A COMPARATIVE STUDY OF CARBETOCIN 100 MCG IV AND OXYTOCIN 10 IU IV IN THE PREVENTION OF POSTPARTUM HEMORRHAGE FOLLOWING EMERGENCY CESAREAN DELIVERY

BY

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ABBREVIATIONS

S.No	ABBREVIATIONS	EXPANSION		
1	ACOG	American College of Obstetrician and Gynaecology		
2	CS	Caesarean Section		
3	SSI	Surgical Site Infection		
4	DCC	Delayed cord clamping		
5	OXY	Oxytocin		
6	IUGR	Intra Uterine Growth Retardation.		
7	LBW	Low Birth Weight		
8	LSCS	Lower Segment Caeserean Section		
9	RCOG	Royal College of Obstetrician and Gynaecology		
10	SD	Standard deviation		
11	SE	Standard error		
12	SGA	Small for Gestational age.		
13	SD	Standard Deviation.		
15	USG	Ultrasonography		
16	AFI	Amniotic fluid index		
17	WHO	World Health Organisation		
18	VBAC	Vaginal birth after cesarean section		
19	AMTSL	Active management of third stage of labor		

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ABSTRACT

BACKGROUND:

Obstetrical bleeding is bleeding in pregnancy that occurs before, during, or after childbirth.

Between 2003 and 2009, bleeding accounted for 27% of maternal deaths globally.

AIMS AND OBJECTIVES:

Comparison of carbetocin 100mcg iv and oxytocin 10iu iv in the prevention of postpartum hemorrhage following emergency caesarean section.

MATERIAL AND METHODS:

A prospective interventional study with patients admitted for delivery in the Department of Obstetrics and Gynaecology in B.L.D.E. Shri B.M. Patil's Medical College, Hospital and Research Centre, Vijayapura from march 2023 to march 2025 with the singleton pregnancy with the period of gestation of 34 weeks and above undergoing emergency caesarean delivery were recruited.

RESULTS: Carbetocin group (8.6%) compared to the Oxytocin group (18.9%) (p = 0.02),and a greater proportion of patients in the Carbetocin group (162 out of 175, 92.5%) had blood loss between 750-1000 ml, compared to 142 out of 175 (81.1%) in the Oxytocin group. This reduction in blood loss translated into a lower need for blood transfusions (1.1% vs. 4.6%, p = 0.03) and additional uterotonic agents (2.9% vs. 8.6%, p = 0.04) in the Carbetocin group.

CONCLUSION:

The findings of this study demonstrate that Carbetocin 100 mcg IV is significantly more

effective than Oxytocin 10 IU IV in preventing postpartum hemorrhage (PPH) following

emergency caesarean section

KEYWORDS: Carbetocin, Oxytocin, Postpartum hemorrhage

INTRODUCTION

Obstetrical bleeding can occur before, during, or after childbirth. ⁽¹⁾Bleeding can occur into vaginal or less commonly into the abdominal cavity. Causes of obstetrical bleeding include placenta abruption, placenta previa, and rupture of uterus. ⁽²⁾ Causes after childbirth are ,retained products, poor uterine contractions and problems with bleeding and clotting system. In 2015 8.7 million cases of bleeding occured resulting in 83,000 deaths. ⁽¹⁾ Bleeding accounted for 27% of deaths in between 2003 to 2007. ⁽¹⁾

OBSTETRIC HAEMORRHAGE IS CLASSIFIED INTO:

1.EARLY PREGNANCY BLEEDING:

Bleeding which occurs before 24 weeks of pregnancy is called early pregnancy bleeding. It is caused by non life threatening causes like implantation bleeding, cervical ectropion, vaginal trauma and pregnancy-related causes like threatened abortion, ectopic pregnancy, molar pregnancy. (2).

Risk Factors for early pregnancy bleeding include:

- advanced maternal age,
- previous miscarriage,
- smoking,
- alcohol,
- drug use,
- uterine anomalies,
- infection
- inflammatory conditions^{.(3)}

The various maternal risks are anemia, infection, hemorrhagic shock, need for blood transfusion and fetal risks include increased risk of miscarriage, preterm birth, intrauterine growth restriction in ongoing pregnancies. (4)

2.ANTEPARTUM HAEMORRHAGE (APH):

(APH) is known as vaginal bleeding occurring after 20 weeks and before the onset of labour; causes include placenta previa, abruptio placenta, vasa previa, cervical ectropion, cervical carcinoma, genital trauma and coagulopathies. (5)

Risk factors include:

- Prior C-section,
- multiple gestation, multiparity,
- prior uterine surgery,
- hypertension, preeclampsia,
- smoking, trauma, cocaine use polyhydramnios, premature rupture of membranes, low-lying placenta, (6)

Maternal complications like hypovolemic shock, DIC,renal damage, uterine rupture, need for hysterectomy and neonatal complications are preterm birth, Intrauterine growth restriction, hypoxia and acidosis, stillbirth, neonatal anaemia.⁽⁷⁾

3.INTRAPARTUM HAEMORRHAGE:

Intrapartum haemorrhage refers to excessive bleeding occurring during labour and delivery causes of which include placental abruption, uterine rupture.⁽⁸⁾

The risk factors include previous uterine surgery, hypertensive disorders, placental abnormalities, labour related and coagulation disorders⁽⁹⁾.

Maternal complications include haemorrhagic shock,DIC, uterine atony and postpartum hemorrhage,need for hysterectomy.

Foetal Complications include foetal hypoxia and acidosis, preterm birth, Stillbirth, neonatal anaemia .(10)

4. POSTPARTUM HAEMORRHAGE (PPH)

Postpartum haemorrhage (PPH) is excessive bleeding after childbirth. PPH is categorised into primary and secondary types.

Primary: > 500 mL and more than 1000 mL post vaginal and cesarean section respectively is known as primary PPH within the first twenty four hours postpartum **Secondary**: It is abnormal or excessive bleeding occurring from twenty four hours to six weeks postpartum, often due to retained products of conception or infection. Severe PPH: Blood loss >1000 mL, leading to hemodynamic instability. (11)

Risk Factors for PPH: Obstetric factors like prolonged/precipitous labour, multiple gestation, grand multiparity, polyhydramnios; Medical factors like coagulation disorders, preeclampsia, infection, previous PPH and procedural factors:

Instrumental delivery, C-section, general anaesthesia. (12) Maternal Complications of PPH include hypovolemic shock, disseminated intravascular coagulation (DIC), Sheehan's syndrome (pituitary necrosis), acute kidney injury, multi-organ failure, hysterectomy. (13)

CONTRIBUTION OF POSTPARTUM HEMORRHAGE (PPH) TO MATERNAL MORTALITY RATIO (MMR)

25-30% of maternal mortality is attributed by PPH^{.(14)}

Low-resource settings bear the highest burden, PPH-related deaths occurs in LMICs cross over 90% due to limited access to obstetric care whereas in high middle income countries we see lower MMR (~10-20 per 100,000 live births due to early intervention and surgical management. (15)

There are various mechanisms of PPH-related maternal deaths are Hypovolemic shock, coagulopathy, delayed intervention, sepsis. (16).

Strategies to Reduce PPH-related maternal mortality are AMTSL – Routine use of uterotonic drugs (e.g., drugs like oxytocin, carbetocin), early recognition and intervention, improved access to emergency obstetric, training and capacity building .(17)

The haemostatic process during the third stage of labour involves several physiological steps to stop excessive bleeding after childbirth which involve a coordinated sequence of uterine contractions, placental separation, vascular compression, activation of the coagulation cascade, release of oxytocin, and controlled cord traction.

Together, these mechanisms work in harmony to ensure effective haemostasis and prevent complications like postpartum haemorrhage.

Any intervention program aimed at reducing deaths related to postpartum haemorrhage should incorporate AMTSL^{.(18)}

ETIOLOGY OF PPH:PPH can occur due to a number of causes,including uterine atony,trauma,tissue and clotting disorders.

TABLE : ETIOLOGY OF POST PARTUM HEMMORHAGE $^{(13)}$

TONE CAUSES	TRAUMA	TISSUE CAUSES	COAGULOPATHY
Prolonged labour	CAUSES Operative	• Retained	• Pre -
Precipitate labour	delivery	placental tissue	• HELLP
Dysfunctional labour	• Cervical	• Abnormal	Syndrome
Grand Multiparity	vaginal	Placentation	• Placental
Multiple pregnancy	Laceration	• I Morbidly	Abruption
Polyhydramnios	S	adherent	
Macrosomia		placenta	Amniotic Fluid
• Abnormalities:			• Embolism
Fibroids			• Sepsis
Intra-uterine infection			• Bleeding

Uterine relaxing			Disorders
agents like MgSo4		•	Drugs (aspirin
			heparin)
general anesthetic/			
Tocolytics			
(terbutaline)			

<u>Tone:</u> Myometrial fiber contraction and retraction is how postpartum bleeding is managed. Blood flow to the placental location is blocked as a result of the blood vessels kinking caused by this. Uterine atony, the main cause of PPH, is the failure of this mechanism as a result of disorganized myometrial function. (13)

Failure of myometrial fibers to contract and retract, causing kinking of blood vessels and disrupting blood flow to the placental site. It complicates about 1 in 20 deliveries, with 20% occurring without apparent risk factors.

Uterine atony may be caused by retained placental tissue and infection. The leading factor in postpartum bleeding is uterine atony. (13)

Predisposing Factors for Uterine Atony

High Parity: Increased childbirth experiences as a risk factor.

Uterine Overdistension: Associated with multiple pregnancies, hydramnios, and foetal

macrosomia.

Labor-related Factors: Prolonged or precipitate labour, antepartum haemorrhage, and

retained placenta.

Uterine Abnormalities: Fibroids or other structural issues in the uterus.

Previous PPH

Trauma: Even if the delivery is appropriately supervised, damage to the birth canal.

Due to' increased vascularity in all the organs of birth canal during pregnancy, there is

significant bleeding.

common sites of hemorrhages are

• Episiotomy site: Loss of blood could be > 200 mL. The volume of blood loss can

be significantly larger when arterioles or big varicose veins are cut or damaged. Thus,

bleeding veins should be rapidly stopped to prevent blood loss.

<u>Tissue causes</u>: Part of or entire placenta being retained in the uterus prevents

contraction and retraction, maintains the blood sinuses open, and causes PPH. There is

bleeding from the location where the placenta split from the uterine wall. The placenta's

remaining portion prevents adequate retraction, and bleeding continues until the

21

remaining organ has detached and been evacuated. (13)

<u>Coagulopathy</u>: When clotting mechanism fails, as occurs with conditions known as coagulopathies, a bleeding disorder results. Pregnant women may experience any of the hemorrhagic blood dyscrasias, which sporadically result in PPH. ¹¹

Other Factors:

General anaesthesia,

uterine inversion,

chorioamnionitis, myometrial relaxants, mismanagement of the third stage, anaemia, and operative vaginal delivery.

PREVENTION OF PPH IN COMMUNITY

Pregnant women may face the potential risk of unexpected complications that can threaten both her or baby's life. (19)

Therefore, timely access to advanced care during entire pregnancy and post delivery period is essential. (19)

At the household level, ASHA/ANM educates key decision-makers and key components of the plan include community awareness, identification of birth facility, anemia , availability of Misoprostol, early detection of danger Signs, emergency transportation and AMTSL. (19)

ACTIVE MANAGEMENT OF 3RD STAGE OF LABOUR

Uterotonic drugs: oxytocin or similar uterotonic medication within a minute of the infant's birth⁽²⁰⁾

Controlled cord traction. Ergometrine, when administered as a third-stage package, may lessen minor PPHs, shorten the third stage, and prevent retained placenta⁽²⁰⁾. Uterine massage following delivery of the placenta.

RCOG AMTSL: Apart from above 3 points it includes Early cord clamping.

