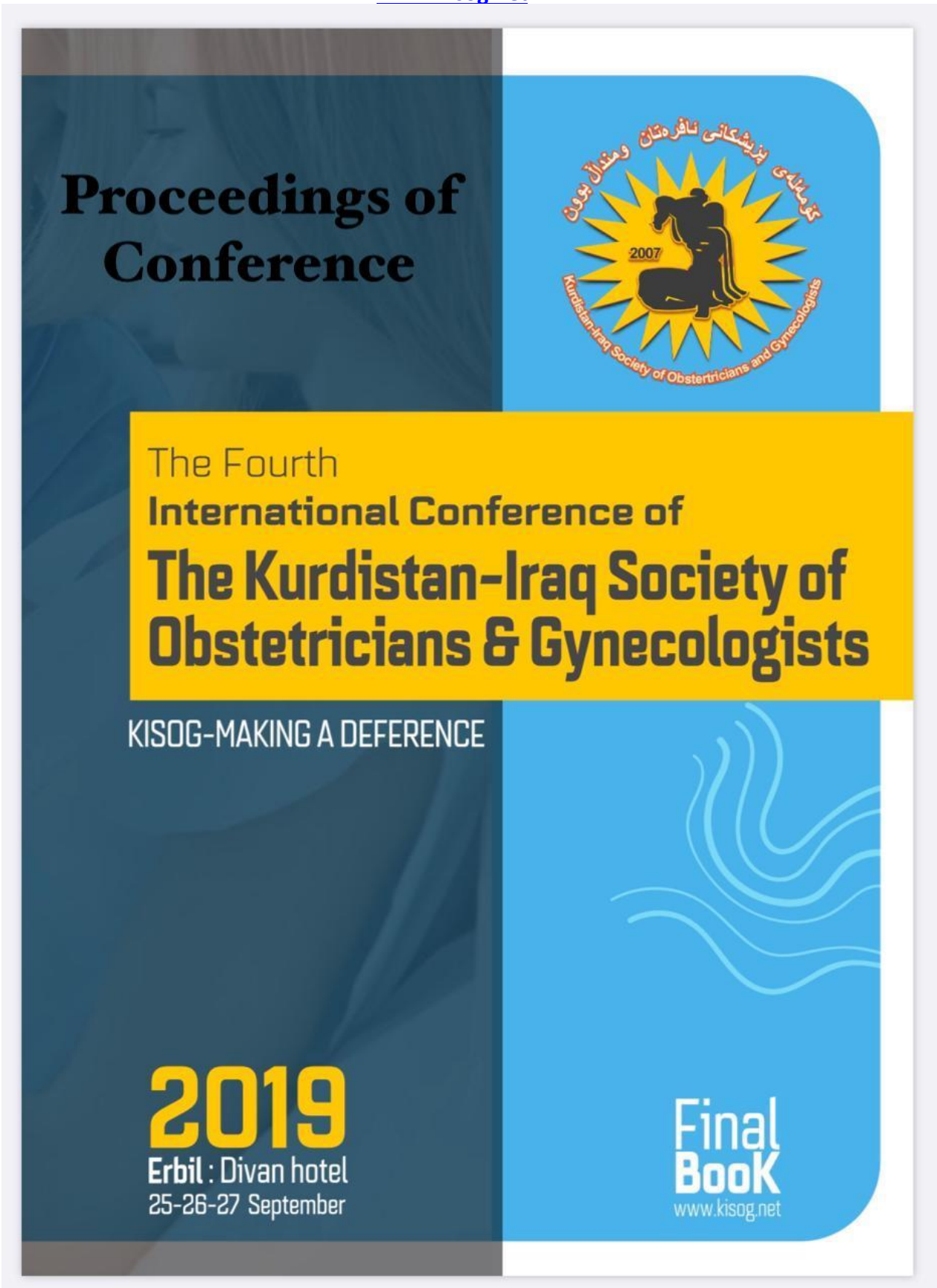
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Role of Prophylactic use of Intravenous Tranexamic Acid in Preventing Postpartum Haemorrhage after Vaginal Delivery: a Randomised Controlled Study

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ABSTRACT

BACKGROUND

Tranexamic acid is complementary component acts on haemostatic process. It can be used in third stage of labour to prevent postpartum haemorrhage.

OBJECTIVES

To know whether prophylactic usage of tranexamic acid after vaginal delivery would decrease postpartum haemorrhage.

