



Oxytocin vs. carbetocin at caesarean delivery in women with Class III obesity: Double-blind, Randomised control, non-inferiority trial

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Introduction

- Obesity in pregnancy, has an increasing incidence worldwide: 26.1% in 2016 to 29.0% in 2019.¹
- Class III obesity is defined as body mass index (BMI) above 40 kg/m²
- Maternal comorbidity includes higher rates of gestational diabetes, macrosomia, postpartum hemorrhage and caesarean delivery,² and neonatal comorbidity includes low Apgar scores, hypoglycaemia and sepsis.³
- The 90% effective doses (ED90) of uterotonics for adequate uterine contraction in women with class III obesity are:
 - Oxytocin: **0.75 IU** (95% CI = 0.5-0.93) 2x higher than non-obese.⁴
 - Carbetocin: **68 mcg** (95% CI = 57-68.7) 4x higher than non-obese.⁵

Methods

Primary objective: To determine if carbetocin 80 mcg is non-inferior to oxytocin 1 IU at elective caesarean delivery in parturients with Class III obesity.

We hypothesized that with equipotent dosing, carbetocin would be non-inferior to oxytocin in these patients.

Study design: Double-blind, Randomised control, non-inferiority trial

Population: Parturients with BMI >40 kg/m² who had no additional conditions predisposing to uterine atony and PPH undergoing elective caesarean delivery under neuraxial anaesthesia, except gestational diabetes and macrosomia (as these conditions almost are commonly associated with high BMI).

Exclusion criteria: Refusal to consent, allergy, labour, general anaesthesia, and other conditions predisposing to uterine atony and PPH.

Randomization: Parturients were randomised into two groups - Oxytocin and Carbetocin groups - using block randomization of 4 using computer generated scheme of random numbers with the 1:1 allocation.

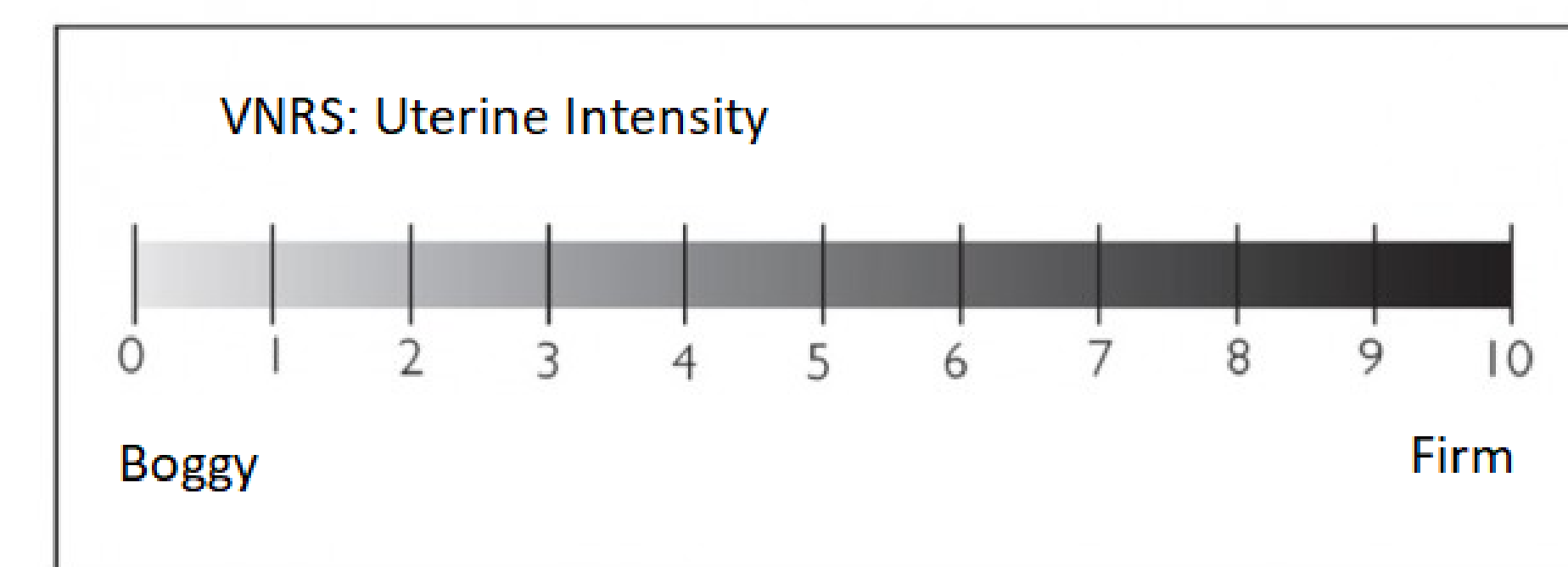
1. Oxytocin group: Oxytocin 1IU bolus followed by infusion of 40 IU in 1000 ml Ringer’s lactate.

