

The effect of pre-operative intravenous Cyklokapron on the amount of blood loss during and after caesarean section for anemic patients At Al Yarmouk teaching hospital in Baghdad.

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Abstract

Back ground: caesarean section carries significant morbidity and mortality over vaginal delivery. Anemia with hemorrhagic complications add significantly for this morbidity and mortality.

Aim of the study: to assess the effectiveness of Cyklokapron in reducing the intra-operative blood loss at time of caesarean section and postpartum hemorrhage in anemic patients and to evaluate its safety when used prophylactically.

Patients and method: A hundred pregnant women aged 19 - 41 years with term gestation were recruited in this randomized, case control, prospective therapeutic trial, which was conducted for a period of one year at Al Yarmouk teaching hospital \ Baghdad \ Iraq, the participants were admitted for caesarean section. They were divided randomly into two groups; the study group 50 patients received intravenous Cyklokapron pre-operatively and a control group matched for the indication of caesarean section, the intra-operative, post-operative blood loss and hematocrit were evaluated and compared for both groups.

Results: The intra-operative blood loss was measured in both groups, the total loss was significantly lower in the study group (170.12 ± 68.4 ml) compared to the control group (420.39 ± 130.6 ml) as P value was 0.0001. Concerning the post-operative blood loss, it was comparable in both groups and blood transfusion was required for two patients in the control group because of severe anemia (hemoglobin less than 8 gm/dl) with no transfusion in the study group and this difference was not significant statistically. The mean reduction in hematocrit was significantly lower in the study group compared to control group ($1.52 \pm 0.81\%$) versus ($2.58 \pm 0.85\%$) respectively and P value was less than 0.05.

Conclusion and recommendations: The current study revealed that Cyklokapron is significantly effective in reducing blood loss at time of caesarean section. We recommend further studies with higher doses and more patients to evaluate its effect in reducing the intra-operative loss and preventing postpartum hemorrhage.

Key words: Caesarean section, Cyklokapron, Postpartum hemorrhage

INTRODUCTION

Caesarean section is now one of the most common surgeries performed in Obstetrics, the cesarean delivery rate in the United States rises from early seventies to this decade to about 31 percent from all deliveries.⁽¹⁾ In 2007 the primary caesarean rate was

more than 30%.⁽²⁾ In Iraq and according to the Iraq Multiple Indicator Survey 2006, about 20% of deliveries were by Caesarean section.⁽³⁾ The mortality rate for Caesarian delivery was 13 per 100,000 in the developed countries.⁽⁴⁾ However in the UK the risk of death for the mother from caesarean delivery was three

times that of a vaginal birth.⁽⁵⁾ Hemorrhage contributes significantly for these mortalities, which were much higher in the developing world.⁽⁶⁾ The incidence of anemia during pregnancy depends on preexisting iron states and prenatal supplementation. It is more common among undernourished women and influenced by dietary intake.⁽⁷⁾ In our country and according to the Nutrition research institute in Iraq in 2014, anemia was a very common health problem occurring in 37.9% of pregnant women, 35.5% of non pregnant women and in lactating women for about 25.8% which adds significantly to maternal morbidity and mortality especially with caesarean delivery.⁽⁸⁾ Postpartum hemorrhage also contributes to morbidity because of the need for blood transfusion with all its hazards, about, 1% of women with uncomplicated vaginal deliveries received a blood transfusion, but the rate increases to about 5% for women undergoing a cesarean delivery.⁽⁹⁾ A blood loss of up to 1000 ml is seen on the average rate of blood loss during caesarean birth.⁽¹⁰⁾ After delivery of the the placenta , physiologic and hemostatic changes occur to decrease the amount of bleeding; strong myometrial contractions, increased platelet activity, massive release of coagulation factors and altered fibrinolytic activity.⁽¹¹⁾ After oxytocin administration, the first mechanism enhanced the haemostatic process, where as administration of Cyklokapron may facilitate this process by its effect on fibrinolytic system.⁽¹²⁾ It is an antifibrinolytic agent, which causes reversible and competitive inhibitor of plasminogen activation, and at much higher concentrations, a noncompetitive inhibitor of plasmin, the result of its action is to reduce blood loss, it is category B drug according to the FDA grading and is recommended by the WHO for the prevention of postpartum hemorrhage.⁽¹³⁾ In this clinical trial we used the drug to minimize the blood loss at time of surgery in anemic patients undergoing caesarean section.

Aim of the study:

to assess the effectiveness of Cyklokapron in reducing the intra-operative blood loss at time of caesarean section and postpartum hemorrhage in anemic patients and to evaluate its safety when used prophylactically.

PATIENTS AND METHODS

A randomized, case control, prospective therapeutic trial, conducted for a period of one year from July 2015 to June 2016, at Al Yarmouk teaching hospital \ Baghdad \ Iraq. After approval of the scientific committee of Al Yarmouk teaching hospital and Al Mustansiriya Medical college, a hundred pregnant women, aged 19-41 years with term gestation were

included in the study who were admitted for caesarean section. They were divided randomly into two groups; the study group 50 patients received intravenous Cyklokapron and a control group matched for the indication of caesarean section.

