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CONSERVATIVE MANAGEMENT IN THE TREATMENT OF SECONDARY PPH WITH EXCESSIVE BLOOD LOSS OF UNKNOWN ETIOLOGY, COULD IT AVOID SURGERY? A CASE REPORT

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Abstract

Introduction: Tranexamic acid is an antifibrinolytic agent typically used in managing hemorrhage. This is the first reported case to use tranexamic acid as the main treatment protocol in secondary PPH in a case with severe vaginal bleeding which would have rather been only managed by surgical intervention.

Case Presentation: A 38-year-old patient, who had an uncomplicated one pull ventouse KIWI delivery followed by primary PPH of unknown etiology from the common causes. Then ten days post-delivery had secondary PPH with excessive blood loss. Common causes of primary and secondary PPH have been excluded while the only identifiable cause was a bacterial vaginosis; Gardenalia infection detected by high vaginal swap however not sufficient as a main reason to cause such extensive hemorrhage. The case was managed conservatively and medically while avoiding surgical intervention which is usually the inevitable destination of such a case.

Conclusion: In line with the WHO guidelines, we recommend that Tranexamic acid to be considered as a first line treatment of secondary PPH regardless of the etiology. Although treating the cause is a must, but commencing Tranexamic acid with continuous administration until the hemorrhage completely settles is a strong recommendation to control the bleeding and avoid the progression to severe blood loss where hysterectomy or other surgical or radiological interventions will be the remaining treatment options.

Keywords: postpartum hemorrhage, conservative management, KIWI delivery, tranexamic acid

Introduction

Postpartum hemorrhage (PPH) is the most common cause of maternal mortality in all over the world. Primary PPH is generally defined as 500 ml blood loss or may be more among 24 hours after normal delivery of vagina and after Caesarean section loss of blood is more than 1000 ml, it affects almost 5% of all women who gave birth globally (1). In all over the world, among all maternal deaths about one quarter are linked with PPH, and mostly it is the foremost cause of maternal mortality in low-income countries. Routine PPH prevention (by active management of the third stage of labor) and early and efficient PPH therapy, including the use of uterotonics and fluid replacement, could avert the majority of these (2). Secondary PPH, unlike primary has no standard definition for the quantity of blood loss and clinical expressions of this definition vary from increased lochia to massive bleeding. In treating PPH Tranexamic acid, an antifibrinolytic agent, was considered as auspicious drug. (3). WHO now strongly advises women with clinically-diagnosed PPH following vaginal birth

or Caesarean section to utilize IV tranexamic acid as soon as possible (among 3 hours of birth), moreover to normal care. Regardless of whether the bleeding is assumed to be caused by genital tract trauma or other factors, such as uterine atony, in all cases of PPH tranexamic acid must be assumed (4).

Case Report

A 38-year-old patient, Gravida two para 0+1, who is a border line non proteinuria hypertensive patient, who had an uncomplicated pregnancy presented to the delivery suite at thirty-nine weeks gestation with history of leaking liquor and mild uterine contractions with intrapartum augmentation achieved full dilatation of the cervix with normal progression to second stage of labor (5). The indication for KIWI delivery was due to a prolonged second stage of labor and maternal distress which was an uncomplicated one pull ventouse delivery with complete delivery of the placenta by controlled cord-traction (6).

Two hours post-delivery, the patient had a sudden onset of severe vaginal bleeding with clots followed by repeated fainting attacks with quick recovery leading to the diagnosis of primary PPH (7). Initial resuscitation and management of primary PPH was commenced promptly administering 10 units of Syntocinon direct IV and 40 units Syntocinon infusion. The patient was admitted to the ICU following a drop in the Hb; from 13 g/dl to 7 g/dl due to the severe blood loss as well as a hypovolemic shock. She received 2 units blood transfusion as immediate management as well as continuous administration of uterotonics (8).

On observation of increased blood flow, Tranexamic acid 1 gm STAT followed by 1 gm TDS IV daily. Thorough investigation to identify the cause of the bleeding was conducted (9). Full physical examination including Bed side abdominal, vaginal and cervical exploration was performed with no cause of PPH detected. Uterine atony, cervical, vaginal and perineal tears were excluded by clinical examination (10). An Abdominal and Pelvic ultrasound was conducted to rule out retained products of conception, uterine trauma and other causes of primary PPH. The main findings were that there is a postpartum appearance of the uterus, bulky with thickened endometrium and the endometrial cavity distended with clots measuring 2.8 cm 9 (11). Echogenic material with vascularity was noted within the endometrial cavity but was not suggestive of RPOCs. Both ovaries appeared to be normal in size and echotexture. The patient remained hospitalized for 7 days until the bleeding settled and was discharged home in a stable condition (12).

