedure.
- Follow up after 24 hours at outpatient clinic:
  1. Ask patient about any new symptoms.
  2. General examination: pulse,blood pressure and temperature.
  3. Vaginal examination to assess cervical ripening (Bishop score) by the same examiner.
  4. Obstetric ultrasonography to assess fetal condition.
  5. Follow up the mode of delivery.

RESULTS

This study included 100 pregnant women at gestational age 41 weeks, divided into two equal groups, each group contain 50 women.

Demographic data:
Age:

Table (3), shows the age distribution of patients in two groups. In group I the mean age was 28.6 years, in group II the mean age was 26.8 years, there was no significant statistical differences between the two studied groups regarding age (p>0.05).

Table (3): Comparison between the two studied groups regarding the age.

	Study group		Control group	
	No.	**%**	**No.**	**%**
Age				
< 20 years	12	12.0	12	16.0
20 – 25	20	40.0	22	44.0
> 30	18	36.0	16	32.0
Min. – Max.	18.0 – 34.0		19.0 – 33.0	
Mean ± SD.	28.6 ± 6.89		26.8 ± 7.98	
p	0.542			

Maternal weight:

Table (4), shows the maternal weight of patients in the two groups. In group I the mean weight was 76.9, in group II the mean weight was 77.9, there was no significant statistical differences between the two studied groups regarding weight (p>0.05).

Table (4): Comparison between the two studied groups regarding the weight.

	Study group	Control group
Weight		
Min. – Max.	56.0 – 82.0	58.0 – 85.0
Mean ± SD.	76.9 ± 8.6	77.9 ± 9.2
p	0.136	

Maternal history:

Table (5), shows the gravidity, parity and abortion of patients in the two groups. Gravidity in group I and II was 2.01, 1.98 respectively, there was no significant statistical differences between the two studied groups regarding gravidity (p>0.05). On the other hand parity and abortion also show no significant statistical differences between the two studied groups (p>0.05).

Table (5): Maternal history of the studied group.

	Study group	Control group
Gravidity		
Min. – Max.	**1.0 – 6.0**	**1.0 – 6.0**
Mean ± SD.	**2.76 ± 1.53**	**2.70 ± 1.58**
p	0.791	
Parity		
Min. – Max.	0.0 – 4.0	0.0 – 4.0
Mean ± SD.	1.28 ± 1.16	1.20 ± 1.16
p	0.725	

Blood picture and fasting blood sugar:

Table (6) shows the mean blood picture and fasting blood sugar in the two groups. It was found that there was no significant difference between the two groups regarding blood picture and random blood sugar (p>0.05).

Table (6): Blood picture and random blood sugar of the two studied groups.

	Study group	**Control group**
Hb		
Min. – Max.	9.0 – 12.0	9.0 – 12.0
Mean ± SD.	12.65 ± 2.25	12.86 ± 1.98
p	0.425	
WBCs		
Min. – Max.	3.9 – 10.4	3.8 – 10.5
Mean ± SD.	7.51 ± 2.27	7.62 ± 2.85
p	0.226	
RBCs		
Min. – Max.	3.97 – 5.30	4.11 – 5.54
Mean ± SD.	4.85 ± 0.47	4.92 ± 0.56
P	0.365	
	Study group	**Control group**
RBs		
Min. – Max.	75.0 – 92.0	77.0 – 95.0
Mean ± SD.	84.6 ± 8.23	86.5 ± 6.98
p	0.365	

Basic Bishope score:

Table (7), show median of Bishop base score in the two groups before and after 24 hours of NO and placebo respectively, in group I the median value before administration of NO was 4.0 and after administration was 5.0. In the control group the median value was 3.0 and the same after administration of placebo .there was a significant statistical differences between the two studied groups regarding the effect of NO on Bishope score(<0.5).

Table (7): Comparison between the two studied groups regarding the Bishope base score before and after 24 hours of administration

	Study group	Control group
Bishope base score before administration		
Min. – Max.	0.0 – 6.0	0.0 – 6.0
Mean ± SD.	3.72 ± 1.29	3.60 ± 1.54
Median	4.0	3.0
p	0.471	
Bishope score after administration		
Min. – Max.	0.0 – 7.0	0.0 – 7.0
Mean ± SD.	4.40 ± 1.81	3.68 ± 1.73
Median	5.0	3.0
p	0.031*	

Cervical Repining:

Table (8), shows the cervical ripening in two groups after 24 hours of application of NO and placebo respectively, in group I the cervical repining occurred in 60%of cases, in group II the cervical ripening occurred 20% of cases there was a significant statistical differences between the two studied groups regarding the effect of NO on cervical ripening ($p<0.05$).

Table (8): Comparison between the two studied groups regarding to occurrence of cervical ripening.

	Study group		Control group	
	No.	**%**	**No.**	**%**
Cervical ripening				
Positive repining	30	60.0	10	20.0
No change	20	40.0	40	80.0
p	0.001*			

Side effect:

Table (9), shows the incidence of headache in the two groups. In group I the incidence of headache was 70% , in group II incidence was 8%, there was a significant statistical differences between the two studied groups regarding incidence of headache ($p<0.05$). As regard to the incidence of Hypotension. In group I the incidence of hypotension was 24% , in group II incidence was 20%, there was no significant statistical differences between the two studied groups regarding incidence of hypotension ($p>0.05$).

Table (9): Comparison between the two studied groups regarding incidence of headache and hypotension.

	Study group		Control group	
	No.	**%**	**No.**	**%**
Headache				
Yes	35	70.0	4	8.0
No	15	30.0	46	92.0
p	0.001*			
Hypotension				
Yes	12	24.0	10	20.0
No	38	76.0	40	80.0
p	0.368			

The mode of delivery:

Table (10), shows the mode of delivery in the two groups. In group I the normal vaginal delivery was 64% and cesarean section was 36%. In group II normal vaginal delivery was 52% and cesarean section 48%. There was a no significant statistical differences between the two studied groups regarding to the mode of delivery (p>0.05).

Table (10): Comparison between the two studied groups regarding the mode of delivery.

	Study group		Control group	
	No.	%	No.	%
Mode of delivery				
Normal vaginal delivery	32	64.0	26	52.0
C.S.	18	36.0	24	48.0
p	0.224			

p: p value for Mann Whitney test
*: Statistically significant at p ≤ 0.05

Birth weight and Apgar score:

Table (11), shows the birth weight after delivery in two groups. In group I the mean birth weight was 3100.0 ± 385.5, in group II the mean birth weight was 3200.0 ± 425.0, there was no significant statistical differences between the two studied groups regarding birth weight (p>0.05). On the other hand Apger score also show no significant differences between the two studied groups (p>0.05).

Table (11): Comparison between the two studied groups regarding birth weight and APGAR score at 5 min.

	Study group	Control group
Birth weight		
Min. – Max.	2450.0 – 3500.0	2350.0 – 3750.0
Mean ± SD.	3100.0 ± 385.5	3200.0 ± 425.0
p	0.325	
APGAR score at 5 min.		
Min. – Max.	9.0 – 10.0	8.0 – 10.0
Mean ± SD.	9.65 ± 0.65	9.25 ± 0.56
p	0.542	