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Efficacy of Tranexamic Acid to Control of Postpartum Hemorrhage

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Abstract
Background: Postpartum haemorrhage (PPH) is a major cause of maternal mortality, accounting for one-quarter of all maternal deaths worldwide. Uterotonics after birth are the only intervention that has been shown to be effective for PPH prevention. Tranexamic acid (TXA), an antifibrinolytic agent, has therefore been investigated as a potentially useful complement to this for both prevention and treatment because its hypothesized mechanism of action in PPH supplements that of uterotonics and because it has been proved to reduce blood loss in elective surgery, bleeding in trauma patients, and menstrual blood loss. **objective:** The objective of my study was to determine the efficacy of tranexamic acid to control of postpartum hemorrhage. **Material and Methods:** PPH diagnosis was confirmed by a senior Gynecologist and tranexamic acid (1g) was given to the patient by through IV route over 5min and response was checked clinically. One gram further dose was given to the patient after half hour if bleeding continued. Response was assessed after 4hrs of administration of 1st dose to determine the efficacy of the drug. **Results:** Mean age of our study cases was noted to be 28.80 ± 3.72 years. Our study results have indicated that majority of our patients i.e. 103 (65.6 %) were aged equal/less than 30 years of age. Most of our study cases i.e. 103 (65.6%) were from urban areas and 132 (84.1%) belonged to poor families. Mean body mass index of our study cases was 23.67 ± 4.21 kg/m^2 and obesity was present in 31 (19.7 %). Diabetes was present in 18 (11.5%) of our study cases while pregnancy induced hypertension was noted in 49 (31.2%) of our study cases. Mean parity of our study cases was 4.23 ± 2.37, 109 (69.4%) delivered vaginally while cesarean section deliveries were 30.6 %. Mean blood loss after therapy was 382.14 ± 42.34 ml in our study cases and efficacy noted in 145 (92.4%) of our study cases. **Conclusion:** Our study results support the use of tranexamic acid in control of primary postpartum hemorrhage as it was found to be effective, safe and reliable. Blood loss was also within acceptable range of less than 500 ml. Efficacy was significantly associated with obesity, diabetes, pregnancy induced hypertension and gestational age.
Keywords: Tranexamic acid, postpartum hemorrhage, efficacy.

Introduction:

WHO defines postpartum hemorrhage (PPH) as blood loss of more than 500ml after normal vaginal delivery and 1000ml in caesarian section [1]. PPH remains a leading cause of early maternal mortality, accounting for about 300,000 deaths worldwide every year, and of morbidity related to anemia, blood transfusion and hemorrhage related ischemic complications [2,3].Primary PPH is poorly predictable but mainly cause by uterine atony, trauma to genital tract, retained placenta and inverted or rupture uterus after normal vaaginal delivery [4,5].Accordingly, detailed guidelines are available for optimal use of obstetric intervention and utrotonic drugs [7,8].

The incidence of cesarean delivery is also increasing, and the average blood loss during cesarean delivery is double the amount lost during vaginal delivery [5].Thus, The hematocrit falls by 10% and blood transfusion may also be required [5]. Also Delivery by CScan cause more complications than normal vaginal deliveryand one of the most common complications of primary orsecondary postpartum hemorrhage (20%) [6]. It leads toincreased maternal mortality and morbidity as in severe cases, resulting in major obstetrical hemorrhage, hysterectomy and even admission to an ICU. [5, 6].

Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect throughthe reversible blockade of the lysine binding sites onplasminogen molecules [7]. Intravenous administration oftranexamic acid has been routinely used for many yearsto reduce hemorrhage during and after surgical procedures like coronary artery bypass, scoliosis surgery, oral surgery,orthotopic liver transplantation, total hip or kneearthroplasty, and urinary tract surgery [3, 4]. Tranexamic acidhas been shown to be very useful in reducing blood lossand incidence of blood transfusion in these surgeries. InGynecology and Obstetrics, TA have also been used to treat different cases of menorrhagia , placental abruption , previa and PPH[6].But unfortunately The use of TA in PPH has not been considered as first line intervention as hemostatic abnormalities resulting owing to uncontrolled bleeding are not considered to be controlled by administration of this drug. [5-7]

