



Evaluation of Artery Sequential Interventional Therapy on Pernicious Placenta Previa

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Abstract: *Objective:* To evaluate the effect of artery sequential interventional therapy (internal iliac artery catheterization and occlusion/ uterine artery or internal iliac artery embolization) on the hemorrhage of pernicious placenta previa. *Method:* The total of 29 patients with pernicious placenta previa and risk factor of placenta accreta from March 2012 to June 2013 in our hospital were included as control group, who were given traditional method of treatment, while 40 patients with the same disease status from July 2013 to October 2014 as treatment group with artery sequential interventional therapy. The amount of blood loss during operation and red blood cell suspension transfusion, the rate of hysterectomy cesarean time, the amount of cesarean section hemorrhage after 24 hours, duration of postoperative hospital stay, the time of postoperative antibiotic usage and the prevalence of complications (pain, fever, infection and others) of patients in two groups were evaluated, respectively. *Result:* The significant difference of amount of blood loss during operation [(868.5±549.77) ml vs. (1506.90±1417.39) ml for treatment group and control group, respectively] and red blood cell suspension transfusion [(1.50±1.40) U vs. (2.72±2.00) U], the rate of hysterectomy (2.50% vs. 17.24%), cesarean time [(58.86±20.33) min vs. (70.83±29.26) min] and the prevalence of pain (81.25% vs. 48.28%) and other complications (0.00% vs. 10.35%) (all p values < 0.05) were observed, but not for the amount of cesarean section hemorrhage after 24 hours [(271.66±221.55ml) vs. (255.24±249.47 ml)], the duration of postoperative hospital stay [(5.28±1.66) d vs. (5.69±1.58) d], the time of postoperative antibiotic usage [(3.70±2.16) d vs. (3.48±2.06) d], the pain score [(2.64±0.89) vs. (2.67±1.06)], the prevalence of fever (62.50% vs. 55.17%) and inflammation (5.00% vs. 6.90%) (all p values > 0.05). All patients resumed normal menstruation after weaned for 1 to 3 month and the routine newborn physical examination on 42 days after birth, blood analysis, liver function and neurological examination of infants were normal without blood diseases. *Conclusion:* Artery sequential interventional therapy for patients with pernicious placenta previa was safe, effective and feasible for pregnant and newborn.

Keywords: Artery Sequential Interventional Treatment, Pernicious Placenta Previa, Internal Iliac Artery Catheterization, Internal Iliac Artery Occlusion, Uterine Artery Embolization, Internal Iliac Artery Embolization

1. Background

Pernicious placenta previa (PPP) is proposed for the first time by Chattopadhyay, etc. [1] and it is assumed to be a special kind of placenta previa because the placenta is attached to the previous cesarean section scar of the uterus, which may cause placenta implantation, up to 40% ~ 50% [2,

3]. The main performances [4, 5] of PPP are increased placenta implantation and postpartum hemorrhage, which are related to intractable postpartum hemorrhage, shock, diffuse intravascular coagulation (DIC) and directly threatens the safety of mothers and babies [6]. With the development of the imaging diagnostic techniques such as ultrasound and magnetic resonance imaging (MRI), accurate diagnosis of PPP

become easier for obstetric workers, which will help to process more measures to deal with it, such as filling of uterine cavity with yarn or balloon, B - lynch suture, uterine artery and iliac artery ligation and so on. However, the massive loss of blood at the moment of baby-birth and the stripping of the placenta during cesarean section always lead to little time to take the relevant treatments and in order to resave the lives of the mothers, immediately hysterectomy is essential. In recent years, radiological vascular interventional surgery has progressed much in the treatment of postpartum hemorrhage. At present, radiological vascular interventional therapy is mainly used in postpartum in the field of obstetrics [7], but it would lose the best chance because of time delay after the conventional treatment of postpartum hemorrhage. The massive hemorrhage in short time during cesarean section of PPP will lead to cyclic decompensation, then diffuse intravascular coagulation (DIC) and shock, in case of which uterine artery/iliac artery embolization will not work effectively [8]. Since July 2013 artery sequential interventional therapy (internal iliac artery catheterization and occlusion/ uterine artery or internal iliac artery embolization) is applied for treatment of placenta previa at high risk of placenta implantation instead of traditional treatment in the past years in our hospital. Before cesarean section, we will preset tube in the iliac artery and prepare for interventional therapy, at the moment of baby delivery, block iliac artery immediately. Then we choose uterine artery or iliac artery embolization according to the intraoperative and postoperative situation, which will avoid the movement of parturients and save the time for effective rescue [9]. All the works above significantly reduce the intraoperative and postoperative blood loss/ hysterectomy/ hysterectomy-related-complications and ensure the safety of

parturients [10].

