

Comparison between Placental Site Injection of Vasopressin and Bilateral Internal Iliac Artery Ligation to Reduce Blood Loss during Cesarean Section for Placenta Praevia, A Randomized Controlled Trial

Omar, KA and Galal, M

Obstetrics and Gynecology Department, AL-Azhar Faculty of Medicine (Damietta)

Corresponding author: Mohammad Galal, email:mohammed.30028@yahoo.com

ABSTRACT

Background: placenta praevia is an obstetric complication in which the placenta is inserted partially or completely in the lower uterine segment, A significant proportion of these cases is associated with life threatening hemorrhage during delivery, often by caesarean section in the vast majority of cases, many procedures introduced to overcome this problems, none of them is completely successful.

Aim of the work: this study aimed to compare between local vasopressin injection in the placental bed and bilateral internal iliac artery ligation on the blood loss during caesarean section for placenta praevia.

Patients and Methods: this a randomized-controlled prospective trial included 60 pregnant women with a diagnosis of placenta praevia, they were categorized into 3 equal groups according to methods to control blood loss during cesarean section for placenta praevia. **Group 1** included 20 pregnant women who underwent vasopressin injection at placental site. **Group 2** included 20 pregnant women who underwent bilateral internal iliac artery ligation. **Group 3** included 20 pregnant women who underwent caesarean section without internal iliac artery ligation or local injection of vasopressin (The control group), comparison between groups were done and statistically analyzed.

Results: there were statistical significant differences between the intervention and the control groups as regard estimated blood loss, P value was <0.001 ; **group 3**(Control) had more amounts of blood loss, there were no statistical significant differences between **group 1** and **group 2** as regard estimated blood loss, P value was > 0.05 . Comparison between **group1** and **group 2** showed that internal iliac artery ligation was significantly associated with prolonged operative time than vasopressin injection(P value was <0.001).

Conclusion and Recommendation: local injection of vasopressin at placental site seemed to be a promising modality for reducing blood loss during cesarean delivery for placenta praevia and was associated with similar reduction of blood loss and less operative time when compared with internal iliac artery ligation, may be done first before trying internal iliac artery ligation and needs no experience.

Keywords: Vasopressin, Bilateral Internal Iliac Artery Ligation, CesareanSection, Placenta Praevia.

INTRODUCTION

Placenta praevia (pp) is a potential life threatening pregnancy complication that may cause various clinical situations, serious adverse outcomes include: excessive obstetrics haemorrhage, massive transfusions and need for extension of surgical procedure leading to injury of the adjacent organs like bladder or bowel ,mainly due to the abnormal invasion of the placenta⁽¹⁾. Placenta praevia is an obstetric complication in which the placenta is inserted partially or completely in the lower uterine segment⁽²⁾. Major placenta praevia is recognized by the presence of an abnormal placenta overlying the internal cervical os and it is considered as one of the most anxious adverse maternal and fetal-neonatal complications in obstetrics⁽³⁾.The incidence of placenta praevia has been recently increased over the past few decades, correlating with the elevated caesarean section rate⁽⁴⁾.One of the most serious complications of placenta previa is the development of placenta accreta. This condition involves trophoblastic invasion beyond the normal

boundary established by the Nitabuch fibrinoid layer. If invasion extends into the myometrium, the term placenta increta is used; placental invasion beyond the uterine serosa (at times involving the bladder or other pelvic organs and vessels) is termed placenta percreta⁽⁵⁾. Cesarean delivery is essential in nearly all cases of placenta previa and the amount of blood loss during surgery is significantly higher than in cases of normal placental presentation, also the rate of blood transfusion was also significantly increased⁽⁶⁾. Different conventional approaches had been used to stop hemorrhage, including continuous uterine massage, uterine packing, and uterotonic agents, including oxytocin, prostaglandin and ergometrine. However, in patients with placenta praevia , hemorrhage from the placental implantation site may continue after placental delivery because the lower uterine segment has poorer contraction than the uterine body⁽⁶⁾.There were multiple modalities that have been evolved to minimize blood loss during CS, which had directed towards reducing

blood flow to the pelvis through bilateral ligation of internal iliac arteries or their branches⁽⁷⁾. Vasopressin is a naturally occurring hormone produced by magno-cellular neurons in para ventricular and supraoptic nuclei within the hypothalamus and secreted by the posterior lobe of the pituitary gland, where it is stored in granules present in the axon terminals⁽⁸⁾.

