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ORIGINAL ARTICLE

A prospective cohort study evaluating the cost-effectiveness of carbetocin for prevention of postpartum haemorrhage in caesarean sections

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ABSTRACT

Postpartum haemorrhage (PPH) is the leading cause of maternal mortality worldwide. Prophylaxis with oxytocic medication is recommended by the WHO to prevent its occurrence. Carbetocin is a newer oxytocic, with potential to lower PPH rates, reduce the total use of oxytocic drugs and lead to financial savings. Meta-analyses have confirmed a reduction in the use of additional oxytocic medication with the use of carbetocin compared to oxytocin. However, there are few studies evaluating the costs of carbetocin prophylaxis. We carried out a prospective cohort study evaluating the financial impact of carbetocin, following its introduction at our centre for caesarean section. We collected data for 400 patients in total, making this, to our knowledge, the largest study conducted on this topic. We found a significant reduction in PPH rates and the use of additional oxytocics with projected overall financial savings of £68.93 per patient with the use of carbetocin.

IMPACT STATEMENT

- It is well established that carbetocin reduces the use of secondary oxytocics compared to oxytocin alone in the active management of the third stage of labour. Evidence for reduction of post-partum haemorrhage and its cost effectiveness are more equivocal. Our study demonstrates that carbetocin also reduces post-partum haemorrhage, use of blood and blood products and midwifery recovery time in the setting of caesarean section. We have also demonstrated that despite the increased index cost of carbetocin it delivers an overall substantial cost benefit. The implications of these findings are of reduced morbidity, faster recovery and cost savings in these times of austerity in the UK. It allows more efficient labour distribution of midwives, particularly in the setting of staff shortages across the NHS. A randomised control trial in this area needs to be conducted to determine the cost benefit of carbetocin and with this and post-partum haemorrhage rates as the primary outcome measures.

KEYWORDS
Carbetocin; oxytocin; postpartum haemorrhage; caesarean section; cost evaluation

Introduction

Postpartum haemorrhage (PPH) is the major cause of maternal death and morbidity worldwide, attributable for 27.1% of deaths (Say et al. 2014). Oxytocin is a peptide hormone secreted by the posterior pituitary gland, whose chief physiological effects are to 'let down' milk in lactating mothers and stimulate myometrial contraction in the last two stages of labour. The latter effect also serves the purpose of reducing bleeding in labour, as myometrial contraction reduces blood flow to the uterus (Gimpl & Fahrenholz 2001). This effect is clinically useful and the WHO recommends prophylactic administration of oxytocin to prevent PPH following Caesarean section (WHO 2012). However, bleeding often occurs regardless, necessitating the use of further oxytocin or other treatments to maintain haemodynamic stability.

Carbetocin is a synthetic analogue of oxytocin, with a longer half-life, that has increasingly seen wider use in preference to oxytocin in the UK. Several randomised controlled trials investigating the effect of carbetocin on women undergoing caesarean section have found a single bolus to be as effective and more reliable than continuous oxytocin infusion in preventing PPH (Boucher et al. 1998; Borruto et al. 2009). NHS Improving Quality, UK recommends its use in the enhanced recovery programme after elective caesarean sections (NHS IQ 2012).

A Cochrane review found carbetocin to reduce the use of additional uterotonics and uterine massage when compared to oxytocin (Su et al. 2012). Its use could therefore potentially lead to significant financial savings, however, there is little data on its cost effectiveness in comparison to oxytocin. We have therefore performed a cost evaluation on the use of carbetocin following caesarean section based on prospective observation following the introduction of carbetocin at our centre in October 2014.

Materials and methods

Prospective data collection began in November 2014 and finished in October 2015, using a standardised proforma.

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Data were collected at Poole Hospital, UK, a District General Hospital with approximately 5000 deliveries annually. Of these, 28% are delivered via caesarean section.

Initially, carbetocin was only given to patients undergoing elective caesarean section under regional anaesthesia, whilst other patients were administered oxytocin. In June 2015, carbetocin prophylaxis was rolled out to all patients undergoing caesarean section. As a result, carbetocin and oxytocin cohorts contained both elective and emergency patients.

Data were collected on the volume of blood loss, additional oxytocic use, high dependency unit (HDU) and intensive care unit (ICU) admission and the length of stay in recovery. Information on the parity of each patient was also collected as a confounding factor.

Blood loss was measured by weighing blood soaked swabs and subtracting the dry weight of the swabs. This was then added to the weight of the blood collected in the suction container, the blood drawn here includes that collected from the side pockets of special drapes used at caesarean section. Care was taken to avoid drawing up amniotic fluid into the same container, different suction containers are used for amniotic fluid and blood in caesarean sections at our trust.

