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Safety of the use of uterotonics in caesarean section

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At present oxytocin (OT) is known as a first line treatment for post-delivery bleeding prevention and therapy. Beside its uterotonic activity OT provides a range of other effects: parasympathetic neuromodulation, vasodilation, negative inotropic and chronotropic effects as a consequence of blood pressure (BP) drop [1]. Considerable decrease of mean BP was shown to develop 30 seconds post-administration while elevated HR and cardiac output emerge within 1 to 5 min. after infusion onset [2]. In clinical settings OT-related hemodynamic changes are usually inconsiderable (15-20%), short-term and well tolerated by healthy women. There are some studies showing that long OT infusion results in increased troponin, myocardium damage marker, and depressed ST segment on ECG [3].

Use of lower OT doses to prevent post-partum bleedings have been made attempted also for quite a while. M.C.Sarnac et al. in their study administered OT dosing 0.4 IU min-1. OT ED90 was 0.405 IU min-1. OT dose increase is a conventional practice having in mind that larger OT dose should improve uterine contractions. The authors showed that higher OT doses did not improve uterine contractile function and, thus, cannot be considered as post-partum bleeding prevention methods since OT receptor number not only remain unaltered but they also turned to be sensitized. E.Zarzur already in 1998 organized a study enrolling 20 pregnant patients with elective CS and suggested that OT dose of 0.024 IU min-1 results in favorable outcome without arterial hypotension, nausea and vomiting. We suppose patient sample was too small, thus, limiting reliability of conclusions produced [4]. However, this study is worth to pay attention to since those days only few researchers considered such risk

factor for hemodynamic complications as oxytocin. In the research by R.B.Hodge et al. OT ED90 was 0.405 IU min-1 (95% CI 0.3864–0.4125). About 25.6% of parturients had short-term hypotension, while 9.4% had short-term tachycardia. In the study puerperants didn't show headache, face redness, chest pain and vomiting. Assumed blood loss was within normal range. OT dose increase did not provide improved uterine tone [5].

The given study results differ from the work by M.Balki et al. who determined minimal effective OT dose required for adequate post-CS uterine contraction in 30 puerperants. OT was given as slow IV bolus (0.5 IU ml-1 with the rate of 1 ml per 5 sec). OT bolus ED90 was estimated as 2.99 IU that was 9 times higher vs. puerperants after elective CS in primipara with full-term pregnancy. It suggests that OT used to stimulate labor might desensitize uterus making it less sensitive to OT during CS [6].

Randomized, double blinded, placebo-controlled comparison of oxytocin and carbetocin given during elective CS interventions with spinal anesthesia showed that 5 IU of oxytocin and 100 μg of carbetocin had concomitant hemodynamic effects with similar onset timing. When given these agents decreased systolic blood pressure and systemic vascular resistance while heart rate, cardiac output and stroke volume increased [7]. In our study the general group showed a trend to higher risk for arterial hypotension (1.62-fold) when giving OT of 10 IU vs. 5 IU dose. Besides, in 5-IU treated groups uterotonic effect was satisfactory with no additional dosing required [8]. The same was seen in the study by L.Tsen. et al. where bolus administration of 3 OT IU during CS was found to be similarly effective to IV drip feed of 30 OT IU in 500 ml of saline solution [9]. Recently published study showed that effective OT dose in 90% of patients necessary to reach adequate uterine tone after emergency CS in patients with high risk of uterine atony was 0.405 IU min-1 (CI 95% 0.3864–0.4125) [10].

Now many tragedies turned to have clearer explanation when acute post-delivery bleeding developed in the settings of sympathetic blockade caused by spinal anesthesia in combination with acute circulatory hypovolemia. Arterial hypotension develops due to OT effects on

vascular smooth muscles through calcium-dependent nitrogen oxide release, which, in turn, decreases general peripheral vascular resistance, increasing vascular bed volume, tachycardia, compensatory increased stroke volume and cardiac output. In such settings myocardium need for oxygen sharply increases along with dramatic fall of oxygen delivery due to massive post-delivery bleeding and hemorrhagic shock [11]. Besides, in the neuraxial anesthesia settings unfavorable hemodynamic OT effects might intensify [12]. Reprimands that OT can cause sudden circulation arrest with intensive care for massive post-partum bleeding emerged quite a while ago and even are reflected in some official documents [13].