Ten days post-delivery, the patient presented to the Emergency department with heavy vaginal bleeding and clots, low grade fever and high non proteinuria blood pressure. Resuscitation procedure were immediately commenced (13). The patient was re-admitted to the ICU due a drop in the hemoglobin from 11 to 7 g/dl. She received another 2 units of blood transfusion. Medical treatment of secondary PPH commenced including Tranexamic acid, Syntocinons, Prostaglandin E2, and antihypertensive medications (14). Triple antibiotics were administered as the vaginal swap was positive for bacterial vaginosis Gardenalia infection. The case was managed conservatively so as to avoid any surgical interventions; while tranexamic acid remained as the main treatment protocol (15) Transvaginal sonography was conducted where the findings came back showing that there is an anteverted uterus which is bulky in size with a heterogenous area measuring 12 * 6.6 * 3.7 cm noted within the endometrial cavity however without evidence for increased vascularity. Cervical was found to be open (16). Both ovaries appeared to be normal with minimal free fluid noted. The TVS concluded that the large heterogenous area within the endometrial cavity is a suggestion of blood clots rather than retained products of conception. Then to confirm the findings, an MRI Pelvis Scan + C was carried out the following day (17). Pre and Post Contrast Images have been obtained using axial, sagittal and coronal planes. The findings confirmed the result of the TVS scan and the main findings were significant filling of the endometrial cavity with heterogenous material measuring 10 cm at its

maximum height and 4 cm at its maximum sagittal extension and 5.5 cm at its maximum coronal extension (18).

The MRI Pelvis Scan + C concluded that a large heterogenous material was seen occupying the endometrial cavity; the signal characteristic of which is consistent with bleeding of variable ages and the high signal changes consistent with recent hemorrhage (19). Pelvic TVS ultrasound and pelvic MRI were both showing clots in the cavity of uterine with no reserved conception products or AV malformation detected (20)

The case was a challenging case to manage as the patient was at high risk due to the excessive bleeding of unknown etiology. However, any surgical intervention such as evacuation of the uterus and/or hysterectomy was to be avoided, and controversial treatment remained the therapeutic goal to control the bleeding (21). The blood clots by the aid of uterotonic agents were slowly expelled and the bleeding was massively controlled by tranexamic acid (22). The Gardenalia infection was treated with broad spectrum triple antibiotics, was the only identifiable finding and thought to be the sole cause for the secondary PPH. The patient was discharged stable however on labetalol 100 mg TDS and tranexamic acid 1 gm TDS for 3 weeks (23).

Discussion

Postpartum hemorrhage is the most mutual type of major obstetric hemorrhage, responsible for about 25% of maternal deaths worldwide. [1] It refers to an estimated blood loss of 500 mL or more after delivery. There are two types of PPH: Primary and Secondary. Primary PPH occurs within 24 hours after delivery and is characterize by a blood loss of 500ml or more. While secondary Postpartum hemorrhage is blood loss following 24 hours up to 6 weeks after delivery and has no standard definition for the quantity of blood loss. Clinical expressions of this definition vary from increased lochia to massive bleeding (24).

The four Ts defined the causes of postpartum hemorrhage that involves.

- **Trauma:** birth canal injury that can even happen when delivery is properly monitored. The bleeding is substantial because during pregnancy the vagina, perineum, cervix and uterus become more vascular
- **Tissue:** fetus or placenta tissue retention as well as abnormalities of placental i.e., placenta uterine or accreta inversion is the major cause of bleeding.
- **Thrombin:** it is bleeding disorder that occurs due to failure of clotting.
- **Tone:** Uterine atony a uterus incapability to indenture leads to unceasing bleeding. Reserved placental infection and tissue may lead to uterine atony. The most common secondary and primary cause of postpartum hemorrhage is uterine atony.

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Primary PPH major causes involves retained placenta, hematomas, consumptive coagulopathy, lower genital tract lacerations uterine atony, uterine rupture and uterus acute inversion. Late and Immediate problems of primary postpartum hemorrhage involve renal failure, cerebral anoxia, anemia, Sheehan's syndrome and hypovolemic shock puerperal sepsis. The status of antepartum hemoglobin and total loss of blood effect hemorrhage result. While in secondary postpartum hemorrhage the major cause is likely to be an infection or retained products of conception not identified earlier (25).