2. Material and Methods

There were 46 patients with PPP from March 2012 to June 2013 in our hospital and 29 of whom with risk factor of placenta accreta were included as control group, who were given traditional method of treatment, while 40 patients from 105 with the same disease status from July 2013 to October 2014 as treatment group with artery sequential interventional therapy. All the patients who were taken for sequential interventional therapy were without blood coagulation dysfunction, serious surgical and medical disease. Patients with placenta increta who were considered as high risk of placenta implantation in this study were chosen according to the following factor: ultrasound/MRI-indicated placenta increta and implantation, ≥ 2 times uterine curettage, ≥ 2 times cesarean delivery, vascular engorgement of lower uterine and richness of blood flow were risk-signs of placenta implantation during cesarean section. Moreover, all the patients were single pregnancy. The patient's age, gestational weeks, gravidity, uterine curettage times, prior cesarean sections, time from the last cesarean delivery in two groups were evaluated, respectively and there were no statistically significant difference (Table 1). All data were expressed as means \pm SD and examined by Student's t-test for statistical significance. $p < 0.05$ was considered statistically significant. This research was based on the ethics standards of Chengdu Women's and Children's Central Hospital. All the patients were informed and signed that data concerning the case would be use for clinical research and submitted for publication, and they consented.

Table 1. General situations of two groups of patients.

	Treatment group	Control group	t	p
Age, y	32.83 \pm 4.38	30.55 \pm 4.43	2.017	>0.05
Gestational weeks, w	36.37 \pm 2.03	36.24 \pm 1.49	0.292	>0.05
Gravidity, n	3.80 \pm 1.52	4.07 \pm 2.01	0.633	>0.05
Uterine curettage times, n	2.65 \pm 1.42	3.03 \pm 1.48	1.09	>0.05
Prior cesarean sections, n	1.08 \pm 0.35	1.03 \pm 0.19	0.568	>0.05
Time from the last cesarean delivery, y	6.58 \pm 3.34	4.93 \pm 2.81	2.155	>0.05

Imaging equipment (Allure Xper FD X-ray) was from Philips Company, Dutch, Iopamidol Injection was from Jiangsu Hengrui Pharmaceutical Company, Ultra-soft SV was from American Cook Company, catheter and godet for angiography were from TERUMO Manufacturers (TERUMO) Co., LTD, 560 ~ 710 μ m (diameter) medical gelatin sponge embolization agents were from Hangzhou Eric kang Pharmaceutical Technology Co., LTD.

Based on enhancement of contractions, patients of control group were given traditional treatments, such as filling of uterine cavity with yarn or balloon, 8 suture, B - lynch suture, ascending branch of uterine artery/uterine artery ligation and iliac artery ligation, alone or cobinationg of them. However, patients of observer group were pretreated with Seldinger's technology: Patients were taken the horizontal position, after

routine disinfection and the asepsis turban spreading, they were punctured bilateral femoral artery and Cook PTA5 balloon were implanted in bilateral iliac arteries through C2 catheter and artery sheath under local anesthesia with 0.1 g lidocaine. Then we need to take out the guide wire, record the position, exhaust the balloon and fix C2 catheter and artery sheath with 3M applicator. After the baby was taken out from the uterus during cesarean section, balloon should be expanded to block the artery. The patients with high risk of postpartum hemorrhage through intraoperative evaluation were treated by uterine artery embolization, or embolization of bilateral iliac arteries with gelatin sponge and gelfoam in case of uterine artery embolization did not work effectively. Otherwise, catheter and artery sheath would be taken out and deal bilateral groin puncture point with compression bandage

after the postoperative angiography indicated that bilateral uterine artery was blocked and the rest branches of iliac artery were usual. The patients were transferred to the ICU after the operation and double lower limbs should be braked 8 hours along with the observation of bilateral puncture point and status of dorsalis pedis artery pulse.

