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Carbetocin versus oxytocin for the prevention of postpartum haemorrhage during caesarean section-A study of 100 cases in Combined Military Hospital, Momenshahi

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Abstract
Postpartum bleeding or postpartum hemorrhage (PPH) is often defined as the loss of more than 500 ml in vaginal delivery or 1,000 ml of blood in caesarean section within the first 24 hours following childbirth. It occurs more commonly in those who: already have anemia, obesity, multiple pregnancy, older than 40 years of age. It also occurs more commonly following caesarean sections, during medications are used to start labor, during the use of a vacuum or forceps. In the developing world about 1.2% of deliveries are associated with PPH and when PPH occurred about 3% of women died. Globally it occurs about 8.7 million times and results in 44,000 to 86,000 deaths per year making it the leading cause of death during pregnancy. In UK, during2000–2002, PPH was the second most frequent cause of maternal death. Caesarean section is an agonized risk factor for PPH and the worldwide caesarean delivery rate is increasing It has been found that a hormone named oxytocin, plays an important role to stimulate the uterus to contract shortly after the baby is born. Another drug named carbetocin is also used to control postpartum hemorrhage. So, in this study our main objective to find most crucial and effective drug of PPH prevention by comparing effectiveness of carbetocin vs. oxytocin.
Keywords: *Postpartum hemorrhage, caesarean sections, carbetocin, oxytocin.*

Introduction

Postpartum haemorrhage (PPH) remains a major cause of maternal deaths worldwide, and is estimated to cause the death of a woman every 10 minutes[1]. The risk of postpartum haemorrhage is much higher for women, when they are undergoing caesarean section. In most cases, uterine atony is responsible for the occurrence of excessive bleeding during or following childbirth[6]. There are signs or symptoms of low blood volume for the condition to exist[8]. Initial signs and symptoms are; an increased heart rate, feeling faint upon standing, and an increased breath rate[7]. Primary postpartum bleeding is defined as blood loss in excess of 500ml following vaginal delivery or 1000ml following caesarean section in the first 24 hours following birth[2]. Secondary postpartum bleeding is that

which occurs after the first day and up to six weeks after childbirth[3]. As more blood is lost the women may feel cold, their blood pressure may drop, and they may become restless or unconscious[7].

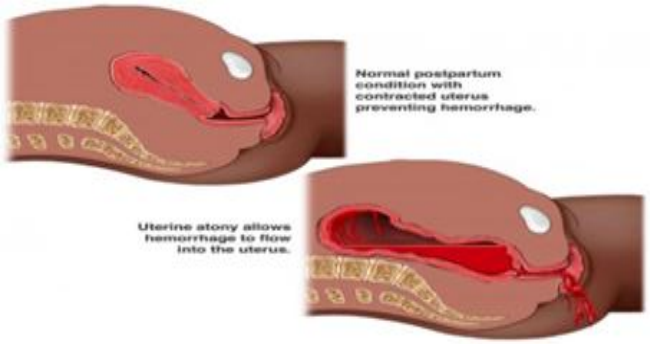

Figure 1: This figure shows normal postpartum condition with contracted uterus preventing hemorrhage (upper) and uterine atony allows hemorrhage to flow into the uterus (lower).

Prevention involves decreasing known risk factors including procedures associated with the condition, if possible, and give the medication oxytocin to stimulate the uterus to contract shortly after the baby is born[2]. Oxytocinis a peptide hormone and neuropeptide. It is normally produced by the paraventricular nucleus of the hypothalamus and released by the posterior pituitary and plays a role in social bonding, sexual reproduction in both sexes, and during and after childbirth[9],[10]. The administration of oxytocics after the delivery of the neonate reduces the likelihood of PPH and10 IU oxytocin through slow intravenous injection is currently recommended for all caesarean sections. The use of additional oxytocin medication is common to arrest bleeding, or prophylactically if there are risk factors for PPH. It has been revealed that an additional 8-hour oxytocin infusion was used in more than 20% of caesarean sections in an adult.

Figure 2: Chemical structure of oxytocin with labeled amino acids and oxytocin injection.

Carbetocin is compared with oxytocin produced a reduction in women who needed uterine massage and further uterotonic drugs for women having caesarean sections. Carbetocin is a synthetic analogue of human oxytocin with structural modifications that increase its half-life thereby prolonging its pharmacological effects. Two double-blind randomized trials compared 100 µg carbetocin (the licensed dose) with different combinations of oxytocin, bolus and infusion, following caesarean section. The first trial found that significantly more women needed additional oxytocic interventions in the oxytocin group. The second trial found no significant differences in the intraoperative blood loss. This study compared carbetocin directly with the currently recommended (and licensed) dose of oxytocin (10 IU) so the performance of this comparison in a double-blind randomized trial[2].