Therefore, identifying the cause is crucial in order to control the bleeding. The very first approach is to overcome the primary cause is surgical correction for lacerations and uterotonics for atony (30). On the basis of pharmacological and biological principles oxytocin and ergometrine was considered

[1]Mousa HA, Blum J, Abou El Senoun G, Shakur H, Alfirevic Z.,Treatment for primary postpartum haemorrhage., Cochrane Database Syst Rev,2014;(2):CD003249

as PPH treatment. The recognition and identification of their uterotonic structures that uterine atony acts as an important part in PPH directed to their wide acceptance as first line drugs in its supervision. Therefore, their use as preventative measures during labor's third stage constituted an expansion of their role in treatment. It is intriguing, though, that there are more trial data supporting their use in prophylaxis than in treatment. Later, when prostaglandins' uterotonic properties were discovered, PPH was also treated with them. (26).

Low fibrinogen due to loss, dilution, or fibrinolysis evidence can foretell the development of major bleeding (>1500 ml). Obstetric or postpartum hemorrhage (PPH) can become extremely hazardous in the context of coagulopathy, necessitating repeated blood transfusions, hysterectomy, or even death. Surgical management of intractable post-partum hemorrhage used to be the standard management plan by undergoing hysterectomy. However, a major advance has set the use of Tranexamic acid as the key to avoiding any surgical intervention and actively managing the bleeding; while also treating the cause with needed medications.

Agents of Antifibrinolytic, primarily tranexamic acid, have been confirmed to lower the loss of blood in PPH patients. Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules therefore used in the management of hemorrhagic episodes (27)

In bleeding trauma patient tranexamic acid helps to lower death and is efficient in lowering surgical patients bleeding.

According to the recently released World Maternal Antifibrinolytic (WOMAN) trial, women with PPH who received intravenous TxA experienced a markedly lower risk of bleeding fatalities (Risk ratio 081) than those who got a placebo. Neither moms nor breastfed infants saw an increase in post-partum thrombotic rates. This experiment has demonstrated that intravenous TxA can be used to safely and efficiently treat PPH, and that it should be widely utilized to lower PPH-related death rates. Treatment and prevention recommended by WHO in 2012 involved a restrictive recommendation to utilize TXA when uterotonics miss to overcome bleeding.

Consequently, there has been a main development where the WHO sturdily mentions primary habit of arterial tranexamic acid (in 3 h of birth), Moreover to typical women care with clinically identified post-partum hemorrhage ensuing caesarean section or vaginal birth. The GDG endorses treatment with tranexamic acid at a fixed dose of 1 g (100 mg/mL) intravenously at 1 mL/min (i.e., given over 10 min), with a second dose of 1 g intravenously if bleeding persists after 30 min or if bleeding resumes within 24 h of finishing the first dose. This recommendation is based on the dosing regimen used in the WOMAN trial (28).

Tranexamic Acid has a supportive protection profile for the quantity used in the trial of WOMAN. As compared to the control group of the study Venous thromboembolic renal complication, seizures, and events were NOT perceived at developed rates (29).

Beside PPH treatment of Tranexamic Acid, with uterotonics and antibiotics is also available:

- **Antibiotics** – mostly it is a combination of metronidazole and ampicillin. In case of overt sepsis or endomyometritis Gentamicin must be added to the above combination.
- **Uterotonics** – examples involve syntometrine (oxytocin ergometrine), syntocinon (oxytocin) misoprostol (Prostaglandin E1) and carboprost (prostaglandin F2) (30)

The World Health Organization reorganized its 2012 PPH handling endorsements to involve the TXA use for PPH treatment in retort to this new indication, suggestion from the approaching Cochrane

systematic assessment on TXA effectiveness for PPH3, and evidence from a distinct participant meta-analysis data of 40,138 bleeding patients4 (31). The current 2012 World Health Organization recommendations for the treatment and prevention of PPH supersede this advice, which replaces the recommendation on TXA. (32).

Conclusion

After vaginal delivery in women with conventional PPH, TXA use lowers hysterectomy risk and does not enhance thrombotic events risk. We commend that Tranexamic acid to be used regardless of the cause until bleeding settles and to be continued even after the patient being stably discharged. Further studies on the safety of long-term use of Tranexamic acid in cases of secondary PPH needs to be conducted.

Conflict of Interest

In this study there is no conflict of interest

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