The amount of blood loss during operation and red blood cell suspension transfusion, the rate of hysterectomy, cesarean time, the amount of cesarean section hemorrhage after 24 hours, duration of postoperative hospital stay, the time of postoperative antibiotic usage and the prevalence of complications (pain, fever, infection and others) of patients in two groups were evaluated, respectively. Moreover, information about menstruation recovery, ovarian function (with and without hot flashes, night sweats, mood swings, etc.), and neonatal blood system diseases was also collected through reexamination or telephone follow-up from half a year later to 2 years. Routine physical examination, blood picture, liver function tests (liver enzyme blood levels) and neurologic examination were applied for 42 days old newborns.

Difference of measurement data was compared with analysis of t-test and enumeration data was detected by analysis of variance, $\alpha=0.05$. All data were examined by SPSS 13.0 software for statistical significance. $p<0.05$ was considered statistically significant.

3. Results

There are significant differences between the two groups (treatment group and control group) in terms of amount of blood loss during operation [(868.5±549.77) ml vs. (1506.90±1417.39) ml and red blood cell suspension transfusion [(1.50±1.40) U vs. (2.72±2.00) U], the rate of hysterectomy (2.50% vs. 17.24%), cesarean time [(58.86±20.33) min vs. (70.83±29.26) min)] ($p<0.05$). In the treatment group, there was less amount of blood loss during operation/red blood cell suspension transfusion/the rate of hysterectomy and cesarean time. However, there is no significant differences between the two groups in terms of the

amount of cesarean section hemorrhage after 24 hours [(271.66±221.55ml) vs. (255.24±249.47 ml)], the duration of postoperative hospital stay [(5.28±1.66) d vs. (5.69±1.58) d], the time of postoperative antibiotic usage [(3.70±2.16) d vs. (3.48±2.06) d]. ($p>0.05$) (Table 2). The difference of occurrences of postoperative pain (48.28% vs 81.25%, 33/40, 33/40), and other complications (10.35% vs 0.00%, 0/40, 0/40) had statistical significance between therapeutic group and control group ($p < 0.05$). There is no other complications occurred treatment group, while 1 case of bladder injury, 2 cases of ischemia-reperfusion injury in control group. In therapeutic group, the occurrences of postoperative pain was dramatically higher than that of control group ($p < 0.05$), but the rate of occurrences of other complications was obviously less. Moreover, there was no significant statistical significance ($p > 0.05$) difference of the pain score [(2.64±0.89) vs. (2.67±1.06)], prevalence of fever (62.50%, 25/40 vs 55.17%, 16/29) and inflammation (5.00%, 2/40 vs 6.90%, 2/29) (all p values > 0.05) between the two groups (table 3). In summary, for patients with PPP, artery sequential interventional therapy could significantly reduce the amount of blood losses during operation, also the occurrence rate of hysterectomy and other complications. Compared with control group, artery sequential interventional therapy could induce higher occurrences of pain, but the pain score is not higher and no special treatment was needed. Although the amount of cesarean section hemorrhage after 24 hours, the time of postoperative antibiotic usage, the prevalence of fever was increased in the treatment group, duration of postoperative hospital stay, the pain score, the prevalence of fever and inflammation was less in control groups, and there was no significant difference among all of them. Two groups of the patients (exception of hysterectomy) restored them their menstruation after 1-3 months since they stopped breast-feeding and there was no symptoms of menopause. The babies were healthy and without obvious anomalies on normal newborn physical examination, blood picture/ liver/ neurological examination and blood system diseases after 42 days later.