PATIENTS AND METHODS

Double-blinded randomized controlled trial performed on 418 pregnant women in labour who had planned vaginal delivery at Sulaimani Maternity Teaching Hospital from August 2018 through August 2019. Participants were randomly allocated into two groups; 209 women received 10 mg/kg tranexamic acid with oxytocin within 10 minutes after vaginal delivery, and 209 patients received only oxytocin. Inclusion criteria were singleton pregnancy, live foetus and cephalic presentation at ≥38 gestational weeks. Exclusion criteria were: placenta abruption, significant medical diseases, coagulopathy, auto-immune disease, intrauterine foetal demise, and history of postpartum haemorrhage. Primary outcome was postpartum haemorrhage (blood loss of ≥500 ml). Patients' ages, body mass index (BMI), and pre-/post-delivery vital signs were recorded.

RESULTS

There were no significant differences between intervention and control groups in regard of age, BMI, and gravidity (P-values of 0.14, 0.23 and 0.63 respectively). The primary outcome occurred in 12 (5.7%) women in intervention group and in 31 (14.8%) women

in control group (relative risk = 0.39; 95% confidence interval [CI] = 0.32 to 0.56; P-value = 0.04). Mean±SD blood loss (ml) was significantly lower in intervention group (P-value of <0.001). Post-delivery haemoglobin and haematocrit were significantly higher in intervention group (P-value of <0.001).

CONCLUSIONS

Use of tranexamic acid resulted in significantly decreasing rate of postpartum haemorrhage.

KEYWORDS: Labour; Postpartum haemorrhage; Tranexamic acid; Vaginal Delivery.

INTRODUCTION

Although labour is a physiological process, it is sometimes associated with severe morbidity and mortality. Bleeding during deliveries is a normal physiological event, but if bleeding exceeded 500 millilitres (ml), it is considered as postpartum haemorrhage (PPH) [(1)].

The most common cause of maternal death is PPH [(2)]. Moreover, about 125000 women die annually due to obstetrical haemorrhage [(3)]. The incidence of PPH was reported as 2-4% to as much high as 38% after vaginal deliveries [(2)]. Furthermore, both mechanical and clotting mechanisms are involved in the pathophysiology of PPH [(4)].

To solve this real issue, researchers worldwide tried to find solutions for it. One of the agents that have been used for this purpose was tranexamic acid [(5-6)]. Moreover, it had been used to treat different medical and surgical conditions since the 1960s [(4)].

Tranexamic acid is one of the derivatives that synthesized from lysine amino acid [(7-8)]. Its mechanism of action, i.e., antifibrinolytic effect, is exerted by blocking lysine binding sites on plasminogen; thence, inhibiting the interaction between the heavy chains of plasmin with lysine on fibrin surface [(7-8)]. Hence, although plasmin can still be formed, it cannot bind and degrade fibrin [(7-8)].

The efficacy of tranexamic acid had been assessed in gynaecology and obstetrics for reducing blood losses [(9)]. It had been used in conditions like menorrhagia, myomectomy, caesarean section, and ovarian tumors [(4, 10-11)]. Furthermore, studies showed that tranexamic acid had decreased the rate of PPH [(12-14)]. Besides, tranexamic acid is readily available and cheap [(15)]. Although there is concern about the thromboembolic effect of tranexamic acid, many studies mentioned its safety and showed no risk of thrombosis [(9, 16)].

In the current study, we wanted to know whether prophylactic usage of tranexamic acid in addition to oxytocin in pregnant women after vaginal delivery would decrease the rate of postpartum haemorrhage and to evaluate any potential adverse effect among the patients receiving tranexamic acid.

PATIENTS AND METHODS

The study is a single-center, double-blinded randomised controlled trial performed on 418 pregnant women in labour who had planned vaginal delivery. The study was conducted at Sulaimani Maternity Teaching Hospital from August 2018 through August 2019. All participants included in this study were randomly allocated into two equal groups; 209 women received 10 mg/kg tranexamic acid in addition to oxytocin (intervention group) within 10 minutes after vaginal delivery, and 209 women received oxytocin only (control group).

Inclusion criteria were pregnant women with a singleton pregnancy, live intrauterine foetus and cephalic presentation at 38 or more weeks of gestation. Exclusion criteria were: placenta abruption, history of significant medical diseases such as; heart, liver, renal diseases, coagulopathy and bleeding tendency, auto-immune disease, intrauterine foetal demise, pregnancy-induced hypertension and diabetes, history of postpartum haemorrhage and patients who were on anticoagulants within a week prior to the delivery.

The primary outcome was PPH, and it was defined as a blood loss of equal to or more than 500 ml. Blood loss was calculated by the differences in the weights of surgical pads that were pre-weighed and then weighed two hours after delivery (1 mg = 1 ml). The secondary outcomes were the requirement of maternal blood transfusion and maternal and foetal complications. Furthermore, all patients had their vital signs (Blood pressure, pulse rate, and respiratory rate) recorded before and at two hours after delivery. Patients' demographic features including age and body mass index (BMI) were recorded on admission.