The vasopressin V1 α receptor (VP1 α R) has been demonstrated to be present in the myometrium of both non-pregnant and pregnant women and contributes to myometrial contraction⁽⁶⁾. In placenta praevia, bleeding is thought to be due to poor contraction of the lower uterine segment and the subsequent inability to compress the torn vessels⁽⁶⁾. The immune reactivity of oxytocin receptor was faint in the lower segment compared to the upper segment of the uterine body, which might contribute to the poor contractility of the lower segment and subsequent blood loss. However, immune reactivity of the vasopressin V1 α receptor (VP1 α R) was strongly localized to the smooth muscle cells obtained from both the upper and lower segments of the uterine body. The reduction of blood loss after vasopressin injection into the placental implantation site may be caused by not only peripheral vasoconstriction, but also by contraction of uterine smooth muscle⁽⁶⁾.

So, the aim of this study was to compare between local diluted vasopressin injection and bilateral internal iliac artery ligation on the blood loss during caesarean section for placenta praevia.

PATIENTS AND METHODS

The present study was a randomized-controlled prospective trial that was conducted at Obstetrics and Gynecology Department, Al-Azhar University Hospital (New Damietta) between April 2015 and April 2017 and it included 60 pregnant women diagnosed with placenta praevia and were randomly categorized into 3 equal groups according to the methods of intervention during caesarean delivery for placenta praevia

Group 1: included 20 pregnant women who underwent vasopressin injection at placental site.

Group 2 included 20 pregnant women who underwent bilateral internal iliac artery ligation.

Group 3 included 20 pregnant women who underwent caesarean section without internal iliac artery ligation or local injection of vasopressin (control group).

Inclusion criteria

Age: 18-40 years, gestational age: >32 wks, singleton pregnancy, placenta praevia (partial or complete).

Exclusion criteria

Placenta praevia percreta diagnosed prenatally or during surgery, multiple gestations, significant obstetric disease (preeclampsia), known risk factors for postpartum hemorrhage (including uterine fibroids), inherited or acquired coagulation disorders and thrombocytopenia, urgent bleeding from placenta praevia or other causes of antepartum haemorrhage.

For all pregnant women included in the study an informed written consent were taken after explanation of the nature of the study, underwent elective caesarean delivery between 36 and 37 weeks of gestation according to delivery-timing guidelines⁽⁹⁾ and they were subjected to the following before elective cesarean delivery:

Thorough history taking and clinical examination, laboratory investigation: including complete blood count (CBC) and coagulation profile to exclude any systemic disease, Routine obstetric ultrasound: using a Voluson 730 Pro machine (GE, Milan, Italy to confirm gestational age, detect grade of placenta praevia and presence of accretion.

Operative details

Four units of packed red blood cells and two units of FFP were saved during expectant management as well as during surgery. **Anesthesia:** general anesthesia was the method used. Patients were received a 500-mL infusion of Ringer's lactate solution during the 30-min period just before induction. They were pre-oxygenated with 100% oxygen via face mask for 2 min before induction. General anesthesia was induced with i.v. sodium thiopentone 4–5 mg/kg and succinylcholine 1 mg/kg to facilitate intubation, followed by vecuronium to maintain relaxation during surgery.

The patients were ventilated with 50% nitrous oxide in oxygen and 1% enflurane. After delivery, anesthesia was maintained with 0.5% enflurane and 50% nitrous oxide in oxygen, A Pfannenstiel's incision was done for the cesarean section. After entering the peritoneal cavity, uterine incision was done in the upper part of lower uterine segment away from the placenta, the placenta is left in situ after clamping of the cord; then, the placenta was removed manually. Double-layer closure of the incision is made with 1.0 Vicryl. Then the operation is completed using traditional technique. All patients received five units of oxytocin in 500 mL of a 5% glucose solution. Placental invasion was accurately detected during surgery. Cases with placenta percreta were excluded from this study.