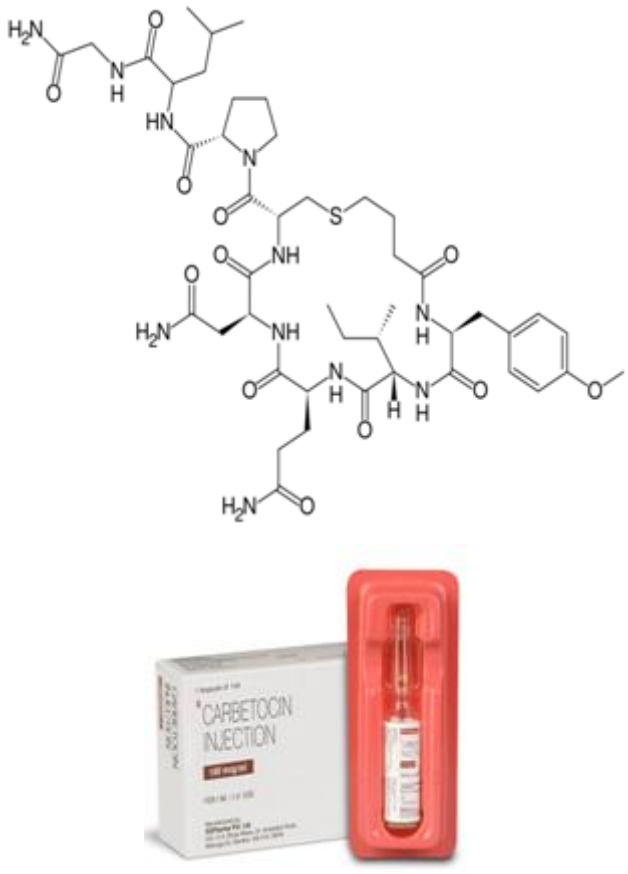

Figure 3: Skeletal formula of carbetocin and carbetocin injection.

Objective

To compare the effectiveness of carbetocin and oxytocin, when they are administered during caesarean section for prevention of postpartum haemorrhage (PPH).

Methodology

Study design

- Double-blind randomized single centre study (1:1 ratio).

Setting

- The study took place in Combined Military Hospital-Momenshahi, Mymensingh for one year May 2017 to May 2018.

Primary outcome

- The proportion of women in each arm of the trial that needed additional pharmacological oxytocic interventions.

Secondary outcome

- Estimated blood loss, difference in preoperative and postoperative hemoglobin, vital signs during and after the operation, uterine tone, incidence of blood transfusion and adverse effects.

Inclusion criteria

- Women with a singleton pregnancy undergoing elective or emergency caesarean section after 37 weeks of gestation.

Exclusion criteria

- Women with multiple gestation, placenta praevia and placental abruption were excluded because there is a higher risk of hemorrhage with these conditions and it was therefore felt to be inappropriate to recruit these women. Women undergoing caesarean section with general anesthesia were also excluded, because carbetocin is licensed for use with regional anesthesia only. Furthermore, we excluded women undergoing caesarean section at less than 37 weeks of gestation (likely to be emergency caesarean sections; a different smaller group from term pregnancies) and women having emergency caesarean section for fetal or maternal distress where, due to time constraints, it was not possible and/or appropriate to recruit or randomize.

Methods

- Women were randomized to receive either carbetocin 100 µg or oxytocin 10IU intravenously, after the delivery of the baby. Perioperative care was otherwise normal and use of additional oxytocic was at the discretion of the operating obstetrician. Analysis was by intention to treat. Primary outcome measurement of this study was the proportion of women in each arm of the trial that needed additional pharmacological oxytocic interventions

Data collection

- Demographic, pregnancy and postnatal data were recorded by the researchers on the study preformats. Data relating to the operation [indication, estimated blood loss, additional oxytocic (s) used, uterine tone and adverse effects] were recorded on preformats filled in by the operating obstetrician. Blood loss was estimated by the surgeon in the usual way (visual estimation, number of used swabs and amount of aspirated blood). Blood pressure and pulse readings were recorded on the anesthetic and recovery charts. Women were followed up to discharge from the hospital[2].