Data analysis was performed using the "IBM SPSS Statistics version 25" program. Both descriptive and inferential statistical tests were performed. Also, a P-value of ($\leq$0.05) was considered a statistically significant association.

ETHICAL CONSIDERATION

All participants included in this study had written informed consent. Research Ethical Committee of Kurdistan Board of medical Specialties approved the study proposal and formal acceptance letter was obtained from Sulaimani Maternity Teaching Hospital prior to the start of the study.

RESULTS

There were no significant differences between the intervention and control groups in regard of age (year), BMI before pregnancy (kg/m^2), and gravidity (Table 1).

Table (1): demographic features among the studied groups

Demographic features	Intervention group (n = 209) (mean±SD)	Control group (n = 209) (mean±SD)	P-value
Age (year)	25.6±3.6	26.2±4.1	0.14
BMI (kg/m^2)	24.6±2.1	25.3±1.6	0.23
gravidity	2.3±0.9	2.4±0.3	0.63

BMI = body mass index; n = number; SD = standard deviation

Overall, 43 patients had the primary outcome (blood loss of equal to or more than 500 ml). Moreover, it significantly occurred less frequent in the intervention group as compared to the control group (Table 2).

Table (2): the frequency of PPH in between the studied groups

Primary outcome (PPH)	Frequency (%)	P-value	relative risk	95% CI
Intervention group (n = 209) (%)	12 (5.7)	0.04	0.39	0.32 to 0.56
Control group (n = 209) (%)	31 (14.8)			

CI = confidence interval; n = number; PPH = postpartum haemorrhage

The post-delivery blood loss (ml) was significantly lower in the intervention group as compared to the control group. In addition, the post-delivery haemoglobin and haematocrit were significantly higher in patients receiving tranexamic acid (intervention group) as compared to the control group (Table 3).

Table (3): post-delivery haematological assessment of the studied groups

Haemogram	Intervention group (n = 209) (mean±SD)	Control group (n = 209) (mean±SD)	P-value
Blood loss (ml)	281±34	392±44	<0.001
Hb (gm/dl)	11.8±0.9	10.11±0.15	<0.001
HCT (%)	36±3.2	32±1.4	<0.001

HCT = haematocrit; Hb = haemoglobin; n = number; SD = standard deviation

The frequency of vomiting and/or nausea in the delivery room was not significantly different between the intervention and the control groups (Table 4). Furthermore, other adverse effects did not happen in the study participants.

Table (4): adverse effects among the participants

Adverse effects	Intervention group (n = 209)	Control group (n = 209)	P-value
Vomiting and/or nausea (%)	7 (3.4)	5 (2.4)	0.43

DISCUSSION

Postpartum haemorrhage is one of the leading causes of maternal mortality [17]. Although the definition of PPH by World Health Organization (WHO) is a blood loss of equal to or more than 500 ml of blood after delivery [9, 18-19], postpartum blood loss estimation is a matter of debate [20]. Moreover, it was measured either by graded collecting bags or visual estimation [19, 20]. A direct visual estimate of the blood loss was considered the unreliable method in many studies [21-25], and graded collecting bag was impractical for us; therefore, we used the method of weighing the surgical pads before and two hours after delivery.

Prophylactic use of tranexamic acid before surgery had been shown to reduce blood loss by inhibition of fibrinolysis [4, 9]. Therefore, it had been used in gynaecology and obstetrics conditions [4, 10-11]. The ease of administration, availability, and relatively low cost of tranexamic acid make it more attractable to be routinely used in women during vaginal delivery [15].

Studies showed decreased vaginal blood loss and less need for blood transfusion during vaginal birth after the usage of tranexamic acid, and they also showed no serious side effects associated with its usage [15, 18, 26]. The results of the current study showed a significant decrease in blood loss after administration of tranexamic acid in women following vaginal delivery as compared to the control group. Although there were concerns about thromboembolic adverse effects after tranexamic acid usage [17, 27-29], we did not face such an event in this study.

Based on our finding, we, therefore, recommend the usage of tranexamic acid as a prophylactic measure during vaginal deliveries.

CONCLUSIONS

Among women with vaginal delivery who received prophylactic oxytocin, the use of tranexamic acid resulted in decreasing frequency of postpartum haemorrhage, and that was significantly lower than the frequency with the control group. Furthermore, extensive scaled, multicenter studies are justified to allow the use of tranexamic acid to be part of a local and national protocol for the management of pregnant women in labour.

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