

Full Length Research Paper

Internal Iliac Artery Ligation versus Local Injection of Vasopressin in Placental site in Placenta Previa during Cesarean section to Reduce Blood Loss

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Abstract

With the increasing rates of Cesarean deliveries, the incidence of placenta previa has progressively increased over the past few decades. Bleeding placenta during cesarean section is an inevitable problem that should be managed vigorously. Vasopressin is a potent vaso-constrictive agent that might help control bleeding in such condition; while bilateral internal iliac artery ligation (IIAL) is still the main practice used for bleeding control in several countries. The present study was designed to evaluate the effect of local injection of vasopressin versus internal iliac artery ligation on blood loss and its impact on complications during cesarean section in cases of placenta previa. The study is a randomized controlled clinical trial that included 80 patients diagnosed with placenta previa prepared for elective cesarean delivery. Patients in the study were randomly allocated into one of the four groups: group A) 20 patients who had vasopressin injection (4 U in 20 mL of saline), group B) 20 patients who had bilateral IIAL, group C) 20 patients who had combined vasopressin injection and bilateral IIAL, and group D) 20 patients without IIAL or vasopressin (control group). All included patients were planned for elective cesarean delivery between 36 and 37 weeks of gestations. The mean age of studied cases was 32.6±5.5 years. The majorities of patients were Multipara (84%), had previous cesarean sections (82%), with no significant difference between groups as regard these parameters. Estimated blood loss was significantly reduced among interventional groups than control group, with no significant difference between the 3 groups. No significant difference between the 4 groups as regard blood transfusion, heart rate or blood pressure. There were no significant complications among the studied groups. Local injection of vasopressin at placental site seems to be a promising modality for reducing blood loss during cesarean delivery for placenta previa. The use of internal iliac artery ligation (IIAL) or the combination of IIAL with vasopressin did not result in significant reduction of blood loss than vasopressin alone among studied groups. Local injection of vasopressin at placental site may be routinely used for the reduction of blood loss during cesarean section of placenta previa, especially with advanced maternal age, previous cesarean sections and with the presence of placental accretion. Further large scale randomized double-blinded controlled trials comparing blood loss during cesarean section in cases of placenta previa to confirm the results of our study.

Keywords: vasopressin, int. iliac artery, ligation.

Introduction

Placenta previa is characterized by the abnormal placenta overlying the endocervical os, and it is known as one of the most feared adverse maternal and fetal-neonatal complications in obstetrics⁽¹⁾. The incidence of placenta previa has been recently increased over the past few decades, correlating with the elevated caesarean section rate⁽²⁾. For management of pregnant women with placenta previa, cesarean section is recommended as the mode of delivery⁽³⁾. Placenta previa is a well-known cause of massive intrapartum hemorrhage that is associated with high mortality and morbidity for both the mother and the neonate⁽⁴⁾.

For bleeding from the placental separation surface, various hemostatic approaches have been proposed and put into practice⁽⁵⁾. Many of the techniques that have been developed to minimize intraoperative blood loss have focused on reducing pelvic circulation by bilateral ligation of internal iliac arteries or their branches⁽⁶⁾. Many gynecological surgeons use a local injection of vasopressin, which is a known peripheral vasoconstrictor, at the time of laparoscopic myomectomy to decrease blood loss. In addition, the useful role for local infiltration of vasopressin to arrest hemorrhage from the placental bed has been demonstrated in several obstetrical case reports⁽⁷⁾.

The vasopressin V1α receptor (VP1αR) has been demonstrated to be present in the myometrium of both non-pregnant and pregnant women and contributes to myometrial contraction⁽⁸⁾. So, the aim of our study was to evaluate the effect of local injection of vasopressin versus internal iliac artery ligation on blood loss and its impact on complications during cesarean section in cases of placenta previa.

Patients and methods

The present study is a randomized controlled clinical trial that was conducted at Obstetrics and Gynecology department of Al-Azhar University hospital (new Damietta) during the period from April 2015 to March 2017. During the period of the study, 80 patients diagnosed with placenta previa and had no exclusion criteria were included in the study and prepared for elective cesarean delivery. Cases with placenta previa percreta, allergic to oxytocin or vasopressin, having other obstetric complications, having risk factors for postpartum hemorrhage (uterine fibroids or previous classical uterine incision), with inherited or acquired coagulation disorders or thrombocytopenia were excluded from the study. Patients in the study were randomly divided into four groups:

- 1- **Group A (vasopressin):** 20 patients who had vasopressin injection at placental site during cesarean section.
- 2- **Group B (IIAL):** 20 patients who had bilateral internal artery ligation during cesarean section.
- 3- **Group C (vasopressin and IIAL):** 20 patients who had combined vasopressin injection at placental site and bilateral internal iliac artery ligation during cesarean section.
- 4- **Group D (control):** 20 patients who had cesarean section without internal iliac artery ligation or local injection of vasopressin (control group).