This concept has been recently challenged by the demonstration of a relationship between fibrinogen decrease and outcome. [7] Thus, antifibrinolytic agents, mainly TA, have been demonstrated to reduce blood loss and transfusion requirements in various emergency procedures. [7] The Clinical Randomization of an antifibrinolytic in significant hemorrhage (CRASH-2) has demonstrated that TA safely reduces the risk of death in bleeding trauma patients. In the field of obstetrics, a randomized control trial recently performed in France have suggested that TA administration in women after viginal or CS reduces blood loss and the incidence of PPH to about 93% [4,5]. This study has been carried out in western population in 2008 and thus gives no account of figures in South Asian population. Also, there is gap in knowledge regarding the efficacy of this drug in managing primary PPH. Although this drug in conjunction with uterotonics has frequently being used but the record regarding the outcome of its usage in the most recent years is lacking especially in South Asian population [7 - 11].

Material and Methods:

Patients coming the obstetrics and gynecology emergency department, Nishtar Hospital Multan, meeting inclusion criteria (All women of 20 to 40 age group with primary PPH, primigravida and multigravida having singleton pregnancy with gestational age more than 24 weeks) were enrolled for study. Women with history of thromboembolic disease and women with known allergy to drug were excluded from our study. PPH diagnosis was confirmed by a senior Gynecologist and tranexamic acid (1g) was given to the patient by through IV route over 5min and response was checked clinically. One gram further dose was given to the patient after half hour if bleeding continued. Response was assessed after 4hrs of administration of 1st dose to determine the efficacy of the drug. Primary Postpartum Hemorrhage: was defined as bleed loss of more than 500 ml after vaginal delivery measured as one full kidney tray and more than 1000 ml after cesarean section. blood loss of more than 500ml after delivery measured as one full kidney tray. Efficacy of Tranexamic acid was defined as blood loss of less than 50 ml measured by weighing presoaked and soaked pads and difference in weight indicated blood volume. 1g = 1 ml after 4 hours of TA administration or pads soaked are less than 2 in number. The data was entered and analyzed by computer software version 20. Frequency and percentages were calculated for categorical variable like age groups, parity, residential status, diabetes, socioeconomic status, obesity, PIH, efficacy and mode of delivery. Descriptive statistics was applied to calculate mean and standard deviation like age, gestational age and BMI.

Results:

Our study included a total of 157 cases of primary post partum hemorrhage meeting inclusion of our study. Mean age of our study cases was noted to be 28.80 ± 3.72 years ranging from 23 years to 36 years while 103 (65.6 %) were aged equal/less than 30 years of age. Most of our study cases i.e. 103 (65.6%) were from urban areas and 132 (84.1%) belonged to poor families. Mean body mass index of our study cases was 23.67 ± 4.21 kg/m^2 and obesity was present in 31 (19.7 %). Diabetes was present in 18 (11.5%) of our study cases while pregnancy induced hypertension was noted in 49 (31.2%) of our study cases. Mean parity of our study cases was 4.23 ± 2.37 and 76.4 % of our study cases had parity more than 3. Of these 157 study cases, 109 (69.4%) delivered vaginally while cesarean section deliveries were 30.6 %.

Mean gestational age in our study was 38.43 ± 1.12 weeks. Mean blood loss after therapy was 382.14 ± 42.34 ml in our study cases and efficacy noted in 145 (92.4%) of our study cases.

Table No. 1

Stratification of Efficacy with regards to mode of delivery.

Mode of delivery	Efficacy		P – value
	Yes (n = 145)	No (n = 12)	
Vaginal (n = 109)	103	06	**0.189**
C. section (n = 48)	42	06	
Total	**157**		

Table No. 2
Stratification of Efficacy with regards to age.
(n = 157)

Age groups	Efficacy		P – value
	Yes (n = 145)	No (n = 12)	
20 – 30 Years (n =103)	97	06	**0.342**
31 – 40 Years (n =54)	48	06	
Total	**157**		

Table No. 3
Stratification of Efficacy with regards to obesity.
(n = 157)

Obesity	Efficacy		P – value
	Yes (n = 145)	No (n = 12)	
Yes (n = 31)	20	11	**0.000**
No (n = 126)	125	01	
Total	**157**		

Table No. 4
Stratification of Efficacy with regards to diabetes.
(n = 157)