Statistical analysis was conducted using SPSS version 23 and Microsoft Excel 2016 for Macintosh. p Values were calculated using the Mann–Whitney U test for continuous data and the Chi-squared test for proportions of categoric variables, with the threshold for significance set at $p < .05$. Averages were presented as medians and interquartile ranges were given to indicate variability.

Drug costs were calculated using the hospital supply price of £10 per dose of carbetocin and other drug costs using the British National Formulary list price. Blood and blood product price was also added. The average cost per patient in carbetocin and oxytocin groups was then derived. Midwifery staff costs were calculated at 3 h per additional oxytocin infusion, excluding the first of the 4 h it was given, as all women in our unit spent first 45–60 min on an average in the theatre recovery area. Women who were admitted to HDU or ITU were excluded from this group and their costs were calculated separately based on the time spent. In some cases where this data was missing, the time spent was assumed to be 12 h as most of our women admitted to our HDU spent this time as a minimum. A rate of (Band 6 midpoint including on costs) per hour £18.78 was used. The actual bed, amenity, food or consumable costs of recovery in the delivery suite/HDU/ITU were not included. The costs were then extrapolated with 1120 caesarean sections eligible for carbetocin per annum.

Results

Demographics

Data were collected for a total of 400 patients, with 227 receiving carbetocin and 173 given oxytocin. Of these, 24 of the carbetocin group had emergency caesarean sections compared to 65 in the oxytocin group. The median parity for both groups was one previous pregnancy. 28.6% of women in the carbetocin group had more than one previous pregnancy compared to 21.4% in the oxytocin group ($p = .099$, not significant). The main indications for elective caesarean sections were previous caesarean section, breech presentation, maternal request followed by twin pregnancy. The indications for emergency caesarean section were failure to progress during the first stage, suspected foetal compromise, breech presentation in labour and antepartum haemorrhage.

Blood loss

There was a significantly lower rate of PPH (blood loss >500 ml) in the carbetocin cohort (Table 1) with only 28% developing a PPH compared with 43% for oxytocin ($p = .002$; RR 1.5). Major bleeding with blood loss greater than 1 and 2 l was also reduced in the carbetocin group (RR 2.2 and 7.9, respectively). The median volume of blood loss was 575 ml (IQR 300–600 ml) in the carbetocin cohort vs 650 ml (IQR 350–730 ml) for the oxytocin cohort ($p = .001$).

However, when comparing elective caesarean sections only, the difference in PPH rates was not statistically significant ($p = .19$). For emergencies, the difference between the groups for the rate of PPH with more than 1 l blood loss was significant with $p = .029$. However, that was not significant for blood loss greater than 500 ml or 2 l (Table 2). There was no need for blood or blood products in the carbetocin cohort. In contrast, 17 units of packed red cells, 4 units of platelets and 6 units of fresh frozen plasma were used in the oxytocin group.

Additional oxytocic use

A large reduction in the use of additional oxytocic medication was observed with the use of carbetocin (Table 1), with only 7% requiring this compared to 48% in the oxytocin cohort ($p < 10^{-20}$). Additional oxytocin infusions were used in 46.2% of the oxytocin group as opposed to 6.2% of the carbetocin group. Subdividing the cohorts into elective sections revealed an even lower use of oxytocics in the carbetocin group relative to the oxytocin group (Table 2). The difference was also

Table 1. Outcomes of oxytocin and carbetocin cohorts.

	Oxytocin	Carbetocin	p Value
Number of patients (N)	173	227	n/a
Number multiparous (N)	37 (21.4%)	65 (28.6%)	.099
Median total blood loss (ml)	650 (IQR 350–730)	575 (IQR 300–600)	.001*
Patients with PPH >500ml (N)	74 (43%)	63 (28%)	.002*
Patients with PPH >1 l (N)	22 (13%)	13 (6%)	.01*
Patients with PPH >2 l (N)	6 (3%)	1 (0.4%)	.02*
Patients requiring additional oxytocics (N)	83 (48.0%)	16 (7.0%)	< 0.001*

*Indicates statistical significance at $p < .05$.

Table 2. Outcomes in elective and emergency caesarean sections.