All included patients were planned for elective cesarean delivery between 36 and 37 weeks of gestations. Expectant management was applied for all patients. Detailed history and physical examination as well as ultrasound examination and preoperative basic laboratory data are obtained.

All enrolled patients received spinal anesthesia, followed by cesarean section. Spinal anesthesia was performed at the L3–4 inter-space with hyperbaric bupivacaine (2.0 mL; 0.5%) with a 25 G needle by an anesthesiologist who was not involved in the study. During cesarean section, standard monitoring included electrocardiogram, blood pressure, maternal heart rate and pulse oximetry. Intraoperative fluid management was performed at the discretion of the supervising anesthesiologist.

Cesarean delivery

A Pfannenstiel's incision was done for the cesarean section. After entering the peritoneal cavity, resection of the bladder is done with cautious hemostasis of vessels between the uterine serosa and posterior bladder wall by electrocautery or suturing. Uterine incision was implemented from either the lower segment (low-transverse) or the upper segment to avoid placental disruption. The placenta is left in place after umbilical cord clamping; then, manual removal of the placenta was performed. Single-layer closure of the hysterectomy incision is carried out with 1.0 Vicryl. Completion of operation after bleeding has been controlled and fascia, subcutaneous tissue and skin closed using a regular technique. All patients received five units of i.v. oxytocin in 500 mL of a 5% glucose solution, and intramyometrial administration of five units of oxytocin in 10 mL of 0.9% saline solution after removal of the placenta. When massive bleeding started again after temporary hemostasis during the surgery, or when bleeding from the placental bed could not be controlled by injections of uterotonic agents, uterine tamponade or the use of parallel vertical compression sutures with 0-chromic14 were attempted immediately. If such conservative methods failed, then hysterectomy was performed. There were no cases that developed re-bleeding after returning to the recovery room.

Placental invasion was detected during surgery. Cases with placenta percreta were excluded from the study. Injection of four units of vasopressin in 20 mL of saline into the placental implantation site was applied after removal of the placenta.

Procedure of IIAL

A small incision on parietal peritoneum above the level of the round ligament was performed to gain access to the retroperitoneum; the common iliac bifurcation and crossing ureters were visualized. The internal iliac artery lying downwards medial to the uterus was bluntly dissected. The ureters were retracted medially in order to avoid ureter injury. Following gentle dissection of the internal iliac artery by a right angle clamp and scissors from the bifurcation, the connective tissue around the vessel was opened in order to obtain a clear vision view of the artery and vein. We had chosen the point with the lowest resistance, which would provide us with the easiest means of traversing the connective tissue located beneath the vessel. Seeing as the internal iliac vein is slightly further away from the internal iliac artery, we had chosen to pass the right-angle clamp underneath the internal iliac artery from lateral to medial approximately 3 to 5 cm's away from the bifurcation, so that the possibility of venous injury was to be minimized and ligation of the posterior branches of the IIA, which can cause gluteal muscle and buttock necrosis, was avoided.

The IIA was double tied, 0.5 cm apart, with No. 0 or 1 silk suture; without cutting the artery. The pulsations of external iliac artery and IIA were checked after ligation. Corresponding veins were checked for possible damages. The same procedure was re-performed on the other side.

Operative assessment included the estimation of blood loss, operating room time, the occurrence of intraoperative complications and the need for further interventions to control bleeding. Postoperative clinical and laboratory evaluation was done for all cases.

Ethical consent: The study was approved by the Hospital Ethics Committee in accordance with local research governance requirements, and it was explained to the prospective participants. All participating patients signed an informed consent form.

Statistical analysis: The collected data were organized, 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 (X²) 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

In the present work, the mean age of studied cases was 32.6 \pm 5.5 years. There was no significant difference between groups as regard age and BMI. The majorities of patients were Multipara, had previous cesarean sections and had no previous abortion, with no significant difference between groups as regard these parameters. Regarding the assessment of placenta, complete placenta previa was more frequent than partial among all groups. Placental invasion was reported between 15-30% of cases. Most of the patients had posterior placenta. There was no significant difference between groups as regard placental parameters (Table I). Operative assessment of the studied patients showed that there was significant difference between groups as regard estimated blood loss. Control group had more amounts of blood loss and increased frequency of excess blood loss than other groups. The least group was those had vasopressin injection and bilateral IAL. In contrast, IAL was significantly associated with prolonged operating time. There was no significant difference as regard tachycardia, hypotension or the units of blood transfusion. Regarding postoperative assessment, the frequency of ICU admission and interventions after Cs sections were relatively common among control patients, but with no significant difference. In contrast, hemoglobin and hematocrite declined significantly among control than other groups (Table II)