2. Carbetocin group: Carbetocin 80 mcg bolus followed by placebo infusion.

Bolus diluted to 10 ml with normal saline and administered over 1 min, infusion delivered at 125 ml/h.

Primary Outcome: The primary outcome was the uterine tone at 3 min.

Intensity of uterine tone was evaluated at 3, 5, 10 minutes using Verbal numerical rating score (VNRS) scale of 0 (boggy) to 10 (firm) assessed by the obstetrician.



- Firm (10) = obstetrician could not depress the uterus or it sprung back upon depression with fingers
- Boggy (0) = uterus did not spring back upon depression

Secondary outcomes:

- Uterine tone at 5 and 10 min
- Need for additional uterotonic drugs
- Calculated Blood loss = Estimated blood volume (75ml/kg) x pre-operative haematocrit (Hct) - postoperative Hct / pre-operative Hct.
- Side effects: hypo/hypertension, tachycardia, bradycardia, arrhythmia, nausea, vomiting, chest/abdominal pain, shortness of breath, flushing or headache

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Results

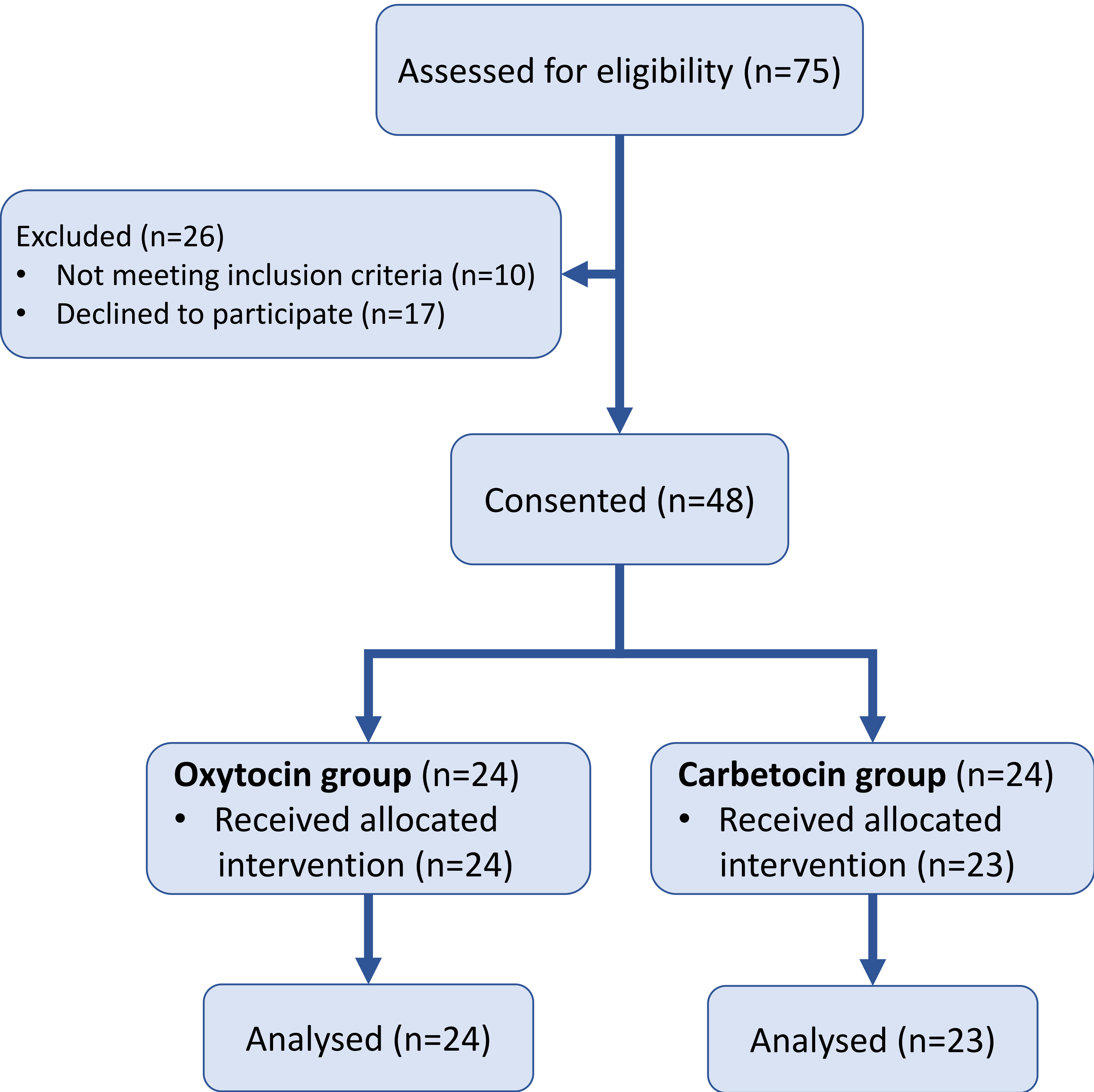
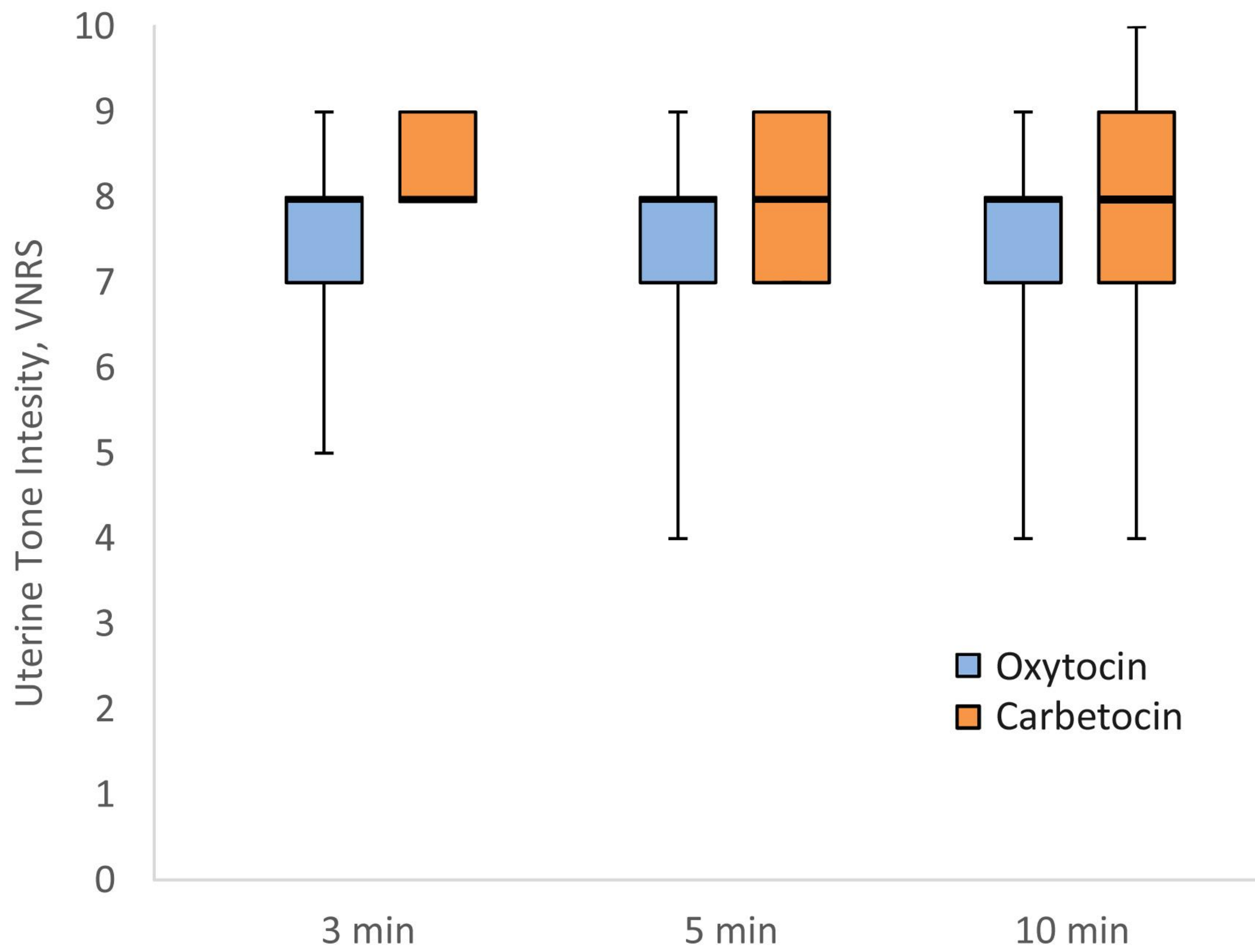