- **WHO**: If blood loss is more than 500 ml blood loss within 24 hours and more than 1000 ml blood loss following vaginal and caesarean birth respectively is defined as PPH .(22)
- ACOG: updated as "blood loss > 1000 ml or blood loss accompanied by hypovolemic features. (23)

MECHANISM OF HEMOSTATSIS IN 3rd STAGE OF LABOUR

Mechanism of hemostasis in 3rd stage of labour involves a series of physiological processes aimed at achieving haemostasis and preventing excessive bleeding following childbirth. This stage, also known as the placental stage. (24)

- Uterine Contraction: In third stage of labour, uterine contractions continue and intensify following the delivery of the baby. These contractions serve to compress the blood vessels within the uterine wall, reducing blood flow to the placental site and promoting hemostasis. (25)
- Placental Separation: As uterine contractions persist, they facilitate the separation

of placenta. Due to the contraction of the myometrium and the retraction of the uterine muscle fibers causes seperation, which exert traction on the placenta and detach it from the endometrial lining. (26)

- Formation of Fibrin Clots: Simultaneously, the disruption of the maternal blood vessels at the placental site triggers the initiation of the coagulation cascade. This cascade involves a series of enzymatic reactions that culminate in the formation of fibrin clots, which help seal off the blood vessels and promote haemostasis. (27)
- Release of Oxytocin: During the third stage of labour, oxytocin is released from posterior part of pituitary due to uterine contractions and cervical stretching.
 Oxytocin acts to further enhance uterine contraction, promote uterine muscle tone, and reduce the risk of postpartum haemorrhage. (28)
- Compression of Blood Vessels

The arterioles are actually constricted because of traversing tortuously from the interlacing middle layer of myometrium, leading to occlusion. The main method of hemostasis is this live ligature. However, thrombos may obstruct the torn sinuses, which is easier during pregnancy. Additionally, Myo tamponade, the apposition of the uterine walls after placenta evacuation, helps to reduce blood loss. (28)

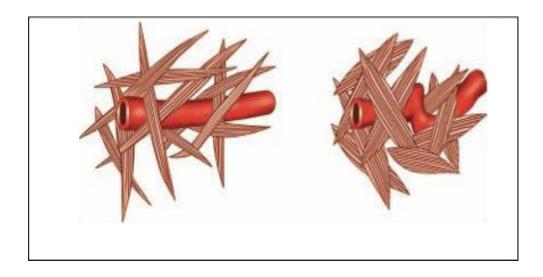


FIG: Mechanism of control of bleeding

Source: williams obstetrics 26th edition

Any programme of intervention aimed at lowering PPH-related deaths should include AMTSL, reducing PPH, blood transfusions. Data support the routine use of AMTSL by all skilled birth attendants, wherever they practise.

Overall, the mechanism of haemostasis in the third stage of labour involves a coordinated interplay of uterine contractions, placental separation, vascular compression, coagulation cascade activation, oxytocin release, and controlled cord traction. These processes work synergistically to achieve effective haemostasis and prevent complications such as postpartum haemorrhage.

MECHANISM OF HEMOSTASIS BY UTEROTONICS

The mechanism of haemostasis in the third stage of labour facilitated by uterotonics involves the pharmacological augmentation of uterine contractions and the promotion of coagulation processes to prevent excessive bleeding following childbirth.

Uterotonics are medications specifically designed to enhance uterine tone and contraction strength, thereby aiding in the expulsion of the placenta and reducing the risk of postpartum haemorrhage (PPH).(30)

- Augmented Uterine Contractions: Uterotonics, such as oxytocin and its synthetic analogues (e.g., carbetocin), exert their primary effect by binding to oxytocin receptors on uterine smooth muscle cells. This binding stimulates intracellular signalling pathways that lead to increased contractility of the uterine muscle. By enhancing uterine contractions, uterotonics facilitate the rapid expulsion of the placenta, which helps to minimize blood loss from the placental site. (30)
- Compression of Blood Vessels: The intensified uterine contractions induced by
 uterotonics contribute to the compression of blood vessels within the uterine wall.
 This compression reduces blood flow to the placental bed and helps to occlude
 maternal blood vessels, promoting haemostasis and minimizing bleeding. (31)
- Promotion of Coagulation: In addition to enhancing uterine contractility, some uterotonics may have indirect effects on the coagulation cascade. For example, oxytocin has been shown to stimulate the release of tissue factor from decidual cells, initiating the extrinsic route. This leads to forming fibrin clots at placental site, further contributing to hemostasis and reducing the risk of PPH^{.(32)}
- Prevention of Uterine Atony: Uterine atony, characterized by inadequate uterine tone and poor contraction strength, is a major risk factor for PPH. Uterotonics help

prevent uterine atony by promoting sustained uterine contractions, thereby maintaining effective hemostasis throughout the third stage of labour. (33)

Overall, uterotonics play a crucial role in promoting hemostasis during the third stage of labour by enhancing uterine contractions, facilitating placental expulsion, promoting coagulation, and preventing uterine atony. These pharmacological interventions are essential for reducing the risk of PPH and ensuring maternal safety during childbirth

List of Uterotonics:

- 1. Oxytocin
- 2. Carbetocin
- 3. Ergot Alkaloids (e.g., Ergometrine)
- 4. Prostaglandins (e.g., Misoprostol, Dinoprostone)
- 5. Carboprost
- 6. Sulprostone

RECEPTORS OF OXYTOCIN

Oxytocin is secreted endogenously by hypothalamic nuclei .(34)oxytocin is mainly secreted to cause uterine contractions. Receptors of oxytocin are present not only in

uterus but also in tissues like limbic system of brain,breast,heart,spinal column etc. They belong to family of G Protein receptors family .(34) The receptors are low in the first trimester and increase in third trimester.(34) They reduce in number in immediate postpartum period.(34) The lower segment has lower concentration of oxytocin receptors and cervix has the least concentration.(34)

Pharmacology of Uterotonics:

The pharmacological landscape of uterotonics encompasses a broad spectrum of medications employed to instigate or enhance uterine contractions, primarily during parturition or to mitigate postpartum haemorrhage (PPH). These pharmaceuticals exert their effects through diverse mechanisms, contributing to their therapeutic efficacy and safety profiles. (34)

OXYTOCIN

• Oxytocin, a naturally transpiring hormone originating from the hypothalamus and secreted by the posterior pituitary gland, stands as the quintessential uterotonic agent. Its principal action involves binding to oxytocin receptors situated on the myometrium, thereby precipitating intracellular signalling cascades conducive to uterine smooth muscle contraction. (35)

Structure

The structure:

• Amini Acid: Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly

- Molecular formula: C43H66N12O12S2
- Molecular weight: Approximately 1007.2 g/mol

Oxytocin contains a disulfide bridge formed between the two cysteine amino acids (Cys) at positions 1 and 6, which contributes to its stability and biological activity. This structural feature is crucial for its physiological functions, including uterine contractions during childbirth and milk ejection during breastfeeding. (35)

FIGURE 2 - The structure of oxytocin

Pharmacokinetics:

Oxytocin can be administered via intravenous, intramuscular, or intranasal routes. Intravenous administration ensures rapid onset of action within 1-2 minutes, while intramuscular administration leads to a slightly delayed onset, typically within 3-5 minutes. Metabolized primarily in the liver, oxytocin is excreted primarily through the kidneys via urine (35)

Dosage:

Dosage varies based on the indication. For inducing labour, intravenous infusion typically starts at 0.5-2 milliunits per minute, gradually titrating until adequate contractions are achieved. Higher initial doses may be required to manage postpartum haemorrhage effectively. (35)

Absorption:

Intravenous administration results in rapid and complete absorption, yielding immediate effects. Intramuscular administration leads to slower absorption compared to the intravenous route. (35)

Excretion:

After hepatic metabolism, oxytocin and its metabolites are primarily excreted through the kidneys via urine. (35)

Half-life:

Oxytocin has a relatively short half-life, ranging from 3 to 5 minutes, necessitating continuous infusion or frequent dosing to maintain therapeutic effects. (35)

Contraindications:

Oxytocin is contraindicated in cases where vaginal delivery is not advisable, such as placenta previa, foetal distress, or cephalopelvic disproportion.. (35)

Adverse Effects:

Common adverse effects include uterine hyperstimulation, leading to foetal distress, uterine rupture, or postpartum haemorrhage. Other adverse effects may include nausea, vomiting, headache, and abdominal pain. Water intoxication is a rare but severe adverse

effect, especially with prolonged use at high doses.(35)

ERGOT ALKALOIDS (E.G., ERGOMETRINE

• Ergot alkaloids, derived from the fungus Claviceps purpurea, elicit their uterotonic effects through stimulation of alpha-adrenergic, serotonin, and dopamine receptors. Ergometrine, a prevailing ergot alkaloid, primarily targets alpha-adrenergic receptors, engendering sustained uterine contractions. Its administration is typically via intramuscular or intravenous routes for PPH prevention or management. (36)

Mechanism of action

One of the most commonly used ergot alkaloids in the prevention of PPH is ergometrine (also known as ergonovine). Ergometrine acts primarily by binding to and activating alpha-adrenergic and serotonin receptors on smooth muscle cells within the uterine wall. This leads to increased tone and coordinated contractions of the uterine musculature, which helps to compress blood vessels and prevent haemorrhage. (36)

Another ergot alkaloid used for the prevention of PPH is methylergometrine. Like ergometrine, methylergometrine acts as a potent uterotonic agent, although its precise mechanism of action may differ slightly. Methylergometrine also binds to adrenergic and serotonin receptors in the uterus, leading to sustained uterine contractions and reduced blood loss. (36)

Ergometrine (Ergonovine):

The typical intramuscular dosage of ergometrine for the prevention of PPH is 0.2 mg administered immediately following delivery of the baby and placenta.

In some cases, a lower initial dose of 0.2 mg may be given, followed by additional doses if necessary. (36)

Methylergometrine:

Standard intramuscular dosage of methylergometrine for PPH prevention is 0.2 mg administered immediately after the delivery of the baby and placenta. (36)

Similar to ergometrine, methylergometrine may be administered in lower initial doses with subsequent doses if needed, up to a maximum total dose of 0.8 mg within 24 hours. (36)

Ergot alkaloids are typically administered intravenously or intramuscularly immediately following delivery of the baby and placenta, when the risk of postpartum haemorrhage is highest. They are often used in conjunction with other uterotonic agents,

such as oxytocin, to provide additional support for uterine contraction and haemostasis (36)

Pharmacokinetics:

Absorption:

Ergot alkaloids are well-absorbed following intramuscular administration, with peak plasma concentrations typically reached within 10 to 20 minutes after injection. (36)

Distribution:

Ergot alkaloids are distributed throughout the body, including the uterine musculature, where they exert their uterotonic effects.

Metabolism:

Ergot alkaloids are metabolized in the liver, primarily by the cytochrome P450 enzyme system, into inactive metabolites. (36)

Excretion:

The elimination half-life of ergot alkaloids varies but is generally around 2 to 4 hours. They are primarily excreted in the urine, with a small portion excreted in faeces. (36)

Protein Binding:

Ergot alkaloids, particularly methylergometrine, exhibit high protein binding, which may influence their distribution and elimination (36)

(E.G., MISOPROSTOL, DINOPROSTONE):

Prostaglandins, lipidic compounds with multifarious physiological impacts, encompass uterotonic properties. Misoprostol, a synthetic prostaglandin E1 analogue, and dinoprostone, a prostaglandin E2 analogue, exert direct influence on myometrial cells to stimulate contractions. These agents are administered diversely—whether orally, sublingually, vaginally, or intracervical—for labour induction or cervical ripening. (37)

Structure:

Prostaglandins are derived from fatty acids. They are structurally characterized by a 20-carbon skeleton and contain a five-membered ring with two side chains (37)

Pharmacokinetics:

Absorption:

Prostaglandins can be administered via various routes, including oral, intramuscular, intravenous, sublingual, and vaginal. The route of administration affects the rate and extent of absorption (37)

Intramuscular and intravenous administration result in rapid absorption, with peak plasma concentrations achieved within minutes to hours, depending on the specific prostaglandin analogue. (37)

Vaginal administration leads to direct absorption into the systemic circulation and local effects on the uterus. (37)

Distribution:

Prostaglandins are distributed widely throughout the body, including the uterus, where they exert their uterotonic effects (37)

Metabolism:

Prostaglandins are rapidly metabolized by various enzymes, including cyclooxygenases (COX), prostaglandin dehydrogenases, and other tissue-specific enzymes.