Table 2. Therapeutic situation of patients in two groups.

	treatment group	control group	t/ X ²	P value
The amount of blood loss, ml	868.50±549.77	1506.90±1417.39	2.468	<0.05
The red blood cell suspension transfusion, U	1.50±1.40	2.72±2.00	2.914	<0.01
The red blood cell suspension transfusion, %	2.50% (1/40)	17.24% (5/29)	4.601	<0.05
The cesarean time, min	58.86±20.33	70.83±29.26	2.006	<0.05
The amount of hemorrhage after 24 hours, ml	271.66±221.55	255.24±249.47	0.286	>0.05
The duration of postoperative hospital stay, d	5.28±1.66	5.69±1.58	1.032	>0.05
time of postoperative antibiotic usage, d	3.70±2.16	3.48±2.06	0.455	>0.05

Table 3. Comparison of complications between two groups.

	treatment group	control group	t/X ²	P value
The prevalence of pain, %	81.25% (33/40)	48.28% (14/29)	9.067	<0.01
The other complications, %	0.00% (0/40)	10.35% (3/29)	4.326	<0.01
The pain score, n	2.64±0.89	2.67±1.06	0.056	>0.05
The prevalence of fever, %	62.50% (25/40)	55.17% (16/29)	0.374	>0.05
Inflammation, %	5.00% (2/40)	6.90% (2/29)	0.025	>0.05

4. Discussion

The placenta adhesion and placenta implantation—resulted by PPP is the main reason of postpartum hemorrhage [11]. In recent years, with the increasing amounts of cesarean section, the occurrences of PPP is also dramatically increased, which could induce postpartum hemorrhage and lead to emergency hysterectomy, and sometimes endanger the lives of the patients [12]. In 1993, Chattopadhyay etc. ¹reported that proportion of placenta previa with placenta implantation is as high as 59.2% after 2 or more than 2 times cesarean section. In the following researches, it is also indicated that increased rate of cesarean section could result in higher rates of placenta previa and placenta implantation. Sumigama [13] reports that the incidence of placenta previa with placenta penetration or implantation was up to 0.039% and 99.7% of them had a history of uterine surgery. Uterine surgery, especially cesarean section which could lead to endometrial damage, is the important risk factors for placenta previa with implantation. Endometrial damage and poor healthy of incision scar after cesarean section will let the villi and placenta easy to invade the muscularis and serosa, which at last result in pernicious placenta previa with implantation. The more the times of cesarean section, the higher the rate of PPP with implantation [14]. From the foreign literature, we got the information that the incidence of placenta previa in china is higher than other country, which may related to the family planning policy of the different race and religion, and also because of the high rate of cesarean section in our country [15]. Therefore, we should pay more attentions to prevent postpartum hemorrhage resulted by PPP.

4.1. The Therapeutic Action of Artery Sequential Interventional Therapy for Patients with PPP

In 1993, Chattopadhyay etc. [1] reported that proportion of placenta previa is five times higher in the group of patients with cicatricial uterus and 38.2% of them with placenta implantation. Occurrence of placenta previa is 10% after one time of cesarean section, but it is up to 59.2% after 2 or more than 2 times of cesarean section, and the rate of hysterectomy is as high as 66% for patients with placenta previa and placenta implantation in the perinatal period. We choose cesarean section to terminate pregnancy once the patients are diagnosed with PPP. However intractable postpartum hemorrhage and high hysterectomy have been problems during cesarean section all the time. It is reported [16] that traditional treatment for proportion of placenta previa: in case of Uterine massage to contract the uterus and administration of uterotonic drugs cannot effectively strengthen the contractions and reduce bleeding, balloon or yarn tamponade, 8 suture, squares suture, Blynch suture, ascending branch of uterine artery/uterine artery ligation and iliac artery ligation are applied, alone or combination. Bilateral iliac artery ligation or hysterectomy is used if the traditional treatments are not valid and blood bleeding is not contorted. But bilateral iliac artery ligation is difficult to operate which with > 50% of failure rate and big traumatic [17, 18]. Although hysterectomy can control blood bleeding