Group 1 (vasopressin group)

Injection of four units of vasopressin in 20 mL of saline into the placental implantation site was applied after removal of the placenta. If bleeding continued in spite of uterotonic agents, bilateral internal iliac artery ligation was performed. It is necessary to emphasize that it is important to ensure that the needle is not within a blood vessel, because i.v. injection of vasopressin can induce acute arterial hypertension, bradycardia, pulmonary edema⁽¹⁰⁾ or death⁽¹¹⁾. **Group 2** (internal iliac artery ligation group) : an incision over the parietal peritoneum above the level of the round ligament was carried out to reach the retroperitoneum; then, the common iliac bifurcation and crossing ureters were identified. The internal iliac artery was bluntly dissected. The ureters were retracted medially to avoid injury. Following fine dissection of the internal iliac artery by a right angle clamp and scissors from the bifurcation, the connective tissue around the vessel was opened to obtain a clear view of the vessels. From the lowest resistant point, providing an easy mean for crossing the connective tissue below the vessels, a right-angle clamp is passed beneath the internal iliac artery from lateral to medial about 3 - 5 cms away from the bifurcation to minimize the injury of the vein. Ligation of the posterior branches of the internal iliac artery was avoided to prevent gluteal muscle and buttock necrosis. The internal iliac artery was double tied, 1-2 cm apart, with No. 0 or 1 silk suture; without cutting the artery. The pulsations of external iliac artery and internal iliac artery were checked after ligation. Related veins were evaluated for potential injuries. Then, similar steps were done on the other side.

Group 3 (The control group)

Uterine closure without vasopressin injection or internal iliac artery ligation was done. If bleeding continued in spite of uterotonic agents, bilateral internal iliac artery ligation was performed.

The outcome measures were assessed and included:

- 1-Blood loss: losses during cesarean section were estimated as follows: after incision of uterine muscle and rupture of membrane, amniotic fluid was collected so far as possible in the suction bottle. Blood loss was estimated by measuring the volume of blood collected in another suction bottle with additions for weight changes of soaked linen savers, mops and pads.
- 2-Operative time: calculated with onset of skin incision to skin closure.
- 3-The need for further interventions: uterine tamponade compression procedures or hysterectomy.

Postoperative assessment: included : pulse, blood pressure ,CBC, development of DIC and ICU admission.

The study was done after approval of ethical board of Al-Azhar university and an informed written consent was taken from each participant in the study.

Statistical analysis

The collected data were systematized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 19 (SPSS Inc, Chicago, USA), running on IBM compatible computer. Quantitative data were expressed as the mean \pm standard deviation (SD). For comparison between numerical groups, student (t) test was used for parametric or Mann-Whitney test for non-parametric variables. Qualitative data were presented as relative frequency and percent distribution. For comparison between categorical groups, the Chi square (X^2) or Fisher's exact tests were used. Pearson correlation co-efficient (r-test) was used for correlating different numerical variables. For all tests, P values $<$ 0.05 were considered significant. For all tests, P values $>$ 0.05 were considered insignificant.

RESULTS

There were no statistical significant differences in all the 3 groups as regard age , BMI, parity, previous CS, previous abortion, but most of the patients were multipara, had previous cesarean(**Table1**). There were statistical significant differences between intervention and the control group as regard estimated blood loss, p value was $<$ 0.001 ; **group 3** had more amounts of blood loss, there were no statistical significant differences between group 1 and group 2 as regard estimated blood loss, p values was $>$ 0.05 (**Table 2**). Internal iliac artery ligation was significantly associated with prolonged operative time. P value was $<$ 0.001. There were no significant differences between intervention groups as regard tachycardia, hypotension or the units of blood transfusion (**Table 3**).The use of vasopressin resulted in a decrease in the frequency of internal iliac artery ligation, hysterectomy, the occurrence of DIC and ICU admission. However, there were no significant differences between both groups (**Table 4**).The use of bilateral internal iliac artery ligation resulted in a decrease in the frequency of hysterectomy, the occurrence of DIC and ICU admission. However, there were no significant differences between both groups (**Table 5**).