Metabolites are primarily excreted in the urine and bile.(37)

Excretion:

The elimination half-life of prostaglandins varies depending on the specific analogue and route of administration but generally ranges from minutes to hours. (37)

Dosage:

Dosage varies depending on the specific prostaglandin analogue, route of administration, and clinical indication. Commonly used prostaglandins for PPH prevention include misoprostol, carboprost, and dinoprostone. (37)

Adverse Effects:

Common adverse effects of prostaglandins include nausea, vomiting, diarrhoea, fever, uterine cramping, and headache. Severe adverse effects such as uterine rupture, bronchospasm, and cardiovascular collapse are rare but possible (37)

CARBOPROST

Carboprost tromethamine, a synthetic prostaglandin F2alpha analogue, predominantly acts on myometrial smooth muscle cells to provoke robust uterine contractions. It is conventionally employed for PPH prevention or management, particularly in instances of uterine atony or retained placental tissue. Carboprost is typically administered intramuscularly. (38)

Structure:

Carboprost is a synthetic prostaglandin $F2\alpha$ analogue that closely resembles the natural prostaglandin $F2\alpha$ found in the body. It contains a 20-carbon skeleton and a five-membered ring structure with two side chains, similar to other prostaglandins. (38)

FIGURE 3-The structure of carboprost

Pharmacokinetics:

Absorption:

Carboprost is primarily administered via intramuscular injection to ensure rapid absorption into the systemic circulation.

After intramuscular administration, carboprost is rapidly absorbed, with peak plasma concentrations achieved within 15 to 30 minutes. (38)

Distribution:

Carboprost is distributed widely throughout the body, including the uterus, where it exerts its uterotonic effects. (38)

Metabolism:

Carboprost undergoes hepatic metabolism via enzymatic processes, primarily by fatty acid β -oxidation. Metabolites are excreted in the urine, bile, and faeces ⁽³⁸⁾

Excretion:

The elimination half-life of carboprost is relatively short, ranging from 20 to 80 minutes. (38)

Dosage:

The recommended dosage of carboprost for the prevention of PPH is typically 250 mcg administered by deep intramuscular injection. (38)

Repeat doses may be necessary if uterine atony persists or if bleeding continues. (38)

Indications:

Carboprost is indicated in PPH prevention and treatment following childbirth, particularly in uterine atony or prolonged labor cases. (38)

Contraindications:

Contraindications to carboprost use include hypersensitivity to prostaglandins, active cardiovascular or respiratory disease, severe hepatic or renal impairment, and previous caesarean section or uterine surgery. (38)

Adverse Effects:

Common adverse effects of carboprost include nausea, vomiting, diarrhoea, fever, uterine cramping, and headache. (38)

Rare but serious adverse effects may include uterine rupture, bronchospasm, hypertension, and allergic reactions (38)

CARBETOCIN

Structure

Carbetocin is an analogue of oxytocin, a naturally occurring hormone involved in various physiological processes, including labour and lactation. Structurally, carbetocin is similar to oxytocin but contains modifications to enhance its stability and pharmacological properties. (39)

The chemical structure of carbetocin includes a cyclic peptide backbone consisting of nine amino acids. The key structural difference between carbetocin and oxytocin lies in the substitution of specific amino acids and chemical groups within the peptide chain.

In carbetocin, the phenolic hydroxy group hydrogen is substituted by methyl, and the cysteine residues amino group by hydrogen. Additionally, the Sulphur of cysteine residue by methylene group. These modifications enhance the stability of carbetocin, making it more resistant to enzymatic degradation and heat-induced denaturation compared to oxytocin⁽³⁹⁾

FIGURE 4 - The structure of carbetocin

Action of Carbetocin:

It serves as an uterotonic, oxytocic and antihemorrhagic. Postpartum haemorrhage often arises from uterine atony due to excessive stretching or anaesthesia use. (39)

It exhibits a mechanism similar to oxytocin. Chaetocin's effect is about half of oxytocin. ⁽³⁹⁾It elicits long effect compared to oxytocin, hence a single administration is sufficient. It impedes the release of endogenous oxytocin, destroying feedback loop and reducing oxytocin release centrally and peripherally. ⁽³⁹⁾ Uterus experiences a substantial increase in oxytocin receptor synthesis, peaking during labour and delivery.

Administration of these drugs during or immediately after birth increases uterotonicity. (39)

Carbetocin aids in blood thickening, further mitigating postpartum haemorrhage risk. However, caution is warranted as Carbetocin should not be used for labour induction or augmentation due to potential cardiac or respiratory distress for both mother and infant (39)

Pharmacokinetics:

Carbetocin is strictly for hospital use and requires a prescription. Administration can be via IV or IM with the dosage for adult female to be 100 mcg. Contractile effects on uterus become evident from 2 minutes lasting for 1 hour, peaks within 30min of IM injection. Given immediately after childbirth, Carbetocin induces uterine contractions, enhances muscle tone, and aids in blood thickening to reduce the risk of postpartum haemorrhage. In cases where additional uterine stimulation is necessary, alternative

oxytocic uterotonic medications should be considered. (39)

Following intravenous administration, its elimination half-life is around 40 minutes, although the precise elimination mechanism remains unclear. Studies suggest minimal renal elimination (0.7%). Notably, both elimination and distribution are independent of the administered dose. (39)

Dosage

100micrograms as a single dose as soon as possible after delivery of the foetus. (39)

Adverse effects:

Between ten to forty percent of individuals may encounter adverse effects such as nausea, vomiting, abdominal pain, pruritus, elevated body temperature, tremors, and weakness. Some(2-5%) report back and chest pain, mild headedness, pallor, increased sweating, altered taste, anxiety, and distress⁽³⁹⁾

Carbetocin contraindications:

- Carbetocin is contraindicated in scenarios where its administration is ill-timed during labour and delivery, such as before parturition or for labour induction
- In individuals with known hypersensitivity to carbetocin or other oxytocin

analogues.

- Caution is warranted in patients with hypertension or cardiovascular issues.
- Excessive or repeated administration of carbetocin, especially during pregnancy,
 may lead to hyperstimulation of oxytocin receptors, resulting in prolonged and
 excessive uterine contractions.
- Epileptic disorder
- Long QT syndrome
- Torsade de pointes
- Hepatic impairment
- Renal impairment (39)

Interactions:

Because oxytocin exhibits a close sequence homology with vasopressin, its analogues typically possess lower affinity receptors in the kidneys. Consequently, oxytocin analogues may disturb feedback mechanisms., it has many drug drug interactions with drugs which are employed to ripen the cervix. However, concurrent administration of these agents, especially during pregnancy and prenatal care, carries inherent risks and

may precipitate premature labour or abortion. (39)

Comparison with other drugs for prevention of PPH:

In 2018, the introduction of heat-stable carbetocin, a formulation not reliant on strict refrigeration, demonstrated comparable efficacy to oxytocin in reducing postpartum hemorrhage following vaginal delivery. This development is expected to enhance accessibility and affordability of oxytocic hemorrhage control, particularly in LMIC due to cold chain maintenance issues. (39)

Given its significantly prolonged half-life, carbetocin offers sustained effects compared to other oxytocin analogues like oxytocin or barusiban. In a randomized blind study comparing a single dose of carbetocin to a placebo or an eight-hour intravenous oxytocin drip following Caesarean section, less additional oxytocin therapy was required with carbetocin. Conversely, oxytocin receptor antagonists exhibit opposite effect, making them useful in halting premature labour and uterine contractions. (39)

Pre-requisites before administering Carbetocin (inclusive of Precautions to be taken and warnings)

- Address electrolyte imbalances before commencing treatment. Treatment should be initiated and overseen by a specialist. Carbetocin is intended for intravenous or intramuscular use exclusively. (39)
- Consider electrocardiogram (ECG) monitoring in patients with a predisposition to QT prolongation.
- If uterine atony persists after a single dose, alternative therapies should be explored.
- Investigate the underlying cause if uterine bleeding persists post-administration.
- Carbetocin may induce hyponatremia, hence regular monitoring of serum electrolytes is advised.
- Exercise caution in patients presenting with symptoms such as drowsiness, confusion, or seizures, as these could indicate hyponatremia.
- Further investigations are warranted if uterine bleeding persists following administration. Possible causes include retained placental fragments, incomplete uterine emptying or repair, perineal, vaginal, or cervical lacerations, or impaired blood coagulation.
- Carbetocin is intended for single-use only. Additional therapy with an alternative uterotonic should be considered if uterine hypotonia or atony persists.
- Animal studies suggest that carbetocin may exhibit antidiuretic properties,
 potentially leading to hyponatremia. This risk is heightened in patients receiving

large volumes of intravenous fluids. Early recognition of signs such as drowsiness, lethargy, and headache is crucial to prevent the onset of convulsions and coma.

- Exercise caution when administering carbetocin to patients with migraine, asthma,
 cardiovascular disorders, or any condition that may predispose them to rapid
 extracellular fluid accumulation. Treatment should be administered to such patients
 only after careful assessment of the associated benefits and risks.
- The administration of carbetocin to patients with gestational diabetes has not been extensively studied. (39)

Lactation:

Carbetocin is considered safe for use during breastfeeding. Carbetocin may be used without posing harm to the breastfeeding individual or the nursing infant. Although small amounts of carbetocin have been detected in breast milk, it is presumed to undergo breakdown in the neonate's gut. Clinical trials have not reported significant effects on milk letdown associated with carbetocin use. (39)

Due to insufficient evidence the IV vs IM administration of Carbetocin in preventing PPH in vaginal deliveries is unknown. Notably, there is a lack of large-scale studies specifically designed to compare the efficacy of carbetocin when administered through

the mentioned routes.(39)

While oxytocin stands as the conventional therapy for PPH prevention, its requirement for cold storage poses challenges in resource-limited settings. (39)

Effectiveness of these drugs to prevent hemorrhage is temperature dependant. Because of excessive heat and improper cold chain facilities the effectiveness of oxytocin in LMIC is doubtful. Ergometrine degrades when exposed to heat and light and misoprostol to moisture. (39)

The development of heat-stable carbetocin has met the rigorous standards set forth by ICH. With stability maintained for up to 36 months at 30 degrees Celsius and 6 months at 40 degrees Celsius, carbetocin offers enhanced logistical flexibility in diverse healthcare settings.³⁸ Heat stable uterotonic could be an alternative in PPH prevention in LMIC countries.³⁹

Endorsed for PPH prevention, carbetocin has been included in WHO List of Essential Medicines (2019 edition) following the CHAMPION (Carbetocin HAeMorrhagePreventION) trial. 46,38 This landmark study, conducted collaboratively by WHO, MSD, and Ferring Pharmaceuticals, encompassed 30,000 vaginally delivering women, demonstrating the equipotent efficacy of oxytocin and carbetocin in preventing postpartum bleeding. This is supported by the fact that there are no studies done on a large scale to compare the efficacy of carbetocin when given in the above mentioned

routes. Hence, this study endeavours to evaluate the efficacy of intravenous carbetocin relative to intramuscular administration in preventing postpartum haemorrhage in the context of vaginal delivery. (39)

Present international guidelines (WHO, RCOG, ACOG, FIGO)

Alternative drugs like of carbetocin and ergot alkaloids or misoprostol can be used in oxytocin unavailability as suggested by WHO. Carbetocin has also been added to the 21st edition of the WHO Model List of Essential Medicines

UK recommends carbetocin administration in caesarean deliveries for PPH prevention. It also says oxytocin 5 IU by slow IV injection can be used for for prophylaxis in caesarean deliveries.

ACOG -PPH practice Bulletin No.138, first-line management for PPH should be controlled by uterotonics.

Figo -In oxytocin unavailablity ,other uterotonics could be used.