effectively, it is at the expense of the loss of organ and reproductive function. Besides, 50% ~ 70% of ovarian blood supply is from the ovary branches of uterine artery, hysterectomy may affect ovarian function and quality of life of patients through a series of physiological and psychological changes. Because it is rich in collateral circulation of blood vessels between uterus and pelvic, especially with the healing of abdominal wall scar and uterine scar, inferior epigastric artery of external iliac artery is easily involved in establishing the collateral blood supply, efficient of uterine artery ligation or iliac artery ligation is only about 50%, and with more complications [19]. Multiple pregnancy and scar pregnancy can cause placenta implantation, spiral arteries, especially the scar arteries can not be squeezed and retracted as normal when uterine instauration after baby birth. Internal iliac artery ligation is a difficult operation which need a skilled obstetrics and gynecology doctor who is familiar with pelvic surgery and has the ability to identify the external iliac artery and femoral artery pulsation before and after ligation; in order to avoid damage of iliac vein, if not it will lead to severe pelvic hemorrhage. Some experts agree that the patient who is diagnosed as PPP with placenta implantation should be routine hysterectomy after cesarean section in order to reduce the risk of postpartum hemorrhage [20]. For the patients who is with postpartum hemorrhage (most of them are 20~40 years old), hysterectomy means permanent loss of uterus which is not only a reproductive organ, also has the important function of endocrine. Moreover, 50%~70% of ovarian blood supply is from the ovary branches of uterine artery, hysterectomy may affect the endocrine function of ovary and result healthy problems of patients through a series of physiological and psychological changes. For the first time (1997), interventional treatment has been successfully applied in the postpartum hemorrhage by Brown etc [21]. At present, the technology of pelvic artery embolization for treatment of severe hemorrhage has been widely used in China and abroad, the success rate is as high as 90%~100% [22]. In recent ten years, interventional treatment of artery embolization is relatively popular and selective artery embolization is always used to reduce blood bleeding during operation when conservative treatment is invalid [23]. It is difficult to touch pulses when the patient is under the state of shock, at this time, rapid puncture and catheter indwelling should be instead by the puncture method which is taken under perspective of vein [24]. In recent years, the intervention operation is improved and named as artery sequential interventional treatment in this paper: the balloon is implanted in iliac artery before cesarean section and filled by saline solution to expand the pressure for blocking blood flow once the baby birth. If these doses not work, artery embolism is applied. There are two kinds of selective artery embolization [25], including internal iliac artery embolization (IIAE) and uterine arterial embolization (UAE). Artery embolization blocked the bleeding vessels which could result in decreasing of arterial blood pressure and speed of the organs; at last make it advantageous for

thrombosis information. After embolization of uterine artery/iliac artery, blood flow is decreased, ischemia and hypoxia cause uterine muscle to contract so that get the goal of bleeding control [26]. Using of this method, not only controlled the blood bleeding, but also reduce the complications of interventional embolization [26]. In this report, we got the information that there was less amount of blood loss during operation/red blood cell suspension transfusion/the rate of hysterectomy and cesarean time in the treatment group. While there is no significant differences between the two groups in terms of the amount of cesarean section hemorrhage after 24 hours, the duration of postoperative hospital stay, the time of postoperative antibiotic usage. For patients with PPP, artery sequential interventional therapy can control blood bleeding quickly in short operation time and with fewer complications and higher successful rate, but also reduction of hysterectomy. Especially for the young women who need to retain reproductive function, artery sequential interventional therapy will not increase the incidence of cesarean section hemorrhage after 24 hours, the duration of postoperative hospital stay, the time of postoperative antibiotic usage, but avoid the opportunities of hysterectomy and finally retain the function of fertility. Take all the information above, we got the conclusion that artery sequential interventional therapy is safe and efficient and for patients with PPP can significantly.

4.2. Complications of Artery Sequential Interventional Therapy on PPP

Complications of interventional treatment include fever, pain, hematoma, infection and so on. In order to prevent the complications, local oppression of femoral artery puncture site after operation is need. Besides, we should pay attention to artery pulse and skin temperature of observe dorsalis, and antibiotics using is also involved. Treatments of complications: (1) Pain: Because of tissue ischemia, necroses, the patients always tell a pain of hip and uterus which will last 3-7days, just relieve the plainness. (2) Fever: it is not essential to treat for the reasons that it is associated with drug reaction and necrotic tissue absorption and generally not more than 38°C, but high degree always indicates infection. (3) Nausea and vomiting happens within 48 h after the operation, because of the necrotic tissue absorption, the patients may appears as weakness, fatigue, anorexia, after the surgery, what we need to do is symptomatic treatment and the patients will recover in several days. (4) Allergy: Some patients are allergic to contrast agents and there is no special treatment. (5) Nerve damage: Iliac artery occlusion can cause neurological ischemic damage which could appear as paralysis, limb numbness, Brown - Sequard syndrome, but most of then could alleviate in 7-14days. (6) Ectopic embolization is the most serious complications of the embolization, which may related to choice of embolic agents, failing insert of front catheter, too much artery embolization agent that force the agent reflux roughly. Ectopic embolization may damage the target organs (such as the rectum and bladder, ovarian, etc.) through embolization, ischemia, and necrosis [27]. All the operators