Our research has shown that the risk for ST segment depression above 0.5 mm is 8.6 times higher with oxytocin dose of 10 IU vs. its dose of 5 IU. Administration of 10 IU of oxytocin during elective CS does not decrease blood loss vs. 5 IU of oxytocin [8, 14, 15].

References.

1.Shifman E.M., Kulikov A.V., Krugova L.V., Vartanov V.Ya., Marshalov D.V. Uterotonic drugs use safety: What anesthetist-intensivist should know? Anesthesiology and intensive care. 2017; 62(3):220-224.

2. Thomas J.S., Koh S.H., Copper G.M. Haemodynamic effects of oxytocin given as i.v. bolus or infusion on women undergoing Caesarean section. Br.J.Anaesth. 2007; 98:116-9.

3. Jonsson M., Hanson U., Lidell C. ST depression at ceaesarean section and the relation to oxytocin dose. A randomised controlled trial. Br. J. Obstet. Gynaecol. 2010; 117:76-83.

4. E.Zazur Intravenous oxytocin in patients undergoing elective caesarean section. Anesth Analg 1998; 86:1334.

5. George RB, McKeen D, Chaplin AC, McLeod L. Up-down determination of the ED90 of oxytocin infusions for the prevention of postpartum uterine atony in parturients undergoing cesarean delivery. Can J Anesth 2010; 57:578-82.

6. Balki M, Ronayne M, Davies S, Fallah S, Kingdom J, Windrin R, et al. Minimum oxytocin dose requirement after cesarean delivery for labor arrest. Obstet Gynecol 2006; 107:45-50.

7. Leiv Arne Rosseland, M.D., Ph.D., Tor Hugo Hauge, Ph.D. Changes in blood pressure and cardiac output during cesarean delivery. Anesthesiology 2013; 119:541-51.

8. E.N. Degtyarev, E.M. Shifman, G.P. Tikhova, A.V. Kulikov. The effect of oxytocin dose on the ST segment change, arterial hypotension and blood loss in women of different age groups during cesarean section. Alexandr Saltanov Inetensive Care Herald. 2018; 3:77-87.

9. Tsen L., Balki M. Oxytocin protocols during cesarean delivery time to acknowledge the risk/benefit ratio? IOJA. 2010; 19:243-5.

10. Shashikiran, Kaur H, Bala R, Gupta N. A study to determine minimum effective dose of oxytocin infusion during caesarean delivery in parturients at high risk of uterine atony. J Obstet Anaesth Crit Care 2017.7:75-80.

11. E.J. Baird, Identification and Management of Obstetric Hemorrhage. Anesthesiology Clin 35 (2017) 15–34.

12. Rabow S., Olofsson P. Pulse wave analysis by digital photoplethysmography to record maternal hemodynamic effects of spinal anesthesia, delivery of the baby, and intravenous oxytocin during cesarean section. J. Matern. Fetal Neonat. Med. 2016; 26:1-8.15.

13. Bolton, TJ, Randall, K, Yentis, SM. Effect of the confidential enquiries into maternal deaths on the use of syntocinon at caesarean section in the UK. Anaesthesia. 2003; 58(3):277–279.

14. E.N.Degtyaryev, E.M.Shifman, G.P.Tikhova, A.V.Kulikov, I.V.Zhukovets. The effect of oxytocin dosage on the amount of intraoperative blood loss during caesarean section. Gynecology, Obstetrics and Perinatology. 2018; volume 17; No 6.:51-57.

15. E. N. Degtyarev, E. M. Shifman, I. V. Zhukovets, S. V. Khodus. The effect of oxytocin dose on the development of reversible myocardial ischemia in parturient women of different age groups during cesarean section. Far East Medical Journal. 2019. №1, p. 80–84.