Inclusion criteria: pregnant term gestation anemic patients with hemoglobin 8-11 g\dl, normal BMI depending on prepregnancy weight.

Exclusion criteria: patients had history of coagulopathy and cardiovascular events, those received anticoagulants or aspirin before surgery; patients with renal or hepatic dysfunction and those with hypersensitivity to Cyklokapron.

After a detailed history and examination, laboratory tests including hemoglobin level, hematocrit, fasting blood sugar, renal and liver function tests were carried out in the laboratory of Al Yarmouk hospital. The patients in the study group received Cyklokapron in a dose of 10 mg\kg given by intravenous infusion in 50 ml dextrose solution over a period of 20 min within 2 hrs before the caesarean section as its half-life is 2 hours after intravenous injection.⁽¹⁴⁾ the surgery was performed under general anesthesia and after delivery of the fetus, 10 units of oxytocin in 500 ml normal saline were given for both the study and control groups. Monitoring of the vital signs, oxygen saturation and Electrocardiograph was carried out every 10 min; then every 15 min until the end of the procedure. Blood loss was measured intra-operatively by weighing all surgical materials such as packs and towels with a sensitive weighing scale (\pm 1-2 gm) before and after the surgery. The volume of blood in the suction container was measured only after the fetal delivery to exclude the volume of amniotic fluid sucked. The amount of intra-operative blood loss (ml) was obtained by subtracting the weight of towels before surgery from the weight of the towels after surgery with the addition of the volume in the suction container, the duration of surgery was recorded. Post-operative blood loss was evaluated by observing the number of vaginal pads used by the patient after the procedure up to 24 hrs., all the patients were sent for hematocrit 24 hrs. post-operatively. All the patients were encouraged to start breast feeding, ambulation and early leg exercise as soon as possible post-operatively.

Statistically: The values were expressed in means with standard deviations and medians with ranges. The significance of difference in means was tested by the student t- test for two independent means. A P value <0.05 was considered as significant

RESULTS

The present study included a total of hundred women who were divided into two groups; 50 patients as a study group and 50 patients as a control group and as shown in table 1 below which clarified the demographic data of both groups, there was no statistically significant difference between the two groups concerning their age, BMI, gravidity, gestational age and duration of surgery as the P value was more than 0.05.

Table 1: The demographic data of the study and control groups.

parameter	Study group (n= 50) mean± SD median (range)	Control group (n =50) mean± SD median (range)	P-value
Age (years)	27.04 ± 5.27 28 (19-40)	28.72± 6.58 28 (21-41)	0.125
BMI(Kg\m ²)	22.02 ±3.03 24 (19-25)	21.08 ± 2.17 23 (19-23)	0.88
Gravida	3.65±0.9 3 (2-5)	3.54 ±0.99 3 (2-5)	0.91
Gestational age (weeks)	38.5± 1.4 38 (37-41)	38.8± 1.28 38 (37-40)	0.24
Duration of surgery (minutes)	49.12±7.09 52 (42-56)	51.58± 8.09 55 (43-59)	0.109

In this work both the study and control groups were matched for the indication of caesarean section to minimize the effect of variable amount of blood loss with different indications for caesarean section as shown in table 2 below.

Table 2: Indications of caesarean section in the study and a matched control group

Indication for caesarean section	Study group (n=50)	Control group (n=50)
Breech presentation	6	6
Dystocia	5	5
Fetal distress	4	4
Previous 1 scar	8	8
Previous 2-3 scars	15	15
Previous 4 scars and more	12	12

We estimated the blood loss during the procedure and the total loss was significantly lower in the study group (170.12 ±68.4 ml) compared to the control group (420.39 ±130.6 ml) as P value was 0.0001 and this is shown in table 3

Concerning the blood loss after the procedure, it was comparable in both groups (2-3 pads partially soaked) and blood transfusion was required for 2 patients in the control group because of severe anemia (Hb < 8 gm\dl) with no blood transfusion in the study group and this difference was not significant statistically.

Table 3: Estimated blood loss in the study and control groups.

Parameter	Study group mean± SD median(range)	Control group mean± SD median(range)	P-value
Intraoperative packs wt gain (postop. Wt - preop. Wt) (ml)	68.32 ±44.85 98 (15- 280)	263.8 ±171.37 254 (80-930)	0.0001
Suction drain (ml)	90.8 ± 35.87 110 (50-200)	240.4 ± 115.36 278 (100-450)	0.0001
Total amount of intraoperative blood loss=packs wt+ suction drain (ml)	170.12 ±68.4 230 (75-460)	420.39 ±130.6 410 (190-1120)	0.0001
Postoperative blood loss over 24 hrs (No. of vaginal pads)	2.3	2.8	0.65
Blood transfusion (No. of patients)	0	2	0.15

The hematocrit (PCV) was measured in both groups pre-operatively and 24 hrs post-operatively as it is a better predictor of acute blood loss than hemoglobin level. Preoperative PCV was comparable in the study and control groups (31.96± 3.18 %

Versus 31.08±3.25 % respectively) as P value was 0.175, while the post-operative PCV was lower in the control group (28.84 ±2.07%) than the study group (31 ± 2.49%) and this difference was statistically significant as P value was 0.0001.