should be familiar with pelvic vascular anatomy so that prevent embolism of hips and thrombosis of lower limbs. In most of the literature, it is reported that feel barriers of lower limb, low grade fever and pain is common after gelatin sponge particles embolization [28]. There is no serious complications in our study except postoperative abdominal pain, hip pain, and low thermal reaction and postoperative pain generally do not need special treatment, but can relieve by themselves. Blood loss of PPP during the cesarean section was about 3000~5000 ml, 66% of hysterectomy in the perinatal period, and for the most time it always company with bladder and ureter injury [29]. The difference of occurrences of postoperative pain (48.28% vs 81.25%, 33/40, 33/40), and other complications (10.35% vs 0.00%, 0/40, 0/40) had statistical significance between therapeutic group and control group ($p < 0.05$). There is no other complications in treatment group, while 1 case of bladder injury, 2 cases of ischemia-reperfusion injury in control group. In therapeutic group, the occurrences of postoperative pain was dramatically higher than that of control group ($p < 0.05$), but the rate of occurrences of other complications was obviously less. Moreover, there was no significant statistical significance ($p > 0.05$) difference of the pain score [(2.64±0.89) vs. (2.67±1.06)], prevalence of fever (62.50%, 25/40 vs 55.17%, 16/29) and inflammation (5.00%, 2/40 vs 6.90%, 2/29) (all p values > 0.05) between the two group. The reason of no difference of VAS score between the two groups may be related to using of patient controlled analgesia (PCA). In therapeutic group, pre-placement of iliac artery balloon for the patients were all successful and there are no complications, including pseudoaneurysms in formation and thrombosis of iliac arterial, deep vein thrombosis of lower extremity and so on. Agents for embolization is named as gelatin sponge which is soluble and can be absorbed by the organization in 14~21 days after the embolization so that the blood vessels can restore patency and maintain the blood supply of uterine [30]. For ovarian, radiation of 200-300 cGy will result near future or long-dated injury of, >400 cGy can lead to irreversible damage. It is reported in some studies that blood supply of ovarian will restore quickly after temporarily reduction during interventional treatment and the amount of radiation is too lower to injury ovarian. There is no data support that uterine artery embolization will affect the ovarian function [31]. Brent and his fellows suggest that if the radiation dose is less than 200 mGy, it will not lead to the occurrence of fetal congenital diseases [32]. Proper suing of interventional treatment can make the radiation dose is less than 150 mGy which is safe for the babies [33]. In therapeutic group, the CD of radiation is 10.0~50.6 mGy, average amount is 30.6 mGy, less than 150 mGy is assumed as safety for the babies which is similar with Gonglin Zhang's report [34, 35]. Two groups of the patients (exception of hysterectomy) restored them their menstruation after 1-3 months since they stopped breast-feeding and there was no symptoms of menopause. The baby were healthy and without obvious anomalies on normal newborn physical examination, blood picture/ liver/ neurological examination and blood system diseases after 42 days later, and long-term

observation is in progress. Although artery sequential interventional therapy for patients with PPP can increase the occurrences of postoperative pain, but it significantly reduce the other postoperative complications of surgery and there is no significance of VAS score and inflammation between the two groups. Long-term complications on patients and the babies artery sequential interventional therapy may have still need further studies.

5. Conclusion

artery sequential interventional therapy for patients with PPP not only can significantly reduce the amount of blood loses during operation, but also reduce the occurrence rate of hysterectomy and protect the bladder and ureter. Compared with conventional treatment methods, artery sequential interventional therapy dose not increasing the long-term complications and it could be assumed as a safe and effective new method for patients with ppp.

Conflict of Interest Statement

All the authors do not have any possible conflicts of interest.

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