Diabetes	Efficacy		P – value
	Yes (n = 145)	No (n = 12)	
Yes (n = 18)	12	06	**0.001**
No (n = 139)	133	06	
Total	**157**		

Table No. 5
Stratification of Efficacy with regards to pregnancy induced hypertension.
(n = 157)

Pregnancy induced hypertension	Efficacy		P – value
	Yes (n = 145)	No (n = 12)	
Yes (n = 49)	37	12	**0.000**
No (n = 108)	108	00	
Total	**157**		

Discussion:
Our study included a total of 157 cases of primary post partum hemorrhage meeting inclusion of our study. Mean age of our study cases was noted to be 28.80 ± 3.72 years (with minimum age was 23 years while maximum age

was 36 years). Our study results have indicated that majority of our patients i.e. 103 (65.6 %) were aged equal/less than 30 years of age. Yehia et al [12] also reported 28.4 ± 4.9 years mean age in women with postpartum hemorrhage which is close to our study results. A study conducted in China by Xu et al [13] reported mean age was 26.7 ± 3.7 years which is close to our study results. Goswami et al [14] reported 23.6 ± 2.5 years mean age in women having PPH which is in compliance with that of our study results. Fayyaz et al [15] from Peshawar reported 29.69+7.10 years mean age which is close to our study results. A study conducted by Rasheed et al [16] also reported mean age was 28.86 + 2.94 years which is close to our study results. Chohan et al [17] also reported similar results.

Most of our study cases i.e. 103 (65.6%) were from urban areas and 132 (84.1%) belonged to poor families. Mean body mass index of our study cases was 23.67 ± 4.21 kg/m^2 and obesity was present in 31 (19.7 %). Yehia et al [12] from Kuwait reported mean body mass index to be 27.2 ± 1.6 kg/m^2 which is slightly higher than that being observed in our study. Goswami et al [14] reported mean BMI was 22.4 ± 1.6 kg/m^2 which is in compliance with that of our study results.

Diabetes was present in 18 (11.5%) of our study cases while pregnancy induced hypertension was noted in 49 (31.2%) of our study cases. Chohan et al [17] reported 26 % pregnancy induced hypertension which is close to our study results. Mean parity of our study cases was 4.23 ± 2.37 and 76.4 % of our study cases had parity more than 3. Yehia et al [12] from Kuwait reported mean parity was 2.0 ±1.4 which is slightly lower than that observed in our study. Rasheed et al [16] reported 3.94 mean parity which is close to our study results. Mean gestational age in our study was 38.43 ± 1.12 weeks. A study conducted by Yehia et al [12] reported 39.1 ± 1.1 weeks mean gestational age which is close to our study results. Xu et al [13] reported 38.7 ± 1.0 weeks mean gestational age which is close to our study results. Of these 157 study cases, 109 (69.4%) delivered vaginally while cesarean section deliveries were 30.6 %. A study conducted by Chohan et al [17] also reported 30 % frequency of patients with primary PPH delivered by cesarean section which is close to our study results.

Mean blood loss after therapy was 382.14 ± 42.34 ml in our study cases and efficacy noted in 145 (92.4%) of our study cases. A French study also reported 93 % efficacy with TA which is in compliance with our study results. [5] A study conducted by Yehia et al [12] reported mean blood loss to be 369.5 ± 198 ml in patients treated with TA which was significantly lower than that of placebo group. These findings of Yehiea et al [12] are similar to that of our study results. Xu et al [13] from China reported mean blood loss was noted to be 336.7 ± 151.2 ml in patients treated with tranexamic acid which is close to our study results. Goswami et al [14] reported 376.83±31.961ml mean blood loss after therapy with TA and found that blood loss was significantly less than that of placebo group indicating effectiveness of the TA in the targeted population. A study done in Karachi by Shahid et al [18] also reported mean blood loss with tranexamic acid was significantly lower than placebo (356.44 ± 143.2 ml) which is in compliance with our study results.

Conclusion:

Our study results support the use of tranexamic acid in control of primary postpartum hemorrhage as it was found to be effective, safe and reliable. Blood loss was also within acceptable range of less than 500 ml. Efficacy was significantly associated with obesity, diabetes, pregnancy induced hypertension and gestational age.

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