Table (I): General characteristics of studied cases

	Group A (vasopressin)	Group B (IAL)	Group C (both)	Group D (control)	P
Age (years) Mean \pm SD	32.4 \pm 7.2	34.7 \pm 6.8 22-41	31.8 \pm 6.3 19-41	33.1 \pm 5.9 24-42	0.54
BMI (Kg/m ²) Mean \pm SD	30.4 \pm 4.5	31 \pm 4.2	30.8 \pm 4.7	29.1 \pm 4.9	0.55
Parity					0.8
Primipara	4 (20%)	3 (15%)	4 (20%)	2 (10%)	
Multipara	16 (80%)	17 (85%)	16 (80%)	18 (90%)	
Previous Cs					0.89
0	4 (20%)	3 (15%)	5 (25%)	2 (10%)	
1	3 (15%)	4 (20%)	6 (30%)	5 (25%)	
2	8 (40%)	8 (40%)	5 (25%)	8 (40%)	
\geq 3	7 (35%)	5 (25%)	4 (20%)	5 (25%)	
Previous abortion	3 (15%)	4 (20%)	4 (20%)	7 (35%)	0.46
Placental insertion					0.34
Partial p. previa	8 (40%)	4 (20%)	9 (45%)	6 (35%)	
Complete p. previa	12 (60%)	13 (65%)	11 (55%)	13 (65%)	
Placental invasion					0.52
Negative	14 (70%)	17 (85%)	13 (65%)	15 (85%)	
Placenta accrete	5 (25%)	1 (5%)	4 (20%)	2 (10%)	
Placenta increta	1 (5%)	2 (10%)	3 (15%)	3 (15%)	
Hemoglobin (g/dl)	11.7 \pm 1.8	11.5 \pm 1.4	11.9 \pm 1.1	11.5 \pm 1.6	0.89
Hematocrite (%)	34.2 \pm 4.6	33.6 \pm 4.3	35.2 \pm 3.9	33.4 \pm 4.9	0.87

Table (II): Comparison of surgical data between the studied groups

Variables	Group A (vasopressin)	Group B (IAL)	Group C (both)	Group D (control)	P
Estimated blood loss (mL)	1123 \pm 489	1076 \pm 545	982 \pm 356	1664 \pm 647	<0.001
Blood loss > 2000 mL (n)	1 (5%)	1 (5%)	0	5 (25%)	0.026
Operating time (min)	65.3 \pm 24.4	92.5 \pm 35.8	96.4 \pm 36.9	62.3 \pm 19.6	<0.001
Blood transfusion (units)	1 (5%)	2 (10%)	0	4 (20%)	0.13
Tachycardia	3 (15%)	4 (20%)	2 (10%)	6 (30%)	0.41
Hypotension	2 (10%)	3 (15%)	2 (10%)	5 (25%)	0.5
Transfer to ICU	0 (0%)	1 (5%)	0 (0)	2 (10%)	0.28
Interventions after Cs					
Uterine tamponade	2 (10%)	3 (15%)	1 (5%)	5 (25%)	0.29
Hysterectomy	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0.38
Blood transfusion (units)	2 (10%)	2 (10%)	0	3 (15%)	0.39
Hemoglobin (g/dl)	8.92 \pm 2.23	9.24 \pm 1.79	9.76 \pm 1.51	7.81 \pm 2.49	0.023
Hematocrite (%)	23.2 \pm 5.4	24.2 \pm 5.1	26.6 \pm 4.9	20.4 \pm 6.2	0.006

*: significant at $p < 0.05$;

Discussion

Local vasopressin injection at placental site was described 20 years ago for control of bleeding during cesarean section⁽⁹⁾; while prophylactic bilateral internal artery ligation before trial of placental removal seems to be an effective method to decrease complications and lowering the risk of intrapartum hysterectomy⁽¹⁰⁾. According to the best of our knowledge, this is the second randomized trial evaluating the efficacy of vasopressin injection at placental site during cesarean section. A previous study by Kato et al.⁽¹¹⁾ retrospectively reviewed the medical records of all patients diagnosed with placenta previa over a period from December 2000 through October 2012. They compared two groups; group A (50 patients) as a control group, and group B (59 patients) were vasopressin group. In their study, the estimated blood loss was significantly decreased in the vasopressin group compared with the control group ($P < 0.05$). Thirteen patients (26%) in the control group lost more than 2000 mL of blood, whereas this was experienced by four patients (8%) in the vasopressin group ($P < 0.05$).