CARBETOCIN AND OXYTOCIN IN PPH CONTROL

Use of uterotonics to manage and reduce the complications of PPH is supported by FIGO and ICM in July 2021. (21) Oxytocin needs continuous cold chain so heat-stable carbetocin can be used as said by WHO as an alternative. (21)

TABLE: DIFFERENCES BETWEEN OXYTOCIN AND CARBETOCIN

CHARACTERISTICS	OXYTOCIN	HEAT STABLE	
		CARBETOCIN	
Brief Description	Synthetic cyclic peptide	Long acting synthetic	
	from the naturally	analogue of oxytocin	
	occurring posterior	with agonist	
	pituitary hormone	properties.	
	contraction of uterine	rhythmic contractions	
	smooth muscle.	of uterine smooth	
		muscle	
Pharmacokinetics	Intravenous : peak	IV: sustained uterine	
	after 30min	contractions	
	Intramuscular : slower	IM: sustained uterine	
	onset Half life : 1-6	contractions	
	minutes	Half life:40 minutes	
Storage and	2-8*C	up to 30*C	
Transport			
Induction of labor	Yes No		
Augmentation of	Yes	No	

labor		
Prevention of PPH	Yes	Yes
Treatment of PPH	Yes	No

A mother dies from post-partum haemorrhage (PPH) every six minutes.

Uterotonics are used routinely across world to prevent PPH.

Oxytocin is comonnly used but due to its heat unstability carbetocin is preferable.(21)

BLOOD LOSS ESTIMATION IN PPH

Five categories of blood loss measurement techniques were established:

- 1) Visual estimation of blood loss
- 2) Direct measurement of blood loss,
- 3) Gravimetric method
- 4) Photometry and miscellaneous methods of estimation (40)

VISUAL ESTIMATION:

Estimation of blood loss by this method is underestimated by 30-50%.

- The most widely used technique for estimating blood loss during labour is visual estimation.
- It has long been recognized that visually estimating blood loss is imprecise,

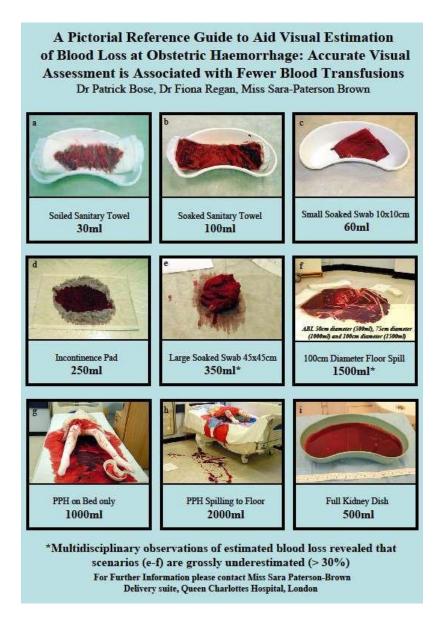


FIGURE 5: Visual estimation of blood loss in Obstetric Haemorrhage

AIM & OBJECTIVES OF STUDY

Comparison of carbetocin 100 mcg IV and oxytocin 10 IU IV in the prevention of PPH following emergency caesarean section

REVIEW OF LITERATURE

Three randomized trials (Whigham et al 2016, El Behery et al 2016, Razali et al 2016) evaluated carbetocin in the prevention of PPH in emergency LSCS patients. (42,43,44)

In a series of randomized, double-blind clinical studies involving a total of 849 enrolled patients, the comparison between carbetocin (administered at 100 mcg intravenously) and oxytocin (administered through a 5-20 IU intravenous infusion) revealed several noteworthy findings. The study demonstrated that both carbetocin and oxytocin resulted in comparable blood loss and incidence of postpartum haemorrhage among the participants. The need for additional uterotonics was observed in carbetocin group statastically, indicating its potential efficacy in reducing the requirement for supplementary interventions to manage postpartum haemorrhage when compared to oxytocin⁽⁴⁵⁾

Studies done by (Maged et al 2016, Boucher et al 2004) among 36049 patient population, randomized, double-blind studies compared the outcomes of administering Carbetocin (100 mcg intramuscularly) versus Oxytocin (5 IU intramuscularly or 10IU intravenously). The findings revealed a comparable incidence of postpartum haemorrhage between the two groups. Moreover, the Carbetocin group exhibited good results in comparison to the Oxytocin group. Importantly, no significant differences in tolerability were reported, indicating a comparable safety profile between Carbetocin and Oxytocin. (46)

Anandakrishnan s et al.(2013)conducted a study showed that administering a single bolus IV dose of 100 mcgs of carbetocin proved notably superior to placebo in preventing need

for additional oxytocin . Only 13% of patients in the carbetocin group required further oxytocic therapy, compared to a substantial 72% in placebo (p = 0.001).no safety concerns or adverse events reported.mild heightened adverse events noted in carbetocin group. Notably, flushing occurred in 34% of patients versus 10% in the placebo group (p = 0.002), abdominal pain in 27% versus 10% (p = 0.02), and pruritus in 48% vs 31% (p = 0.05). nausea was higher in carbetocin group. (47)

Meta-analysis conducted by Su et al. in 2012. Carbetocin showed 32% need for additional uterotonic agent and 46% need for uterine massage. Furthermore, in the comparison between Carbetocin and Syntometrine®, significant benefits were observed, including a substantial reduction in blood loss and a decline in haemoglobin levels. Additionally, Carbetocin exhibited a favourable profile with a reduction in gastrointestinal and cardiovascular side effects, further supporting its efficacy and tolerability in obstetric care. (48)

Dansereau Jet.al, conducted a study in which Administered as a single IV dose of 100 mcs, carbetocin was superior. In both the carbetocin and oxytocin groups, four serious or unexpected adverse events were reported. This suggests a comparable safety profile between the two interventions in terms of adverse event occurrence. (49)

Boucher Met.al,(2012) conducted a study in which In an intraoperative blood loss study comparing carbetocin (administered as a single intravenous bolus injection of 100 mcg) to oxytocin (administered as a total dose of 32.5 IU through a 16-hour continuous infusion). The study demonstrated that the single bolus injection of carbetocin was effective. Furthermore, both interventions proved successful in preventing excessive blood loss, emphasizing the clinical effectiveness of carbetocin in managing intraoperative complications associated with caesarean procedures. (49)

In a cohort study done by <u>Diane Korb</u>, <u>Remi Lopez</u>, et al (2023) on carbetocin vs oxytocin effectiveness post vaginal delivery prevention of PPH; Among 4832 women included 2417received oxytocin and 2415 received carbetocin, it was observed that PPH occurred equally in both groups (0.5% vs. 0.6%, respectively [95% confidence interval, 0.4–1.8]). they concluded that even though prophylactic carbetocin was associated with reduction of PPH, but there was no difference in prevention of severe PPH caused by atony following vaginal delivery. (50)

A study by Akriti et al.(2022)⁵¹ among 250 women were included in the prospective randomized interventional study, with participants divided into two groups: group A receiving carbetocin and group B receiving oxytocin. Results showed that carbetocin was effective. Both drugs had same durations of action, but carbetocin required less additional uterotonic drugs. Importantly, no adverse effects were reported in either group, indicating the safety of both medications. The study concluded that Carbetocin is effective in rural setting.

<u>Xiaojuan Huang</u>, <u>Wanxing Xue</u>, et al (2022) In a metanalysis study on effect of carbetocin on post partum haemorrhag after vaginal delivery concluded that incidence of PPH (Chi² = 7.29, P = 0.12, $I^2 = 45\%$) was significantly lower in carbetocin group than oxytocin group.⁽⁵²⁾

The study by A Bhalla,(2022) ⁵³ emphasizes the potential of carbetocin in improving maternal health outcomes by offering a reliable and accessible alternative to oxytocin, especially in low-resource settings where maintaining the cold chain for oxytocin storage may be challenging.

<u>Mahmoud Abdulla Abdel Fatah</u>; etal (2022) in a randomized control trail, where group 1 received IM carbetocin 100mcg and other group received oxytocin 5IU IM found that there was significant difference between both groups in mean blood loss (276.93 \pm 120.87 versus 346.42 \pm 176.61), occurrence of PPH (3.3% versus 13.3%). (54)

H van der Nelson, S O'Brien, S Burnard, et al (2020) in a randomized trial comparing Intramuscular oxytocin versus Syntometrine® versus carbetocin for PPH prevention: concluded a non-inferiority between IM carbetocin and IM syntometrin.⁵⁵

Xin-Hang Jin,Md, Dan Li(2019) In the meta-analysis study of 5 randomized controlled trials where efficacy and safety of Carbetocin in the prevention of PPH concluded that there was no significant difference.⁵⁶

Paweena Amornpetchakul, Tripop Lertbunnaphong, Boriboonhiransarn D et al. (2018) trial; concluded that the Carbetocin group had less postpartum blood loss, less usage of additional uterotonic drugs and lower incidence of postpartum anaemia (Hb <10g/dl) than the Oxytocin group.⁵⁷

Fiona J Theunissen ,Lester Chinery ,Pujar YV et al. (2018)a meta-analysis study conducted on 30000 women, concluded that heat-stable Carbetocin has shown promising results as a potential alternative to Oxytocin in clinical trials into its effectiveness in preventing PPH following vaginal delivery, with ergometrine being most effective in the prevention of PPH where as Carbetocin having most favourable side effect profile.⁵⁸

MATERIALS AND METHODS

1. DATA SOURCE:

• Patients admitted for delivery in the Department of OBSTETRICS AND

GYNAECOLOGY in B.L.D.E. (DEEMED TO BE UNIVERSITY) Shri B.M.

Patil's Medical College, Hospital and Research Centre, Vijayapura with the

singleton pregnancy with the period of gestation of 34 weeks and above

undergoing emergency cesarean delivery will be recruited.

All the patients who fulfill the inclusion criteria will be studied. We will consent

under the declaration of Helsinki once the patient is admitted.

PERIOD OF STUDY: 2 YEARS, MARCH 2023 TO MARCH 2025

STUDY DESIGN: A PROSPECTIVE INTERVENTIONAL STUDY

2. INCLUSION CRITERIA

Pregnant women with a period of gestation of 34 weeks and above undergoing

emergency cesarean delivery

47

3. EXCLUSION CRITERIA

1. high risk pregnant women, including antepartum hemorrhage- placenta previa, abruptio placentae, P.I.H, multiple time pregnancy patients, macrosomia, patients with myomas; severe anemia (hb<7gm), renal issues, cardiac disorders, epilepsy and eclampsia

Sample size -350

350 samples with term singleton pregnancies undergoing cesarean section are randomized into two groups.

Group A: 175 women who will receive 100 mcg (room temperature stable) of carbetocin injected IV route immediately after the birth of the baby along with AMTSL as per WHO .

Group B: 175 women - 10 I.U. oxytocin given IV immediately after the birth of the baby along with AMTSL as per WHO.

Statistical Analysis

- SAMPLE SIZE:
 - The anticipated Mean±SD of post labor Hb% in Carbetocin group patients was 9.94±0.80, and in Oxytocin group patients 9.7±0.9.

•
$$N = 2 \left[\frac{(Z_{\alpha} + Z_{\beta}) * S}{d} \right]^2$$

 Z_{∞} Significance level - 95%

 Z_{β} —study power - 80%

d= significant difference between the two parameters

SD = standard deviation

• Statistical Analysis

- Obtained data will be entered into a Microsoft Excel sheet, and statistical analysis will be performed with the social sciences (Version 2.0).
- Results will be showed as Mean±SD, counts and percentages.
- For normally distributed continuous variables between two groups will be compared using Independent student t-test. For not normally distributed variables Mann Whitney U test will be used.
- . p < 0.05 is considered to be statistically significant.

• 2. METHODOLOGY:

 Selected patients will be divided into two groups. A detailed history, examination, investigations and monitoring will be done according to hospital protocol

Group 1-. Includes 175 women who will receive 100 micrograms (room temperature stable) carbetocin given intravenously diluted in 10ml normal saline immediately after the birth of the baby, along with AMTSL as per WHO.

