



Editorial

Postpartum hemorrhage: A value of carbetocin



In this June issue of the *Taiwanese Journal of Obstetrics and Gynecology*, a meta-analysis of randomized trials focusing on the comparison of effectiveness of carbetocin and oxytocin in the prevention of postpartum hemorrhage (PPH) during the cesarean section (C/S) has been published [1]. The authors enrolled a total of seven studies containing 2012 women undergoing C/S who were treated with either carbetocin or oxytocin in the prevention of PPH for analysis [1]. The results showed the potential benefits of using carbetocin during the C/S compared to the use of oxytocin, including a significant reduction of rates of PPH (risk ratio (RR) 0.79 (95% confidence interval (CI) 0.66–0.94)), a significant reduction of the need for additional uterotonic agent (RR 0.57, 95% CI 0.49–0.65), and of most importance, a significant reduction of the need of blood transfusion (RR 0.31, 95% CI 0.15–0.64) [1]. Therefore, the authors concluded that carbetocin is effective in reducing the risk of PPH, reducing the need of additional uterotonic agents and blood transfusion when carbetocin is used during the C/S. Due to the high cost of carbetocin compared to oxytocin (USD\$ 18.2 versus USD\$ 0.18), the authors did not recommend the priority of the use of carbetocin to oxytocin. By contrast, the authors suggested that local or regional cost-effectiveness analysis should be performed before the decision was made [1]. This study is interesting and worthy of discussion.

Postpartum hemorrhage, although the different definition is made (either PPH \geq 500 mL or PPH \geq 1000 mL) [2], is still a challenge not only for patients but also for physicians. The majority of PPH can be managed well, but some cannot be. PPH may progress to a life-threatening status. To rescue it, much more invasive procedures might be needed, including embolization, and even total hysterectomy [3,4]. There are three big causes contributing to PPH, including laceration (trauma), retained placenta, and atony [5,6]. The last cause might be preventable. A recent Cochrane review shows there are three most effective drugs for prevention of PPH \geq 500 mL, including the combination of ergometrine and oxytocin (RR 0.69, 95% CI 0.57–0.83), carbetocin (RR 0.72, 95% CI 0.52–1.00), and the combination of misoprostol and oxytocin (RR 0.73, 95% CI 0.60–0.90) [2]. When PPH is defined as \geq 1000 mL, all top three options still work [2]. The combination of ergometrine and oxytocin regimen in the prevention of PPH \geq 1000 mL is strongly recommended, because only it reaches a statistical significance (RR 0.77, 95% CI 0.61–0.95) [2]. Considering the side effects, the Cochrane review found that carbetocin had the most favorable side-effect profile amongst these three above-mentioned regimens [2]. The lower risk of side effect in the use of carbetocin in the prevention of PPH is also confirmed by a recent prospective randomized trial [7]. This trial found that carbetocin induced less nausea and vomiting in patients [7].

In Taiwan, there are at least two reports available to study the value of carbetocin in the prevention of PPH [8,9]. Both studies showed the marginal benefits of this agent. One reported the lower incidence of PPH in the carbetocin prophylaxis group compared to the current standard oxytocin (16.4% versus 30.5%, $p = 0.003$) [8]. The other report showed the mean operative time during the C/S could be statistically significant decreased when carbetocin was used ($p = 0.001$) [9].

In term of cost effectiveness ratio, the same group evaluated this item [10]. Voon and colleagues used the different strategies to evaluate the cost-effective ratio to test carbetocin [10]. The results showed the higher index cost of carbetocin could be mitigated by the reduction in retreatment, staffing requirements, transfusion and potential medication errors, which all needed expense. For example, the incremental cost effectiveness ratio of carbetocin for averting an episode of PPH was USA\$ 278.70, suggesting that carbetocin might be cost effective as prophylaxis against PPH [10]. Finally, in term of psychosocial consideration, quality of life, and the priorities of women and their families, it is much more important to apply the more effective and less side-effects of uterotonic drugs in the prevention of PPH during the C/S or even through normal vaginal delivery. It will be welcome to see future evidence synthesis research, which can offer the better recommendation in the prevention of PPH.

Conflicts of interest

The author declares no conflict of interest.

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References

- [1] Voon HY, Suharjono HN, Shafie AA, Bujang MA. Carbetocin versus oxytocin for the prevention of postpartum hemorrhage: a meta-analysis of randomized controlled trials in cesarean deliveries. *Taiwan J Obstet Gynecol* 2018;57: 332–9.
- [2] Gallos ID, Williams HM, Price MJ, Merriel A, Gee H, Lissauer D, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. *Cochrane Database Syst Rev* 2018;4. CD011689.
- [3] Dogan O, Pulatoglu C, Yassa M. A new facilitating technique for postpartum hysterectomy at full dilatation: cervical clamp. *J Chin Med Assoc* 2018;81: 366–9.

- [4] Tsui KH, Lin LT, Wang PH. An easy method to define the cervical borders during postpartum hysterectomy. *J Chin Med Assoc* 2018;81:295–6.
- [5] Chung JP, Leung TY. Uses of FloSeal® in obstetric hemorrhage: case series and literature review. *Taiwan J Obstet Gynecol* 2017;56:827–30.
- [6] Othman ER, Fayed MF, El Aal DE, El-Dine Mohamed HS, Abbas AM, Ali MK. Sublingual misoprostol versus intravenous oxytocin in reducing bleeding during and after cesarean delivery: a randomized clinical trial. *Taiwan J Obstet Gynecol* 2016;55:791–5.
- [7] Mannaerts D, Van der Veeken L, Coppejans H, Jacquemyn Y. Adverse effects of carbetocin versus oxytocin in the prevention of postpartum haemorrhage after caesarean section: a randomized controlled trial. *J Pregnancy* 2018;2018:1374150.
- [8] Chen CY, Su YN, Lin TH, Chang Y, Horng HC, Wang PH, et al. Carbetocin in prevention of postpartum hemorrhage: experience in a tertiary medical center of Taiwan. *Taiwan J Obstet Gynecol* 2016;55:804–9.
- [9] Seow KM, Chen KH, Wang PH, Lin YH, Hwang JL. Carbetocin versus oxytocin for prevention of postpartum hemorrhage in infertile women with twin pregnancy undergoing elective cesarean delivery. *Taiwan J Obstet Gynecol* 2017;56:273–5.
- [10] Voon HY, Shafie AA, Bujang MA, Suharjono HN. Cost effectiveness analysis of carbetocin during cesarean section in a high volume maternity unit. *J Obstet Gynaecol Res* 2018;44:109–16.

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