Table 1: patient's characteristics

Character	Group 1 (vasopressin)	Group 2 (IIAL)	Group3 (control)	P-value
Age (years) Mean±SD	32.4±7.2	34.7±6.8	33.1±5.9	0.54
BMI (Kg/m²) Mean±SD	30.4±4.5	31±4.2	29.1±4.9	0.55
Parity Primipara Multipara	4 (20%) 16 (80%)	3 (15%) 17 (85%)	2 (10%) 18 (90%)	0.8
previous Cs 0 1 2 ≥ 3	2 (10%) 3 (15%) 8 (40%) 7 (35%)	3 (15%) 4 (20%) 8 (40%) 5 (25%)	2 (10%) 5 (25%) 8 (40%) 5 (25%)	0.89
Previous abortion	3 (15%)	4 (20%)	7 (35%)	0.46

Table 2: blood loss during cesarean section of studied patients

Group	Estimated loss		Major blood loss (> 1500 mL)
	Mean (ml)	SD	
Group 1 (vasopressin)	1123	489	3 (15%)
Group 2 (IIAL)	1076	545	2 (10%)
Group 3 (control)	1664	647	8 (40%)
P value	<0.001 (significant)		0.026 (significant)

Table 3: operative assessment of studied patients

Variables	Group 1 (vasopressin)	Group 2 (IIAL)	Group 3 (control)	P-value
Operative time (min) mean±SD	65.3±24.4	92.5±35.8	62.3±19.6	<0.001
Blood transfusion (units , more than 1)	1 (5%)	2 (10%)	4 (20%)	0.13
Tachycardia	3 (15%)	4 (20%)	6 (30%)	0.41
Hypotension	2 (10%)	3 (15%)	5 (25%)	0.5

N.B: no cases of oliguria were detected

Table 4: comparison between vasopressin group and control group as regard operative outcome

Variable	Vasopressin	Control	P- value
Success rate *	15 (75%)	11 (55%)	0.32
IIAL	3 (15%)	6 (30%)	0.32
Hysterectomy	1 (5%)	2 (10%)	0.41
DIC, ICU admission	1 (5%)	1 (5%)	1

* Success : no further intervention is needed.

Table 5: comparison between bilateral internal iliac artery ligation group and control group as regard operative outcome

Variable	IIAC	Control	P –value
Hysterectomy	1 (5%)	5 (25%)	0.18
DIC	0 (0%)	2 (10%)	0.49
ICU admission	0 (0%)	3 (15%)	0.23

DISCUSSION

The incidence of placenta previa has been recently increased over the past few decades, correlating with the elevated caesarean section rate⁽⁴⁾. Major placenta previa was recognized by the presence of an abnormal placenta overlying the endocervical os, and it is considered as one of the

most anxious adverse maternal and fetal-neonatal complications in obstetrics⁽³⁾. In the present study, the mean age of the studied patients was 32.6±5.5 years, The mean BMI of the patients was 30.4±4.5, the majority of patients were multipara with previous cesarean sections, which is consistent with a study that evaluated 25 patients with placenta

previa, The mean age of the patients was 30.2±5.6, The mean BMI of the patients was 26.8±4.9. Five patients (20%) were primigravid, 9 patients (36%) were multipara, 8 patients (32%) have previously been delivered by cesarean section in their first pregnancy and 3 patients (12%) had been delivered by cesarean section twice before their current pregnancy⁽¹²⁾. The use of vasopressin in our study yielded approximate results to other new techniques performed in similar communities compared two protocols for the management of post-partum hemorrhage during CS in placenta previa, using the Bakri balloon versus non-balloon protocols. The balloon alone was successful in achieving hemostasis in 87.5% of cases. Balloon success was associated with the absence of accreta (odds ratio 0.001) and short operation duration.

In general, placenta percreta cases were best treated by total abdominal hysterectomy. In addition, there was an almost widespread agreement that the placenta should be left *in situ* trying to detach the placenta mostly result in massive bleeding⁽¹⁴⁾. The success rate of bilateral internal iliac artery ligation was reported between 40% and 100% in various series⁽¹⁵⁾. The procedure required high skill and experience because the operator must be familiar with retroperitoneal anatomy and potential complications of the procedure. For this reason, in many centers, preoperative placement of balloon occlusion catheter into the bilateral internal iliac arteries was commonly planned to avoid hemorrhagic morbidity. This procedure was available only in a small number of centers with experienced interventional radiologists, and it has been found that the technique is not as efficient as expected⁽¹⁶⁾.