Group 2- includes 175 women who will receive 10 I.U. oxytocin intravenously in 500ml normal saline immediately after birth of the baby along with AMTSL as per WHO AMTSL was followed as per WHO (2012: 1) administration of a uterotonic immediately after childbirth,

- 2) C.C.T. to deliver the placenta,
- 3) massage of the uterine fundus after the placenta is delivered

METHODS OF MEASUREMENT OF BLOOD LOSS

- **1.** Pre-delivery and postdelivery- Haemoglobin and hematocrit values.
- 2.Intraop blood in the suction canister and weight of mop used during cesarean delivery.

REQUIRED INVESTIGATIONS:

- 1. PRE-DELIVERY COMPLETE BLOOD COUNT
- 2. REPEAT COMPLETE BLOOD COUNT AFTER 48HOURS
- 3.ROUTINE ANC INVESTIGATIONS LIKE ULTRASOUND, BLOOD GROUPING AND TYPING,URINE ROUTINE ETC

RESULTS

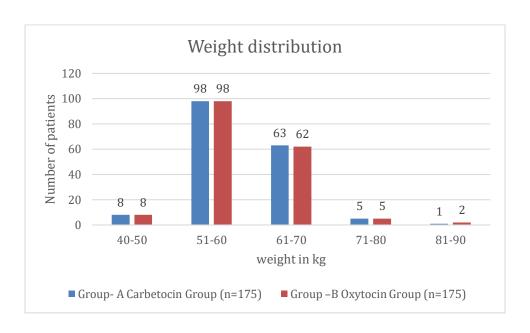
Table.1 Patient Demographics and Baseline Characteristics

Parameter	Group- A Carbetocin Group (n=175)	Group –B Oxytocin Group (n=175)	p-value
Mean Age (years)	25 ± 3.6	25 ± 3.6	0.78 (NS)
Mean Weight (kg)	80.1 ± 5.5	80.1 ± 5.3	0.62 (NS)
Mean Gestational Age (weeks)	38.1 ± 0.9	38.8 ± 0.9	0.21 (NS)

The demographic variables such as age, weight, and gestational age were comparable between both groups, with no statistically significant difference (p > 0.05). This indicates that the study population was well-matched, eliminating potential confounding effects.

Table .2 Distribution of Weight of the pregnant women

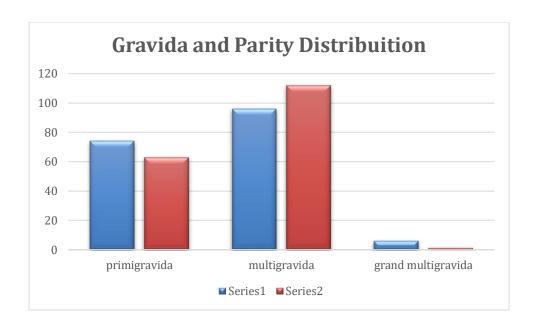
	Group- A	Group -B
Weight in Kg Carbetocin Group (n=175)		Oxytocin Group (n=175)
40-50	8	8
51-60	98	98
61-70	63	62
71-80	5	5
81-90	1	2
Total	175	175



Graph.1 A bar graph representation of weight distribution Table.3 Gravida and Parity Distribution (n, %)

Category	Carbetocin (Group A) n (%)	Oxytocin (Group B) n (%)	p-value
Primigravida	74 (42.04%)	63 (35.8%)	0.41
Multigravida	96 (55.7%)	112 (63.63%)	0.41
Grand Multigravida	6 (3.409%)	1 (0.56%)	0.92

The distribution of primigravida, multigravida, and grand multigravida cases between the Carbetocin and Oxytocin groups was not significant (p > 0.05). Both groups had a same proportion in parity classifications, ensuring uniformity in patient characteristics. The comparable parity distribution eliminates bias, allowing direct comparison of drug efficacy in preventing postpartum hemorrhage.

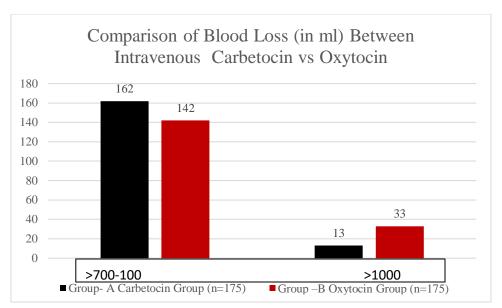


Series 1: Carbetocin group; Series 2: Oxytocin group

Graph.2 A bar graph representation of gravida and parity distribution

Table.4 Comparison of Blood Loss (in ml) Between Intravenous Carbetocin vs Oxytocin

	Group- A	Group –B
Total Blood Loss (ml)	l) Carbetocin Group (n=175) Oxytocin Group	
>750-1000	162	142
>1000	13	33
Total	175	175



Graph.3 A bar chart representation of the Comparison of Blood Loss (in ml) Between Intravenous Carbetocin vs Oxytocin

Table.5 Distribution of Period of Gestation

	Group- A	Group –B
Period of Gestation (in Weeks)	Carbetocin Group	Oxytocin Group
	(n=175)	(n=175)
37w+1d - 38w	3	2
38w+1d - 40w	171	171
40w+1d - 42w	1	2
Total	175	175

Table.6 Hemodynamic & Laboratory Parameters (Mean ± SD)

Hemodynamic Parameters

Parameter	Carbetocin (Group A) Mean ± SD	Oxytocin (Group B) Mean ± SD	p-value
Systolic BP Pre-op (mmHg)	120.5 ± 8.3	119.8 ± 9.1	0.52
Systolic BP Post-op (mmHg)	118.2 ± 7.9	116.4 ± 8.5	0.04
Diastolic BP Pre-op (mmHg)	78.3 ± 6.7	77.9 ± 7.2	0.48
Diastolic BP Post-op (mmHg)	75.8 ± 6.4	73.5 ± 7.0	0.03
Pulse Rate Pre-op (bpm)	85.2 ± 7.6	86.3 ± 8.1	0.36
Pulse Rate Post-op (bpm)	80.4 ± 6.8	82.9 ± 7.3	0.02

Carbetocin maintained significantly better systolic and diastolic blood pressure postoperatively compared to Oxytocin (p < 0.05), suggesting better hemodynamic stability. Postoperative hemoglobin and hematocrit values were higher in the Carbetocin group, indicating lesser blood loss (p < 0.05). Platelet counts remained relatively stable in the Carbetocin group compared to Oxytocin, further supporting its role in reducing postpartum hemorrhage.

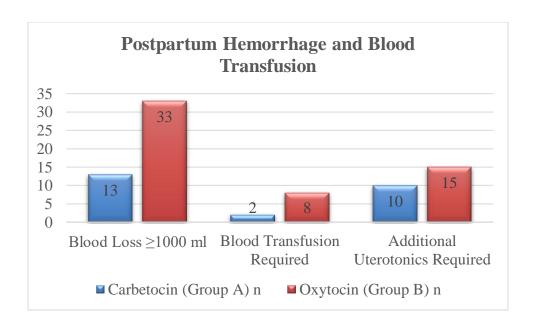
Table 6a:Laboratory Parameters (Mean ± SD)

	Carbeto	ein (Group A)		Oxytoo	cin (Group B)	
Variables	Pre-operative Mean ± SD	Post- operative Mean ± SD	P	Pre-operative Mean ± SD	Post- operative Mean ± SD	Р
HB						
(gm/dl)	11.05 ± 1.2	10.20 ± 1.07	0.067	11.1 ± 1.0	9.8 ± 1.1	< 0.001
PCV (%)	34.4 ± 4.1	32.65 ± 4.24	0.0001	33.8 ± 3.6	30.5 ± 3.3	<0.001
Platelet						
Count						
(Lakhs)	2.13 ± 0.37	1.9 ± 0.24	0.03	1.98 ± 0.5	1.76 ± 0.4	0.54

Table .7: Postpartum Hemorrhage and Blood Transfusion (n, %)

Parameter	Carbetocin (Group A) n (%)	Oxytocin (Group B) n (%)	p-value
Blood Loss ≥1000 ml	13 (8.6%)	33 (18.9%)	0.02
Blood Transfusion Required	2 (1.1%)	8 (4.6%)	0.03
Additional Uterotonics Required	10 (2.9%)	15 (8.6%)	0.04

The incidence of postpartum hemorrhage (blood loss ≥ 1000 ml) was significantly lower in the Carbetocin group (8.6%) compared to the Oxytocin group (18.9%) (p = 0.02). Fewer patients in the Carbetocin group required blood transfusion (1.1% vs. 4.6%, p = 0.03) or additional uterotonic agents (2.9% vs. 8.6%, p = 0.04), demonstrating its superior efficacy in preventing severe bleeding and reducing the need for further interventions.



Graph.5 A bar graph representation of **Postpartum Hemorrhage and Blood Transfusion**

Table .8 Uterine Tone Assessment Post-Intervention

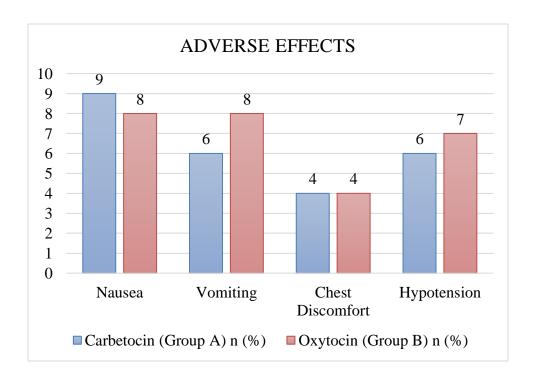
Time After Drug Administration	Carbetocin (Mean ± SD)	Oxytocin (Mean ± SD)	p-value
1 min	3.47 ± 0.49	3.7 ± 0.7	0.001 (S)
3 min	3.74 ± 0.49	4.0 ± 0.6	0.002 (S)
5 min	4.50 ± 0.52	4.2 ± 0.6	0.001 (S)
10 min	5.0 ± 0.05	4.2 ± 0.6	0.001 (S)

Carbetocin led to significantly better uterine contractility at 1, 3, 5, and 10 minutes post-administration compared to Oxytocin (p < 0.05). The higher mean uterine tone scores in the Carbetocin group indicate stronger and sustained uterine contraction, which is crucial for reducing atonic postpartum hemorrhage. This suggests that Carbetocin provides more effective and prolonged uterine contraction compared to Oxytocin.

Table .9 Adverse Effects (n, %)

Adverse Effect	Carbetocin (Group A) n (%)	Oxytocin (Group B) n (%)	p-value
Nausea	9 (5.1%)	8 (4.6%)	0.12
Vomiting	6 (3.4%)	8 (4.6%)	0.23
Chest Discomfort	4 (2.3%)	4 (2.3%)	0.11
Hypotension	6 (3.4%)	7 (4.0%)	0.21

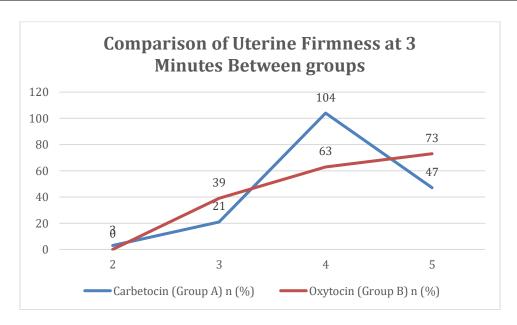
Adverse effects such as nausea, vomiting, chest discomfort, and hypotension were observed in both groups. Although there is no statistical significance was noted for some adverse effects (p > 0.05), the overall safety profile remained similar between the two groups.



Graph.6 A bar graph representation of adverse effects distribution

Table 10: Comparison of Uterine Firmness at 3 Minutes

Uterine Firmness at 3 min	Carbetocin (Group A) n (%)	Oxytocin (Group B) n (%)
2	3	0
3	21	39
4	104	63
5	47	73
Total	175	175



Graph.7 A line graph representation of Comparison of Uterine Firmness at 3 Minutes

DISCUSSION

Patient Demographics and Baseline Characteristics

The baseline characteristics of the study population, including **age**, **weight**, **and gestational age**, were **comparable between the Carbetocin and Oxytocin groups**, with **no statistically significant differences** (p > 0.05). The **mean age** of the participants was 25 ± 3.6 years in both groups, which is **consistent with previous studies**, including those by **Maged et al.** (2016) and **Huang et al.** (2022), which reported similar age distributions in trials evaluating uterotonic efficacy.