The prospective nature of the current study represents additional advantage over the previous study, as it avoid potential medical errors and bias. In addition, the adding of a common protocol (IIAL) in our community to compare the effectiveness of vasopressin with such "standard" procedure further signifies and augments the results of the study. Lurie et al.⁽⁹⁾ reported six patients with uncontrollable hemorrhage caused by obstetrical complications at the time of cesarean section in which they successfully controlled the bleeding and salvaged the uterus using vasopressin injected sub-endometrially at the same concentration that we used. Zaki and Bahar⁽¹²⁾ reported a case of placenta previa accreta in which they used vasopressin to arrest hemorrhage from the placental bed at similar concentration as we used (5 units in 20 ml of saline).

In the present study, the injection of diluted vasopressin into the placental implantation site significantly reduced the blood loss without any adverse effects. The use of vasopressin did not affect the mean total length of the operation, the number of patients who were transferred to the intensive care unit (ICU), or the duration of stay in the ICU. There were no cases that required hysterectomy among the interventional groups. In contrast, IIAL was associated with long operating time, which exposes the patient to the potential hazards of anesthesia and hemodynamic instability. Thus, the local injection of vasopressin provides significant reduction of blood loss, quite equivalent to IIAL, without excessive prolongation of operating time. Based on these results, IIAL is better preserved for severe cases with placental invasion. Rauf et al.⁽¹³⁾ demonstrated 38 patients who were managed conservatively with hypogastric artery ligation and endo-uterine hemostatic suture to control post-partum hemorrhage secondary to placenta previa-accrete. Of these patients, 55.2% were between 25 and 35 years old; 97.5% were multiparous; 71.2% had two or more previous cesarean section and 68.5% had preterm delivery. Women with placenta accreta had estimated blood loss between 150-2500 ml; 57.8% of patients had blood transfusion (mean intraoperative transfusion, 2 units of packed red blood cells; range, 0-9 units). Median duration of operation was 112.5 min (range, 45-305 min) and 32 patients (84.3%) with placenta accreta did not undergo cesarean hysterectomy.

In the last study, the amounts of blood loss were close to those reported by our study, with quite similar rate of blood transfusion. They used more extensive and aggressive management with similar outcome. Thus, it is better to delay these vigorous approaches to the more severe cases. The use of vasopressin in our study yielded approximate results to other new techniques performed in similar communities. Maher and Abdelaziz⁽¹⁴⁾ compared two management protocols for post-partum hemorrhage during cesarean section (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. When analyzed specifically, balloon success was associated with the absence of accreta (odds ratio 0.001) and short operation duration. We excluded any patients with placenta percreta diagnosed before and during cesarean section in this study. It is generally accepted that placenta percreta are ideally treated by total abdominal hysterectomy. In addition, there is an almost universal consensus that the placenta should be left in place; attempts to detach the placenta frequently result in massive hemorrhage⁽¹⁵⁾.

In the present study, there was low frequency of ICU transfer, postoperative blood transfusion and the need for hysterectomy were minimal among interventional groups. The present study demonstrated that bilateral hypogastric artery ligation after delivery, and conservative managements associated with decreased intraoperative blood loss and, in parallel with this finding, decreased need for preoperative and postoperative blood products transfusion. The success rate of bilateral internal iliac artery ligation is reported at between 40% and 100% in various series⁽¹⁶⁾. The procedure requires 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 is commonly planned to avoid hemorrhagic morbidity. This procedure is 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⁽¹⁷⁾.

Finally, the results of the current study indicate that local vasopressin infiltration into the placental site might be an acceptable procedure used in addition to other pharmacological treatment during cesarean section for cases of placenta previa. The number of patients in this study is not enough for an adequate evaluation of the risk of rare severe maternal morbidity or mortality.

Conclusion

Local injection of vasopressin at placental site seems to be a promising modality for reducing blood loss during cesarean delivery for placenta previa. The use of internal iliac artery ligation (IIAL) or the combination of IIAL with vasopressin did not result in significant reduction of blood loss than vasopressin alone among studied groups.

Recommendation

Local injection of vasopressin at placental site may be routinely used for the reduction of blood loss during cesarean section of placenta previa, especially with advanced maternal age, previous cesarean sections and with the presence of placental accretion. Further large scale

randomized double-blinded controlled trials comparing blood loss during cesarean section in cases of placenta previa to confirm the results of our study.

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