Table 1 Demographic and other baseline data for the two study groups; data are presented as n (%), unless stated otherwise

Variable	Carbetocin (n =50)	Oxytocin (n =50)
Age, median (range)	32 (18–42)	32 (18–44)
Parity Primiparous(%)	11(22%)	15(30%)
Multiparous (%)	39(78%)	35(70%)
Previous caesarean section (%)	33(66%)	31(62%)
Emergency caesarean section (%)	23(46%)	32(64%)
Previous PPH (%)	13(26%)	12(24%)
Other PPH risk factors (%)	31(62%)	27(54%)
One risk factor	25(50%)	21(42%)
Two risk factors	06(12%)	06(12%)
Prolonged labour	13(26%)	12(24%)
Birthweight (gm), mean (SD)	3391	3470

Table 2 Outcome data for the two study groups; frequencies and percentages shown unless stated otherwise

Variable	Carbetocin % (n = 50)	Oxytocin % (n = 50)
Additional oxytocic given	13(26%)	39(78%)
ProstaglandinE2	05(10%)	07(14%)
Methergin	06(12%)	08(16%)
Oxytocin infusion	02(4%)	24(48%)
PPH	19(38%)	29(58%)
a.Estimated blood loss(500-1000)ml	12(24%)	20(40%)
b.Estimated blood loss >1000 ml	07(14%)	09(18%)
Women transfused with blood	02(04%)	04(08%)
Haemoglobin (g/dl)		
beforeLUCS	10.6	10.3
afterLUCS	10.2	9.6
Secondary PPH	00 (0%)	02 (0%)
Uterine tone on day 1, median (range)	9 (5–10)	9 (7–10)
Pulse beat/min	100-110	70-100
BP at 0 min(mm of Hg)		
Systole	100	120
Diastole	60	70
BP at 60 min(mm of Hg)		
Systole	120	120
Diastole	70	80
O2 saturation	100%	100%
Nausea/vomiting	06(12%)	20(40%)
Itching	00(%)	00(%)
Flushing	00(%)	03(6%)
Restlessness	03(6%)	12(24%)
Other complications	00(%)	00(%)

Result

Recruitment and randomization took place between May 2017 –May 2018. A total of 100 women were randomized in the study and analyzed. Women had previous PPH and PPH risk factors and the proportions were almost similar between the two groups. Women in the study required additional oxytocics such as 13% of women in the carbetocin group and 39% of women in the oxytocin group. Therefore. Result of this study showed, significantly more women

required additional oxytocics in the oxytocin group. The majority of these women had oxytocin infusion, which were administered over 8 hours. There were no significant differences in the secondary outcomes, including major PPH, blood transfusions and fall in hemoglobin. It could be said that, carbetocin is associated with a reduce use of additional oxytocics. Table2 also summarizes the reported adverse effects of the two interventions. The adverse effect profile appears similar and there was no significant difference in the number of women affected by at least one adverse effect.

Discussion

Historical data from the UK shows that the major reduction in PPH deaths occurred between 1850 and 1920, at a time when Ergometrine was only sporadically available and in an impure format [11]. Much of the reduction in PPH deaths occurred before the arrival of purified oxytocic and the use of prophylaxis that started in the 1940s.The natural history of PPH suggests that most atonic PPHs are self-limiting, and that atonic deaths are relatively rare. Although 10% of women have a PPH without prophylaxis, PPH deaths only occur in around 0.27% of women without access to health care (27% of deaths in low-resource settings are from PPH and the highest maternal mortality rates in the world are around1000 per 100 000; this represents 270 per 100 000 or 0.27%). Of these deaths, most result from untreated placenta praevia, retained placenta, or massive abruption .In South Africa, where access to oxytocics is not universal ,the most common causes of PPH death are bleeding associated with caesarean section (26.2%), uterine rupture (17.9%), abruptio placentae (16%), and retained placenta (9.0%). Only 6% of PPH deaths result from uterine atony[12].

The results suggest that carbetocin may be a more potent then oxytocic, but it is unclear whether this will reduce the rate of PPH in particular major PPH. There was no significant difference in the estimated blood loss, although this can be imprecise, especially for blood loss more than 1000ml but blood loss 500-1000ml is significant as it is almost double in oxytocin group. Women in both groups had their haemoglobin checked on the first postoperative day and found difference .4gm/dl in carbitocin group and 0.6 in oxytocin group. All the previous studies of carbetocin demonstrated a lower rate of additional oxytocic usage, but no study (including this one) has demonstrated a significant difference in the rate of PPH, which is arguably a more important outcome.

Limitation

In this study a potential limitation was that the utilization of extra oxytocics was bizarrely high. In our study, over half of the extra oxytocic drugs were given for PPH prophylaxis given not increasing the dose of carbetocin. Because maximum dose of carbetocin is not known. All things considered Table 2 exhibits that carbetocin diminishes the utilization of extra oxytocics for PPH.