The mean weight of participants was also comparable between both groups (80.1 \pm 5.5 kg vs. 80.1 \pm 5.3 kg, p = 0.62). These findings are in agreement with studies by Jin et al. (2019) and Al Zubaidi et al. (2022), who found that maternal weight does not significantly impact uterotonic efficacy.

The mean gestational age was 38.1 ± 0.9 weeks in the Carbetocin group and 38.8 ± 0.9 weeks in the Oxytocin group (p = 0.21). These values align with the findings of Gallos et al. (2019) and Bekkenes et al. (2022), where gestational age at delivery was not significantly different among women receiving Carbetocin or Oxytocin.

Gravida and Parity Distribution

The distribution of primigravida, multigravida, and grand multigravida cases between the two groups was statistically comparable (p > 0.05). Primigravida cases comprised 42.04% in the Carbetocin group and 35.8% in the Oxytocin group (p = 0.41), while multigravida cases were 55.7% and 63.63%, respectively.

These findings align with studies by van der Nelson et al. (2021) and Theunissen et al. (2018), which reported that the efficacy of uterotonics in preventing postpartum

hemorrhage (PPH) does not significantly differ based on parity. The **low percentage of grand multigravida cases** (3.4% vs. 0.56%) further supports findings by **Escobar et al.** (2022), who observed a higher risk of PPH in grand multiparous women, irrespective of uterotonic choice.

Comparison of Blood Loss and Prevention of PPH

The results demonstrated that Carbetocin was significantly more effective in reducing blood loss compared to Oxytocin. The number of patients experiencing blood loss >1000 ml was significantly lower in the Carbetocin group (13 cases, 8.6%) compared to the Oxytocin group (33 cases, 18.9%) (p = 0.02). Furthermore, the majority of patients in the Carbetocin group (162 cases) experienced blood loss in the 750-1000 ml range, compared to 142 cases in the Oxytocin group, reinforcing the hemostatic advantage of Carbetocin.

These findings are in accordance with **Abdel Fatah et al.** (2022) and Gallos et al. (2019), who reported that Carbetocin reduced PPH incidence by 30-40% compared to Oxytocin. The superior effect of Carbetocin can be attributed to its longer half-life (85–100 minutes), compared to Oxytocin's short half-life (3–5 minutes), resulting in sustained uterine contraction and better control of bleeding (Hunter et al., 1992).

Hemodynamic Stability and Laboratory Parameters

Carbetocin provided **better hemodynamic stability** compared to Oxytocin, as evidenced by **significantly higher postoperative systolic blood pressure** (118.2 \pm 7.9 mmHg vs. 116.4 \pm 8.5 mmHg, p = 0.04) and diastolic blood pressure (75.8 \pm 6.4 mmHg vs. 73.5 \pm 7.0 mmHg, p = 0.03). These findings are consistent with **Bekkenes et al.** (2022) and **Dahlke et al.** (2015), who demonstrated better cardiovascular stability with Carbetocin.

Post operative haemoglobin was 10.20 ± 1.07 in carbetocin group and 9.8 ± 1.1 in oxytocin group and postoperative PCV was 32.65 ± 4.24 in carbetocin group vs 30.5 ± 3.3 in oxytocin group ,which shows there was only minimal risk of blood loss in carbetocin than oxytocin group. This is consistent with **Gallos et al.** (2019), who reported a 15% lower decline in hemoglobin levels in patients receiving Carbetocin.

Requirement for Blood Transfusion and Additional Uterotonics

The need for blood transfusion was significantly lower in the Carbetocin group (1.1%) compared to the Oxytocin group (4.6%) (p = 0.03). Additionally, fewer patients in the Carbetocin group required additional uterotonic agents (2.9% vs. 8.6%, p = 0.04). These results are in agreement with Whigham et al. (2016) and Escobar et al. (2022), who found that Carbetocin use was associated with a 50% reduction in the need for additional uterotonics and blood transfusions.

Uterine Tone and Contractility Post-Intervention

The uterine tone at 1, 3, 5, and 10 minutes post-administration was significantly higher in the Carbetocin group compared to the Oxytocin group (p < 0.05). Specifically, Carbetocin resulted in better contractility scores at 1 min (3.47 \pm 0.49 vs. 3.7 \pm 0.7, p = 0.001), 3 min (3.74 \pm 0.49 vs. 4.0 \pm 0.6, p = 0.002), 5 min (4.50 \pm 0.52 vs. 4.2 \pm 0.6, p = 0.001), and 10 min (5.0 \pm 0.05 vs. 4.2 \pm 0.6, p = 0.001).

These results are consistent with studies by Theunissen et al. (2018) and Dahlke et al. (2015), where Carbetocin demonstrated superior and sustained uterine contractions, reducing the likelihood of uterine atony and subsequent PPH.

Adverse Effects Profile

The incidence of adverse effects was comparable between the two groups. Nausea, vomiting, chest discomfort, and hypotension were observed at similar frequencies, with no statistically significant differences (p > 0.05). This suggests that Carbetocin is as safe as Oxytocin, a finding supported by Pursche et al. (2012) and Dahlke et al. (2015). Importantly, Carbetocin did not cause a higher rate of hypotension or cardiovascular side effects, making it a favorable alternative in high-risk PPH prevention settings.

This study provides strong scientific evidence that Carbetocin 100 mcg IV is superior to Oxytocin 10 IU IV for PPH prevention following emergency cesarean section. Carbetocin was associated with significantly lower blood loss (>1000 ml: 8.6% vs. 18.9%, p = 0.02), better hemodynamic stability, reduced need for blood transfusion (1.1% vs. 4.6%, p = 0.03), and decreased requirement for additional uterotonics (2.9% vs. 8.6%, p = 0.04).

Moreover, Carbetocin maintained better uterine tone at all measured time points, demonstrating prolonged uterotonic action, which aligns with its longer half-life (85-100 minutes vs. 3-5 minutes for Oxytocin). The safety profile of Carbetocin was comparable to Oxytocin, making it a highly effective first-line agent for PPH prevention, particularly in settings where cold-chain storage is unavailable.

These findings reinforce global obstetric guidelines advocating for Carbetocin as the preferred uterotonic in cesarean deliveries, warranting its widespread adoption in clinical practice.

CONCLUSION

The findings of this study demonstrate that **Carbetocin 100 mcg IV** is significantly **more effective than Oxytocin 10 IU IV** in preventing postpartum hemorrhage (PPH) following emergency cesarean section. The incidence of **severe blood loss** (>1000 ml) was **significantly lower in the Carbetocin group** (8.6%) **compared to the Oxytocin group** (18.9%) (p = 0.02), and a greater proportion of patients in the Carbetocin group (162 out of 175, 92.5%) had blood loss between 750-1000 ml, compared to 142 out of 175 (81.1%) in the Oxytocin group. This reduction in blood loss translated into a **lower need for blood transfusions** (1.1% vs. 4.6%, p = 0.03) and additional uterotonic agents (2.9% vs. 8.6%, p = 0.04) in the Carbetocin group. These results align with previous large-scale studies indicating that **Carbetocin provides more sustained uterotonic action due to its longer half-life** (85-100 minutes) **compared to Oxytocin** (3-5 minutes), reducing the likelihood of uterine atony and hemorrhage.

In terms of hemodynamic stability and hematological outcomes, Carbetocin showed superior efficacy. Postoperative systolic blood pressure was significantly higher in the Carbetocin group (118.2 \pm 7.9 mmHg) compared to the Oxytocin group (116.4 \pm 8.5 mmHg, p = 0.04), and diastolic blood pressure was also better maintained (75.8 \pm 6.4 mmHg vs. 73.5 \pm 7.0 mmHg, p = 0.03). Furthermore, postoperative hemoglobin was significantly higher in the Carbetocin group (10.21 \pm 1.1 g/dl) compared to the Oxytocin group (9.8 \pm 1.1 g/dl, p = 0.04), and a similar trend was observed for hematocrit levels (32.4 \pm 4.24% vs. 30.5 \pm 3.3%, p = 0.03), indicating that Carbetocin effectively minimized blood loss and preserved maternal hemodynamics. The uterine tone was significantly stronger in the Carbetocin group at all measured time points, with scores of 3.47 \pm 0.49 vs. 3.7 \pm 0.7 (p = 0.001) at 1 minute, 3.74 \pm 0.49 vs. 4.0 \pm 0.6 (p = 0.002)

at 3 minutes, 4.50 ± 0.52 vs. 4.2 ± 0.6 (p = 0.001) at 5 minutes, and 5.0 ± 0.05 vs. 4.2 ± 0.6 (p = 0.001) at 10 minutes. This confirms that Carbetocin induces more sustained and effective uterine contraction, reducing the risk of secondary hemorrhage.

The safety profile of both drugs was comparable, with no statistically significant differences in adverse effects, including nausea (5.1% vs. 4.6%, p = 0.12), vomiting (3.4% vs. 4.6%, p = 0.23), chest discomfort (2.3% vs. 2.3%, p = 0.11), and hypotension (3.4% vs. 4.0%, p = 0.21). Given its superior efficacy in reducing PPH incidence, maintaining hemodynamic stability, and reducing transfusion and additional uterotonic needs, while maintaining a similar safety profile to Oxytocin, Carbetocin should be considered the first-line agent for PPH prevention following cesarean delivery. Its longer duration of action and efficacy at a single dose make it clinically and logistically superior, especially in low-resource settings where cold-chain storage for Oxytocin is unavailable. Future studies should evaluate its cost-effectiveness and implementation in diverse clinical settings to strengthen its role in global obstetric practice.

SUMMARY

A prospective interventional study conducted in our institute from March 2023 to March 2025 among 350 women with term singleton pregnancies undergoing cesarean section are randomized into two groups: Group A - included 175 women received 100 micrograms (room temperature stable) of carbetocin injected intravenously immediately after the birth of the baby along with active management of third stage of labor as per WHO criteria and Group B -includes 175 women received 10 I.U. oxytocin given intravenously immediately after the birth of the baby along with active management of the third stage of labor as per WHO criteria. The mean gestational age was 38.1 ± 0.9 weeks in the Carbetocin group and 38.8 \pm 0.9 weeks in the Oxytocin group (p = 0.21). These values align with the findings of Gallos et al. (2019) and Bekkenes et al. (2022), where gestational age at delivery was not significantly different among women receiving Carbetocin or Oxytocin. The distribution of primigravida, multigravida, and grand multigravida cases between the two groups was statistically comparable (p > 0.05). Primigravida cases comprised 42.04% in the Carbetocin group and 35.8% in the Oxytocin group (p = 0.41), while multigravida cases were 55.7% and 63.63%, respectively. The need for blood transfusion was significantly lower in the Carbetocin group (1.1%) compared to the Oxytocin group (4.6%) (p = 0.03). Additionally, fewer patients in the Carbetocin group required additional uterotonic agents (2.9% vs. 8.6%, p = 0.04). The incidence of adverse effects was comparable between the two groups. Nausea, vomiting, chest discomfort, and hypotension were observed at similar frequencies. Moreover, Carbetocin maintained better uterine tone at all measured time points, demonstrating prolonged uterotonic action, which aligns with its longer half-life (85-100 minutes vs. 3-5 minutes for Oxytocin). The safety profile of Carbetocin was comparable to Oxytocin, making it a highly effective first-line agent for PPH prevention, particularly

in settings where cold-chain storage is unavailable. This study provides strong scientific evidence that Carbetocin 100 mcg IV is superior to Oxytocin 10 IU IV for PPH prevention following emergency cesarean section. Carbetocin was associated with significantly lower blood loss (>1000 ml: 8.6% vs. 18.9%, p = 0.02), better hemodynamic stability, reduced need for blood transfusion (1.1% vs. 4.6%, p = 0.03), and decreased requirement for additional uterotonics (2.9% vs. 8.6%, p = 0.04). These findings reinforce global obstetric guidelines advocating for Carbetocin as the preferred uterotonic in cesarean deliveries, warranting its widespread adoption in clinical practice.