The mean of the PCV reduction was significantly lower in the study group compared to control group (1.52 ± 0.81%) versus (2.58±0.85%) respectively and P value was less than 0.05 as shown in table 4.

Table 4: Pre-operative and post-operative hematocrit level in the study and control groups.

Parameter	Study group mean±SD median(range)	Control group mean± SD median(range)	P-value
Preoperative PCV%	31.96± 3.18 % 31 (25-34)	31.08±3.25 % 30 (24-34)	0.175
Postoperative PCV%)	31 ± 2.49% 30 (24-33)	28.84 ±2.07% 28 (23-32)	0.0001
Mean reduction in PCV %	1.52 ± 0.81% 1.2 (0-2)	2.58±0.85% 2.5 (1-5)	0.0001

Concerning the safety of the drug studied, two cases in the study group complained from nausea and vomiting which resolved with metoclopramide injection, no other significant adverse events such as vascular events up to 24 hrs post-operatively and the urine output was normal in both groups.

DISCUSSION

N Pregnancy induces some physiological changes that often compensates for the blood loss at time of delivery, one of the most significant changes is plasma volume expansion with a lower red cell increment resulting in a normally decreased hematocrit with the development of physiological anemia; However anemia is an extremely common problem, the World Health Organization reported the prevalence of anemia in pregnancy in the middle east to be 44.2%.⁽¹⁵⁾ We studied anemic patients due to its high prevalence in Iraq, a study done by AL- Shawi showed that (9.6%) of primigravida pregnant women were anemic while (45.8%) of multigravida pregnant women were anemic.⁽¹⁶⁾

Placental delivery is a hyperfibrinolytic state, we decided to conduct a study using a drug which is an antifibrinolytic agent in patients undergoing caesarean delivery and the outcome was that the blood loss at time of surgery was significantly lower than the control group (170.12 ±68.4 ml) versus (420.39 ±130.6 ml) respectively as P value was 0.0001 and this was in agreement with a study carried out by Gaietal in china (2004) who found that cyklokapron statistically reduced the amount of blood loss from time of placental delivery till two hrs postpartum and its use

was not associated with any side effects or complications.⁽¹⁷⁾ A similar study done by Movafegh,et.al. which revealed that mean blood loss was significantly less in the study group compared with the control group for both intra-operative bleeding (262.5 ± 39.6 vs 404.7 ± 94.4 ml) and post-operative bleeding (67.1 ± 6.5 vs 141.0 ± 33.9 ml); P<0.05, respectively.⁽¹⁸⁾ Similar results observed by Abdel-Aleem in Egypt (2013) who studied seven hundred and forty women (373 in study group and 367 in control group) and the blood loss was 241.6 ml in the study group versus 510 ml in the control group.⁽¹⁹⁾

In this study we chose a dose of 10 mg\Kg as we use it prophylactically in patients without bleeding and we found a significant reduction in the lost amount of blood, however other studies used higher doses of cyklokapron like Ducloy-Bouthors et.al. as their study was conducted on patients developed postpartum hemorrhage ,the study showed a significant reduction in the amount of bleeding⁽²⁰⁾,other study in india found that 15mg\Kg was more effective than 10mg\Kg in reducing the amount of blood loss.⁽²¹⁾

We measured the PCV for the patients as it is a better predictor than hemoglobin in cases with acute blood loss and we found that the reduction in PCV was more marked in the control group than the study group(2.58±0.85%) versus (1.52 ± 0.81%) respectively, the reduction was statistically significant and the postoperative PCV was significantly lower in the control than study group (28.84 ±2.07%) versus (31 ± 2.49%) respectively, and these results were similar to the findings of Sekhvat et al who conducted a randomized controlled trial in patients undergoing caesarean section.⁽²²⁾

Concerning the post-operative blood loss, there was no significant difference in the amount of blood loss as P value was more than 0.05 and this in reverse to other studies which found a significant reduction in postpartum hemorrhage,^(17,18,20) and this could be due to variation in sample size and the method of blood loss measurement.

We used 10 units of oxytocin for both groups after the delivery of the fetus, this was sufficient to control the bleeding in contrast to other studies who needed extra dose of oxytocin in the control group.^(18,23)

Concerning its safety, we encountered two cases with nausea and vomiting that resolved with metoclopramide injection, however this is a common problem after general anesthesia which is the mode used in all the cases and this in agreement with Sentürk et.al. who found an extreme safety with this drug in caesarean section.⁽²⁴⁾

Conclusion and recommendations:

The current study revealed that cyklokapron was significantly effective in reducing blood loss at time of caesarean section. Especially in our country where anemia is a common health problem and with rising caesarean section rates, a significant morbidity and mortality from hemorrhagic complications and blood transfusion can be prevented with this medication as it has a good safety profile. We recommend further studies with higher doses and more patients to evaluate its benefit in reducing the intra-operative bleeding and preventing postpartum hemorrhage after caesarean section and vaginal delivery.

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