Table 1. Patient Characteristics

	Oxytocin (N=24)	Carbetocin (N=23)	p-value
Age (years)	33.9 (4.5)	34.9 (4.6)	0.46
Height (cm)	165.4 (7.5)	167.2 (6.2)	0.38
Weight (kg)	146.9 (23.2)	142.4 (20.8)	0.49
Body mass index (kg/m ²)	53.8 (8.3)	50.8 (5.8)	0.20
Gestational age (weeks)	38.3 (0.7)	38.3 (0.7)	0.98
Indication for CS			
Primary	7 (29%)	5 (22%)	0.74
Repeat	17 (71%)	18 (78%)	
Macrosomia	5 (21%)	5 (22%)	1.00
Gestational diabetes mellitus	7 (29%)	8 (35%)	0.68

*Values are presented as mean (SD) or N (%)

Figure 1. Uterine tone with oxytocin and carbetocin



	Oxytocin median (95% CI)	Carbetocin median (95% CI)	Median Difference [Oxytocin – Carbetocin] (95% CI)
3 min	8 (7, 8)	8 (8, 9)	0 (-0.54, 0.54)
5 min	8 (7, 8)	8 (7, 9)	0 (-0.85, 0.85)
10 min	8 (7, 8)	8 (7, 9)	0 (-0.85, 0.85)



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Table 2. Side effects post-delivery

	Oxytocin	Carbetocin	p-value
Hypotension	6 (25%)	9 (39%)	0.3
Hypertension	0	0	
Tachycardia	0	2 (9%)	0.23
Bradycardia	0	0	
Other dysrhythmias	1 (4%)	0	1
Nausea	10 (42%)	4 (17%)	0.07
Vomiting	0	2 (9%)	0.23
Chest pain	1 (4%)	1 (4%)	1
Abdominal pain	2 (8%)	0	0.49
Shortness of breath	0	0	
Headache	1 (4%)	2 (9%)	0.61
Flushing	1 (4%)	2 (9%)	0.61

*Values are presented as N (%)

Table 2. Secondary outcomes

	Oxytocin	Carbetocin	p-value
Estimated blood loss by surgeon (ml)	723 (129)	680 (168)	0.33
Estimated blood loss by formula (ml)	1434 (649)	1211 (787)	0.29
Uterine exteriorization	5 (25%)	4 (17%)	0.72
Need of additional uterotonic intraoperatively	6 (25%)	5 (22%)	1.00
Additional uterotonic medication used:			
Oxytocin	5 (21%)	5 (22%)	1.00
Ergot	1 (4%)	1 (4%)	1.00
Carboprost	1 (4%)	1 (4%)	1.00
Misoprostol	0	0	
Need of additional uterotonics in PACU	0	0	
Need of additional uterotonics in 24hours	0	0	
Tranexamic acid	7 (29%)	3 (13%)	0.29
Norepinephrine dose post-delivery (mcg)	12 (3, 36)	18 (0, 66)	0.57
Phenylephrine dose post-delivery (mcg)	0 (0, 0.3)	0 (0, 0)	0.33

*Values are presented as mean (SD), N (%) or median (IQR)

Discussion

- This is the first double-blind randomized controlled trial comparing oxytocin and carbetocin in women with class III obesity. We chose these doses in accordance with previously published studies from our group by Peska et al⁵ and Drew et al⁴, respectively.
- Our study demonstrates that **carbetocin 80 mcg is non-inferior to oxytocin 1IU in women with class III obesity**, for uterine tone intensity at 3, 5 and 10 min.
- The single shot administration of carbetocin provided equivalent intensity and duration of adequate uterine tone, and may be easier to administer rather than oxytocin infusion.
- Both drugs were associated with a **similar need for additional uterotonic medications, side effects, and blood loss.**

References

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