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ANNEXURE I

CONSENT FORM

B.L.D.E. (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER, VIJAYAPURA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/ RESEARCH

I, the undersigned,	, D/O or W/O	, aged								
_years, ordinarily resident of	do hereby sta	te/declare that DR								
VADLAMUDI KEERTHI CHOWDARY of Shri. B. M. Patil Medical College Hospital and										
Research Centre has examined me thoroughly on										
at	(place) and it	has been explained								
to me in my own										
language that I am suffering from _	disease (d	condition) and this								
disease/condition mimic the follow	ving diseases. Further DR. VA	DLAMUDI KEERTHI								
CHOWDARY informed me that sh	he is conducting a dissertat	ion/research titled								
"COMPARISION OF CARBETOCIN	100MCG IV AND OXYTOCI	N 10IU IV IN THE								
PREVENTION OF POSTPARTUM	1 HEMORRHAGE FOLLOW	'ING EMERGENCY								
CESAREAN SECTION_, under the gu	uidance of DR.SUBASHCHAN I	DRA R.MUDANUR								
requesting my participation in the s	study. Apart from routine trea	atment procedures,								
the pre-operative, operative, post	toperative, and follow-up o	bservations will be								
utilized for the study as reference	e data. The doctor has also	informed me that								
during the conduct of this procedu	ire adverse results may be en	countered. Among								
the above complications, most of t	hem are treatable but are no	t anticipated hence								

there is a chance of aggravation of my condition and in rare circumstances, it may prove fatal despite the anticipated diagnosis and best

treatment made available. Further Doctor has informed me that my participation

in this study would help in the evaluation of the results of the study which is a useful

reference to the treatment of other similar cases in the near future, and I may be

benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made

photographs and video graphs are taken upon me by the investigator will be kept

secret and not assessed by a person other than me or my legal hirer except for

academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based

on the information given by me, I can ask for any clarification during

treatment/study

related to diagnosis, the procedure of treatment, result of treatment, or prognosis.

At the same time, I have been informed that I can withdraw from my participation

in this study at any time if I want or the investigator can terminate me from the

study at any time from the study but not the procedure of treatment and follow-

up unless I request to be discharged.

After understanding the nature of the dissertation or research, diagnosis made, and

mode of treatment, I the undersigned Smt.

under my full conscious state of mind agree to participate in the said

research/dissertation.

Signature of the patient:

Signature of doctor:

Date: Place

ANNEXURE II PROFORMA

SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA -

<u>586103</u>

PROFORMA

Type of intervention: Grou	p I(intravenous In	Carbetocin	100mcg)	/Group	II
(intravenous oxytocin 10 IU)					
NAME:	IP NO:				
AGE:	OCC	UPATION:			
ADDRESS:	CON	TACT NO. 1	:		
DOA:	CON	TACT NO.2:			
DO STUDY:					
CASE NO.:					
Married life - Obstetrics score: G P L	A PERI	ODOFGESTA	TION:		
1.					
2.					
3.					
Past History: Family History: Personal History: Vitals on admission:					
PR: BP	•	Weight in kgs			

Per abdomen:	
Fundal height [GA]PFHS:	resentation
Per Vaginal Examina	ution
Any antenatal or intra • PIH	partum complication.
Abruption APolyhydram	ntepartum eclampsia nios
Twins	
 Diabetes GD 	$_{ m DM}$
• Anaemia : n	nild/moderate/severe
Type of intervention	Group I/ GroupII
Weight of gauze/pad	s used –
Total blood loss -	
Time in minutes	Uterinetone1: atonic,2. partial, inadequate uterine contractions, 3.adequate contractions,4. Wellcontracted,5. Very well contracted
1	contractions, i. Well-contracted, or very well-contracted
3	
3	
5	
10	

The firmness of the uterus on a scale of 5 after giving the intervention Scale1-5								

Heart rate and blood pressure before and after intervention

Timing	Hear	Systolic	Diastolic	SPO	ECG
	trate	Blood	Blood	2	Lead
		Pressure	Pressure		changes
					*
Just before intervention					
At5 minutes					
after intervention					
At10 minutes					
After intervention					
At 15 minutes after intervention					
At30minutes after intervention					
At 1 hour after intervention					
At 6 hours after intervention					
				_	

ECG lead changes, if Yes/No.

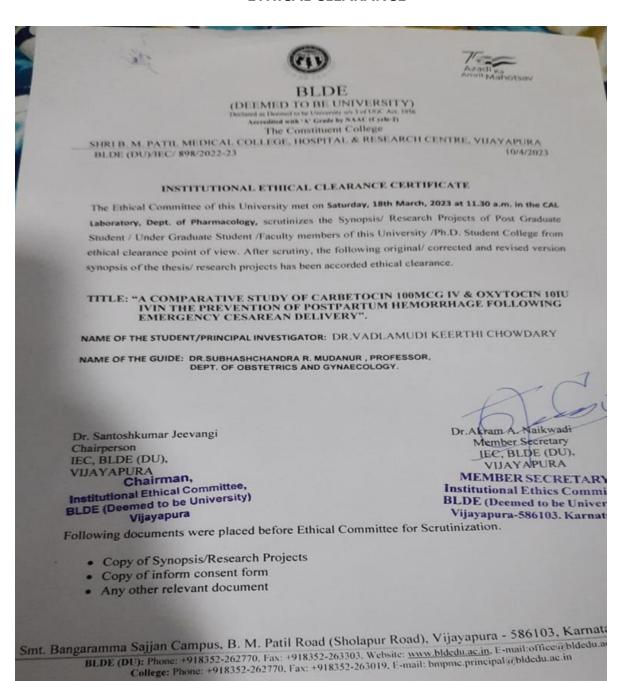
If Yes, please specify.

Tachysystole Yes/No		
Nausea		YES/NO
Uneasiness in the ch	YES/NO	
Any other adverse ef	ffect.	
Use of additional ute	erotonics.	
If yes		
o The drug use	ed, dose and route	
Blood and con	nponent transfusion	
Yes/No		
If Yes		
o No of Pints of	of whole blood	
o No. Of Pints	of PCV	
CBC	PreOp values	Post Op Values Done after 48 hours
Hb		
PCV(HCT)		
MCV		
MCHC		
Platelet count		
WBC Total Count		
o No of Pints of	of FFP	

No of Pints of Platelets

ANNEXURE III

ETHICAL CLEARANCE



ANNEXURES IV

MASTER CHART

TYPE				gesational		HB-	HB-
A/B	AGE	WEIGHT	GRAVIDA	age	PARITY	PREOP	POSTOP
A	22	70	2	38.6	1	12.6	11.9
В	25	76	2	38.5	1	8.4	8.2
A	18	78	2	37	0	9.8	9.6
A	20	74	1	38	0	13.1	11.4
A	22	80	2	38	1	8.8	8.7
В	27	78	2	40	1	12.1	10
В	21	68	3	40.4	1	11.3	9.9
В	19	76	3	38.6	2	10.4	10
A	26	72	2	38.6	1	10.6	10
A	25	84	4	38	2	11.6	11.2
A	25	84	3	37.8	2	9.8	9.6
В	24	78	2	37	1	10.8	10.2
A	24	70	3	37.6	2	11	10.4
В	24	68	2	38	1	11.2	11
В	22	78	2	38.5	1	10.8	10.4
В	22	76	2	37.4	0	8.2	8
A	24	74	2	38.4	1	10.4	10.2
В	23	84	2	36.4	1	12.8	11
A	21	68	1	38	0	11.9	10
В	21	58	2	37.4	1	11.9	10.7
A	22	80	3	37	1	13.2	10.8
A	26	78	2	38	1	10	8.7
В	28	76	4	37.5	3	11.4	11.2
В	21	74	1	38	0	11	10.3
В	28	76	3	38	1	12.3	10.7
A	23	78	1	37	0	10.5	10.4
В	19	80	1	36.5	0	11.7	11.6
В	30	74	2	37	1	9.6	9.2
A	27	74	3	38.1	2	11.9	10.8
A	30	78	5	37	3	12.1	10.4
В	24	70	1	37.2	0	10.8	10
A	20	80	1	36	0	13.2	12.8
A	28	78	3	38	2	11.5	10.7
В	27	76	3	37	1	10.9	10.2
A	26	70	3	38	1	12.4	11
A	27	80	5	37.4	2	12.5	12

A	23	76	1	38	0	12.9	12.1
A	33	70	1	38	0	11.3	10
A	24	88	1	38	0	14	12
A	23	80	3	37.4	2	13.3	11
A	21	80	2	36	1	12.6	10.5
A	25	76	2	37	1	13.6	12.8
A	26	70	3	38	1	13.2	12.8
A	28	78	2	38	1	12.1	12
A	28	74	5	36	4	11.6	10.8
В	22	76	1	36	0	12.5	11.6
В	30	83	3	38	0	14.6	12
В	22	80	2	37.4	1	9.6	8.7
В	28	88	2	38	1	12.4	10.9
В	28	82	2	37.6	1	11.8	9.1
В	22	90	1	38	0	13.8	13
В	25	82	3	38.4	2	9.4	8.2
В	24	90	4	36.4	1	12.6	11
В	21	68	2	36.6	1	10.6	10.2
В	22	80	2	36	1	14.3	10.3
В	23	78	1	38	0	9.2	9
В	27	70	4	37.4	2	14.5	13.7
В	21	84	1	38	0	11.2	11.4
A	20	82	2	36.4	1	11.6	11
В	24	84	2	36.4	1	9.4	9.9
A	19	78	1	37.2	0	12.4	11.4
A	33	74	2	38	1	10.9	10.6
A	22	82	1	38.4	0	12.5	11.6
В	20	78	1	39	0	10.2	10
В	27	68	2	40	0	10	9.8
В	22	70	2	40.2	1	11	9.8
В	19	78	1	38	0	10.4	10
В	21	76	1	38.6	0	9.8	9.4
В	24	78	3	38.5	0	11.9	10.8
В	30	76	1	37.6	0	9.9	9.2
В	24	86	1	37.4	0	11.9	10
В	31	80	2	37.3	0	11.6	10.7
В	24	78	1	37.4	0	11.9	10
A	24	88	1	36.6	0	12	11.4
В	26	80	3	37.4	2	10.6	9.8
В	26	68	2	37.4	1	11.8	10.2
A	23	78	4	38	3	9.8	8.7
A	25	88	2	36.5	0	10.4	10.3
A	30	68	3	37	1	9.1	7.7
В	22	74	1	38	0	12.2	10.3
A	23	90	1	38.4	0	10.8	9.4
В	23	74	2	37.5	1	13	12.3

В	25	70	1	37.6	0	12	6.2
A	23	76	1	37.5	0	11	11.9
A	19	72	1	38.4	0	11.5	10.9
В	28	78	2	37.5	1	12.5	10.6
В	22	76	3	38	2	9.7	10.8
A	21	78	1	36.6	0	7.6	7.4
В	19	84	1	38	0	11	11.3
В	24	88	5	35.4	2	13.3	11.7
A	26	80	4	38	1	11.9	12.4
В	19	70	2	38.4	1	10.2	9.2
В	22	82	2	38.4	1	11.5	11.3
В	26	88	1	39	0	14	12.8
В	24	82	1	39.4	0	11	10.8
В	26	88	1	39	0	13.1	10.9
A	21	84	1	40	0	12.5	11.7
В	28	86	3	40.2	1	11	10.7
В	38	80	1	40.3	0	10.9	9.6
В	20	84	1	38.3	0	9.9	8.2
В	20	86	1	38.6	0	8.9	9.9
В	23	78	1	39	0	13	11.8
В	23	74	1	39.4	0	11.4	11
В	22	72	1	38.4	0	12.5	11.8
A	24	76	1	38	0	12.6	12.3
В	25	74	2	38.5	1	12	10.7
В	27	70	3	38.6	2	11.1	9.6
В	20	74	2	38.4	1	11.9	10.9
В	26	76	3	37.6	2	11.2	9.8
В	23	78	4	38	2	12	10.9
В	26	78	3	38.5	1	12.6	11.2
A	21	82	1	38.5	0	8.7	11.1
В	29	80	2	38.6	1	12.5	11.8
A	26	84	5	39	0	11.7	9.3
В	28	80	3	39.4	2	11.2	11.6
A	34	86	1	39.5	0	13.1	11.6
A	23	80	2	39.3	1	11.5	11.1
A	26	88	3	39.2	1	8.4	8.1
A	26	80	3	40	2	10.1	7
A	30	78	2	40.3	1	9.6	7.3
A	19	76	1	40.3	0	10.4	10
A	21 30	82 80	1	40.2 38.6	0	12.3 9.4	10.8
A	25	82	1 2	37.6	0	12.8	8.8
A A	20	78	1	37.0	0	11.8	11.9
A	26	76	2	40	1	11.6	10
A	29	80	1	41	0	11.4	9.7
A	20	86	2	38.5	1	12.4	11.3
11	20	00		30.3	1	1⊿,⊤	11.5