CONCLUSION AND RECOMMENDATIONS

Local injection of vasopressin at placental site seemed to be a promising modality for reducing blood loss during cesarean delivery for placenta previa and was it associated with similar reduction of blood loss and less operative time when compared with internal iliac artery ligation, may be done first before trying internal iliac artery ligation and needed no experience. The number of patients in this study was not enough for an adequate evaluation of the risk of rare severe maternal morbidity or mortality with vasopressin injection.

REFERENCES

- 1-Ascioglu O, Sahbaz A, Gungorduk K *et al.* (2014): Maternal and perinatal outcomes in women with placenta praevia and accrete in teaching hospitals. *Western Turkey J. Obstet. Gynaecol.*, 34:462-466.
- 2-Matsuzaki S, Yoshino K, Kumasawa K *et al.* (2014): Placenta percreta managed by transverse uterine fundal incision with retrograde cesarean hysterectomy: a novel surgical approach. *Clinical Case Reports*, 2(6):260-264.
- 3- Fan D, Xia Q, Liu L *et al.* (2017): The incidence of postpartum hemorrhage in pregnant women with placenta previa. *PLoS One*, 12(1):170194 -170205.
- 4-Prasanth S, Mehta P and Rajeshwari KS (2016): Maternal and fetal outcome of placenta previa in a tertiary care institute: a prospective two year study. *India J. Obstet. Gynecol. Res.*, 3(3):274-278.
- 5- Silver RM and Barbour KD (2015): Placenta accreta spectrum accreta, increta and percreta. *Obstet. Gynecol. Clin. N. Am.*, 42:381-402.
- 6-Kato S, Tanabe A, Kanki K *et al.* (2014): Local injection of vasopressin reduces the blood loss during cesarean section in placenta previa. *J. Obstet. Gynaecol. Res.*, 40(5):1249-1256.
- 7-Kidney DD, Nguyen AM, Ahdoot D *et al.* (2001): Prophylactic perioperative hypogastric artery balloon occlusion in abnormal placentation. *Am. J. Roentgenol.*, 176(6):1521-1524.
- 8-Robinson AG and Verbalis JG (2016): Posterior pituitary. In: Williams Textbook of Endocrinology. Melmed S, Polonsky KS, Larsen R, editors, Thirteenth Edition. Elsevier, Inc. London, pp: 300-331.
- 9-Spong CY, Mercer BM, D'Alton M *et al.* (2011): Timing of indicated late-preterm and early-term birth. *Obstet. Gynecol.*, 118:323-333.
- 10-Tulandi T, Beique F and Kimia M (1996): Pulmonary edema: a complication of local injection of vasopressin at laparoscopy. *Fertil. Steril.*, 66: 478-480.
- 11- Nezhad F, Admon D, Nezhad CH *et al.* (1994): Life-threatening hypotension after vasopressin injection during operative laparoscopy, followed by uneventful repeat laparoscopy. *J. Am. Assoc. Gynecol. Laparosc.*, 2: 83-86.
- 12-Aydogan P, Kahyaoglu S, Saygan S *et al.* (2014): Does cervical ureaplasma/mycoplasma colonization increase the lower uterine segment bleeding risk during cesarean section among patients with placenta previa? *Eur. Rev. Med. Pharmacol. Sci.*, 18(16):2243-2247.
- 13-Maher MA and Abdelaziz A (2017): Comparison between two management protocols for postpartum hemorrhage during cesarean section in placenta previa: Balloon protocol versus non-balloon protocol. *J. Obstet. Gynaecol. Res.*, 43(3):447-455.
- 14-Fitzpatrick KE, Sellers S, Spark P *et al.* (2014): The management and outcomes of placenta accreta, increta, and percreta in the UK: a population-based descriptive study. *BJOG.*, 121(1):62-71.
- 15-Joshi VM, Otiv SR, Majumder R *et al.* (2007): Internal iliac artery ligation for arresting postpartum haemorrhage. *BJOG.*, 114:356-361
- 16-Shih JC, Liu KL and Shyu MK (2005): Temporary balloon occlusion of the common iliac artery: New approach to bleeding control during cesarean hysterectomy for placenta percreta. *Am. J. Obstet. Gynecol.*, 193:1756-1758.