	Elective			Emergency		
	Oxytocin	Carbetocin	*p* Value	Oxytocin	Carbetocin	*p* Value
Number of patients (*N*)	108	203	n/a	65	24	n/a
Patients with PPH >500 ml (*N*)	46 (42.3%)	71 (35.0%)	0.19	23 (35.4%)	13 (54.2%)	.11
Patients with PPH >1l (*N*)	6 (5.6%)	12 (5.9%)	0.90	16 (24.6%)	1 (4.2%)	.029*
Patients with PPH >2 l (*N*)	2 (0.019%)	1 (0.0049%)	0.24	4 (6.2%)	0	.21
Patients requiring additional oxytocics (*N*)	37 (34.3%)	14 (6.9%)	< 0.001*	46 (70.8%)	2 (8.3%)	< 0.001*

*Indicates statistical significance at $p < .05$.

statistically significant when comparing the emergency cohorts only. Average drug cost per patient in the carbetocin group was £10.33 vs £33.98 in the oxytocin group.

Midwifery staff costs

The average midwifery staffing cost to provide additional 1:1 care per patient was considerably lower at £7.69 in the carbetocin group in comparison to £52.97 in the oxytocin cohort. Additional time spent in recovery was 24 min on average per patient in the carbetocin group vs 169 min in the oxytocin group (a 2 h 25 min difference).

Adverse events

No serious adverse events attributable to carbetocin were observed.

Discussion

Oxytocin is the most widely used and available uterotonic agent used in the active management of the third stage of labour. However, it has a short half-life requiring continuous intravenous infusion to achieve sustained uterotonic activity. In contrast carbetocin's effect lasts four times longer allowing a single intravenous bolus dose.

Additional oxytocin infusion is commonly used either for prophylaxis in women with risk factors or for treatment in 20–35% of caesarean sections according to studies from UK (Attilakos et al. 2010; Shaw et al. 2013b). Our study confirms this, showing a significantly higher proportion of women in the oxytocin group receiving this (46.2% vs 6.2% carbetocin) which is also in agreement with the Cochrane Review by Su et al. and more recent work by Jin et al. (Su et al. 2012; Jin et al. 2016). It has to be noted that both groups were well matched for parity.

Duration of stay in the delivery suite or recovery area requiring 1:1 care has an impact on the efficiency and throughput of busy maternity units, as well as the costs of staff and amenities. Very few studies have evaluated the cost effectiveness of carbetocin in terms of additional uterotonic agents, blood and blood product use. Shaw et al. showed that carbetocin proved to be cost-neutral compared to oxytocin when only additional oxytocic use was taken into consideration (Shaw et al. 2013b). In contrast in our study, additional drug costs were accounted for, including blood and blood products and these made carbetocin a significantly cheaper option with potential annual savings of £26,488 for our unit (£11,569.60 vs £38,057.60).

Our findings exceed the estimate of Shaw et al. (2013a) who also showed significant reduction in recovery times. This was translated into potential savings of £50,713 per annum for our unit. This, combined with savings in drug costs, gives a total saving of £77,201 (£68.93 per patient).

Del Angel Garcia et al. also showed carbetocin to be cost effective in Mexico, as did Pacocha in Poland and Mills in Canada from mathematical models. This was thought to be due to savings from reduced drug costs, reduced blood product use and faster discharge from hospital (Del Angel García et al. 2006; Mills et al. 2014; Pacocha et al. 2016). However, our findings are contrary to Higgins et al.'s finding of a lack of difference in additional oxytocic use or recovery times leading to carbetocin proving more expensive (Higgins et al. 2011).

In contrast to the Cochrane review (Su et al. 2012) and other studies comparing oxytocin with carbetocin, our study found a significant difference in PPH rates including >500 ml, >1 l and >2 l. A particular strength of our study lies in the use of actual measured blood loss as opposed to estimated blood loss used in other studies. Subgroup analysis found that the differences in major PPH >1 l were most likely from the emergency cohort. This was also reflected in blood and blood product use. These results have to be interpreted with caution due to the marked difference in numbers of emergency caesarean sections between the groups.

The major limitation of this study is that carbetocin and oxytocin groups were not matched in terms of demographics and risk factors (other than parity) for PPH due to incomplete collection of data. However, to our knowledge, this is the largest prospective study conducted on this topic. Our demographics are also better reflective of a typical large district hospital in the UK.

Despite the limitations of our study, we have demonstrated the manifold advantages of carbetocin as an effective prophylactic agent with a favourable side effect profile for the third stage of labour in caesarean sections performed under regional anaesthetic. There were reductions in the use of additional uterotonic agents, blood and blood products and time spent in recovery. This has a significant potential for financial savings, decreasing the midwifery workload and improving the flow on delivery suite. These findings are supported by the more recent work by Shaw et al. (2013a, 2013b). Furthermore, the physical and emotional morbidity

for women and the actual running costs of the facilities cannot be underestimated.

Disclosure statement

The authors report no declarations of interest.

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