Conclusion

Notwithstanding enormous interest in maternal wellbeing administrations all through the world, PPH remains a noteworthy reason for maternal demise. The fast beginning and movement of PPH implies that great administrations are required on the off chance that we are to forestall PPH-related mortality and dismalness. The arrangement of uterotonics to all ladies is essential, and the accessibility of misoprostol will achieve ladies who don't something else approach wellbeing administrations. Be that as it may, late investigations recommend that the fundamental advantage of prophylaxis is a lessening in the rate of baby blues frailty, with the impact on maternal passing staying less certain. In women at generally safe, around 7% in carbitocin group and 9% in oxytocin group lose more than 1000 ml of blood regardless of prophylaxis. These ladies require quick access to life-sparing PPH treatment and protect treatments. Be that as it may, the

danger of major PPH is considerably higher in those with placental abrupsio, placenta praevia, multiple pregnancy and these ladies are correspondingly more averse to react to oxytocics. Huge numbers of these ladies will require progressed PPH treatments or on the other hand save medications to counteract dismalness and mortality. The eccentrics of numerous PPHs implies that gifted birth chaperons should go to conveyances, have proper obstetric emergency treatment aptitudes and gear, and the capacity to exchange ladies quickly. On the off chance that real enhancements in PPH-related mortality are to be accomplished, there should be an expanded arrangement of amazing crisis obstetric care administrations. This incorporates the arrangement of careful administrations to avoid PPH during caesarian section PPH therapeutic medicines, physical medicines (uterine pressure, tamponade, surgical medical procedure), and safeguard bundles (blood transfusion and blood items). More research is currently required to decide the most practical method for giving these administrations.

Reference

1. Weeks, A (January 2015). "The prevention and treatment of postpartum haemorrhage: what do we know, and where do we go to next?". BJOG : an international journal of obstetrics and gynaecology. 122 (2): 202–10. doi:10.1111/1471-0528.13098. PMID 25289730.
2. Attilakos, G., D. Psaroudakis, J. Ash, R. Buchanan, C. Winter, F. Donald, L. P. Hunt, and T. Draycott. "Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double- blind randomised trial." *BJOG: An International Journal of Obstetrics & Gynaecology* 117, no. 8 (2010): 929-936.
3. Lockhart, E (2015). "Postpartum hemorrhage: a continuing challenge". Hematology. American Society of Hematology. Education Program. 2015: 132–7. doi:10.1182/asheducation-2015.1.132. PMID 26637712
4. GBD 2015 Disease and Injury Incidence and Prevalence, Collaborators. (8 October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". Lancet. 388 (10053): 1545–1602. doi:10.1016/S0140-6736(16)31678-6. PMC 5055577 . PMID 27733282.
5. GBD 2013 Mortality and Causes of Death, Collaborators (17 December 2014). "Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013". Lancet. 385 (9963): 117–71. doi:10.1016/S0140-6736(14)61682-2. PMC 4340604 . PMID 25530442.
6. Begum, Poly, Dipti Rani Shaha, Lipika Sanjowal, and Md Kamrul Hassan. "Carbetocin versus Oxytocin for the Prevention of Postpartum Haemorrhage." *Faridpur Medical College Journal* 10, no. 2 (2016): 76-83.
7. Lynch, Christopher B- (2006). A textbook of postpartum hemorrhage : a comprehensive guide to evaluation, management and surgical intervention. Duncow: Sapiens Publishing. pp. 14–15. ISBN 9780955228230. Archived from the original on 2016-08-15.
8. Gibbs, Ronald S (2008). Danforth's obstetrics and gynecology (10th ed.). Philadelphia: Lippincott Williams & Wilkins. p. 453. ISBN 9780781769372. Archived from the original on 2016-06-05.
9. Gray's Anatomy: The Anatomical Basis of Clinical Practice (41 ed.). Elsevier Health Sciences. 2015. p. 358. ISBN 978-0-7020-6851-5.

10. Yang HP, Wang L, Han L, Wang SC (2013). "Nonsocial functions of hypothalamic oxytocin". ISRN Neuroscience. 2013: 179272. doi:10.1155/2013/179272. PMC 4045544 . PMID 24967304
11. Registrar General for England and Wales. Annual report of registrar-general of births, deaths and marriages in England. Her Majesty's Stationery Office, London 1847–1926.
12. National Committee on Confidential Enquiries into Maternal Deaths. Saving Mothers 2008-2010: Fifth report on the Confidential Enquiries into Maternal Deaths in South Africa. Pretoria: DoH. 2012.[http://www.health.gov.za/docs/reports/2012/Report_on_Confidential_Enquiries_into_Maternal_Deaths_in_South_Africa.pdf]. Accessed 6 May 2014.