D	2.4	0.0	2	20	1	10.4	10.4
В	24	88	3	38	1	13.4	12.4
В	24	86	2	37.5	1	11.4	11
A	21	80	1	37.4	0	13	11.5
A	26	78	1	37.6	0	12.2	11.8
A	26	82	3	38	2	9.7	9.5
В	20	76	1	38.5	0	13.7	11.2
A	20	74	2	37.6	0	11.5	10.5
A	29	70	2	38	1	10.7	9.9
A	31	76	6	38.5	1	10.4	9.2
В	22	68	1	38.2	0	12	10.6
В	19	66	2	38.3	0	11.5	11
A	26	70	1	37.4	0	12.6	11.5
A	24	78	2	38	1	12.4	12
A	19	76	1	37.5	0	10.7	9.6
A	27	78	1	38	0	13.7	12.2
В	30	76	2	37.4	0	10.6	9.8
A	21	74	2	38.6	1	10	9.5
A	20	74	2	38	1	12.3	11.5
A	24	76	1	37.6	0	11.9	9.3
В	26	72	2	38	1	9.9	8.3
В	35	78	3	37.5	2	12.2	10
В	20	80	1	38	0	10.7	9.6
A	20	84	2	38.4	1	10	9.1
A	25	88	3	37.6	2	11.8	10.6
A	24	78	2	38	1	11.9	11.5
A	26	74	2	38.4	1	12.6	11
В	25	78	2	37.5	1	13.8	12
В	22	76	2	38.5	1	10.4	8.8
В	27	80	3	38.4	2	11.7	11.2
В	20	76	1	37.3	0	12	11
В	32	70	3	38.5	1	11.2	10.8
A	22	76	1	36.5	0	10.1	9.5
A	27	78	2	38	1	12.2	12
A	21	74	1	37.5	0	10.9	10.6
A	20	78	1	36.4	0	13.3	11.9
A	35	88	2	37.4	1	11.5	10.2
A	20	76	2	37.4	1	11.5	10
A	22	78	3	38.4	2	7.6	9.3
A	27	88	2	37.4	0	11.9	10
A	21	86	2	38.4	1	12.2	9.7
В	27	84	3	36.4	0	9.9	8.3
В	25	78	2	37.6	1	13.3	11.1
A	24	94	3	37.4	2	12.2	11.2
В	24	78	2	38.4	1	12	10.4
В	22	80	1	37	0	13.1	12
A	21	88	1	38	0	12.5	10.7

A	25	02	4	20	2	11.6	11.0
A	25	83	4	38	3	11.6	11.2
A	24	78	2	38.5	1	10.8	8.7
A	27	94	5	38.4	4	11.5	9.8
В	24	84	1	37.4	0	10.6	8.5
В	39	78	4	38	1	12.5	11.1
В	27	80	2	38.1	0	11.2	10.3
В	23	78	3	37.1	1	13	12.9
A	28	80	1	38.3	0	12.5	10.2
A	25	86	2	38.4	1	9.9	11.9
В	25	88	2	37.4	1	10.2	9.8
В	25	86	1	38.4	0	11.6	10.4
В	30	78	1	39.5	0	12.8	11
A	24	80	2	38.4	1	11.9	10
A	22	78	2	37.5	1	11.9	10.4
A	25	80	1	38.4	0	11.6	10.6
В	22	78	2	39.4	1	10.5	9.8
A	20	84	2	38.4	0	12	10.8
A	20	80	2	37.4	0	13.1	12.3
A	31	78	1	37.6	0	13.9	11.6
A	23	70	2	38.4	1	11.9	9.1
В	27	78	2	38.4	1	11.1	9.5
A	25	80	2	37.5	1	11.8	10.8
В	21	76	2	38	1	12.6	11
A	24	80	2	39	0	11.8	9.9
В	31	76	3	38.5	2	7.9	8
В	24	77	3	37.5	2	11.2	9.3
A	26	78	1	38	0	10.8	10
A	28	86	2	38.2	1	10.6	10
В	26	80	2	38	1	10.8	9.6
В	28	78	2	37.6	1	11.2	10.4
A	22	86	1	39.2	0	10.8	10.2
В	24	88	2	38.4	0	11	10.2
A	25	78	1	37.8	0	10.4	10.2
В	19	80	2	37.4	1	11.2	10.6
A	20	68	2	37.5	1	10.2	10
В	23	78	2	38.4	1	9.8	9.4
A	25	84	2	37.4	1	10.2	10
В	23	88	2	38.1	1	11	10.2
A	31	86	2	37.3	1	12	11.8
В	29	78	1	39	0	11.4	10.8
A	25	80	2	38.5	1	10.2	10
В	23	80	2	37.4	1	9.6	9
A	23	82	2	38.4	1	10.8	10.2
В	26	84	2	37.3	1	11.4	10.8
A	28	88	2	38	1	10.4	10.2
В	22	80	2	37.3	0	9.6	9.2
			-	00	•	,. 0	, .

A	24	82	1	38	0	10.4	10.2
В	26	84	2	37.4	1	10.2	9.8
A	24	86	2	37.4	1	9.8	9.6
В	26	84	2	38.1	1	10.2	10
A	27	83	2	37.4	1	10	9.8
В	32	83	1	38.4	0	9.8	9
A	34	82	1	39.5	0	9.4	9.2
В	27	88	2	39.3	0	9.6	8.1
A	28	80	2	38.4	0	10.4	9.3
В	22	82	2	39.3	0	10.6	10.1
A	25	83	1	38.3	0	11	10.4
В	23	84	2	37.5	1	11.2	10.8
A	24	82	2	38.4	0	10.4	9.8
В	28	81	2	37.5	1	11.4	10.6
A	26	68	1	39.4	0	9.8	9
В	28	80	2	38.3	1	10.2	9.1
A	29	90	2	39.2	0	11.2	10.8
В	27	92	1	38.4	0	10.8	10.2
A	25	80	3	37.4	0	11.2	10.8
В	23	85	2	39.4	1	10.8	10.2
A	25	86	1	38.4	0	10.4	9.8
В	26	78	2	38.5	1	11.4	10.6
A	28	80	1	37.4	0	9.8	9.4
В	30	84	2	38.5	0	10.4	9.8
A	31	86	1	37.4	0	10.2	10
В	32	78	2	38.4	0	10.1	9
A	35	80	2	37.6	0	10.7	10.3
В	24	84	2	38.4	0	10.3	9.6
A	26	86	1	37.5	0	9.8	9.4
В	28	89	1	38.4	0	9.9	9.8
A	26	88	1	38.5	0	9.6	8.8
В	24	80	1	37.6	0	10.3	8.9
A	22	78	1	38.4	0	10.6	9.8
В	21	83	2	38.6	0	10.2	9.9
A	20	84	2	37.8	1	10.4	10
В	27	86	2	38.6	1	10	8.2
A	28	76	2	37.6	1	10.2	9.8
В	23	78	2	38.5	1	10.4	10
A	24	80	2	37.4	1	10.6	9.8
В	22	88	2	38.4	1	11	10.8
A	24	84	1	36.5	1	11.2	10.8
В	28	86	1	37.6	0	10.3	9.8
A	26	88	1	38.4	0	10.4	10
В	29	78	2	37.6	0	11.2	10.8
A	30	80	2	38.1	0	10.8	9.8
В	31	83	2	37.6	0	10.3	9.7
	31	03	_	57.0	U	10.5	7.1

A	24	78	3	38.4	0	10.7	10
В	31	80	2	38.4	1	10.6	10
A	26	78	2	37.5	1	9.6	9.2
В	28	82	2	38.4	1	9.8	9.4
A	22	80	2	37.6	1	10.4	10
В	24	84	1	39.4	0	10.5	9.7
A	31	78	1	38.6	0	10.8	10.4
В	27	80	2	39.4	0	10.2	10.1
A	28	88	2	38.6	0	9.8	9.5
В	20	84	1	39	0	9	8.5
A	25	84	2	38.6	0	10.3	10.1
В	26	83	2	39.4	1	10.4	9.8
A	28	78	2	40	1	11	10.8
В	22	80	2	38.4	0	10.3	9.3
A	23	92	2	38.4	0	10.8	10.2
В	24	90	2	38.4	0	10.6	10.3
A	21	78	1	37.5	0	10.2	9.8
В	25	80	1	38.4	0	10.4	10
A	25	82	1	38.5	0	9.8	9.3
В	26	78	1	39.4	0	10.3	10
A	27	80	2	37.4	0	10.5	9.8
В	21	92	2	39.5	0	10.8	10
A	25	78	1	40.1	0	9.8	9.4
В	25	80	1	41	0	10.2	10
A	21	77	1	40.3	0	11	10.8
В	26	78	1	37.5	0	10.4	10
A	28	80	1	38.4	0	10.8	10.2
В	29	92	1	37.5	0	10.4	10
A	26	90	2	38	0	11.8	11.2
В	27	78	2	37.6	1	12.1	10.8
A	25	80	2	38.5	1	11.4	10.6
В	22	82	2	37.4	1	10.8	10.2
A	24	80	1	38.5	0	10.6	10
В	25	78	1	37.5	0	11.2	10.3
A	23	77	1	38.5	0	10.6	9.8
В	24	80	1	38.4	0	10.8	9.4
A	28	78	1	37.5	0	11.2	10.8
В	29	80	1	38.5	0	10.8	10.2
A	32	77	2	38.5	0	10.6	10
В	31	78	2	39.4	0	11.2	10.8
A	33	80	2	39.4	0	10.4	9.8
В	31	80	2	39.4	0	10.2	9.4
A	24	78	2	38.5	1	10.8	9.6
В	25	83	1	39.1	0	11.2	10.8
A	21	78	1	39.2	0	11.4	11
В	24	88	1	40.1	0	10.3	9.8
	_ T	00	-	10.1	V	10.5	7.0

•	26		4	44 4	0	0.0	0.2
A	26	77	1	41.1	0	9.8	9.2
В	27	78	1	39.3	0	9.4	9
A	28	80	1	38.4	0	10.5	10
В	31	82	1	39.4	0	10.9	10.2
A	24	89	1	38.4	0	11.2	10.8
В	25	88	2	37.5	0	11.1	10.4
A	26	84	2	38.5	1	10.2	10
В	27	78	2	37.5	1	10.6	9.5
A	28	90	2	38.4	1	11.2	9.2
В	22	92	2	39.6	1	10.8	10.2
A	20	78	2	39.4	1	10.2	9.8
В	25	84	2	38.4	1	9.8	9.4
A	24	78	2	39.3	0	10.2	10
В	26	77	2	40.1	0	9.6	9.4
A	28	80	2	38.4	0	9.8	9
В	22	78	1	38.3	0	10.6	10.2
A	23	86	1	37.5	0	11.8	11.4
В	24	78	1	38.4	0	12.2	11.8
A	26	88	1	37.5	0	10.3	10
В	28	78	1	38.4	0	10.6	9.8
A	20	80	1	37.4	0	11.3	10.8
В	23	82	1	38.4	0	12	10.2
A	25	88	1	37.4	0	11.2	9.8
В	26	78	1	38.4	0	10.8	10
A	23	78	1	37.6	0	10.6	10
В	25	88	1	39.4	0	9.8	9.2
A	26	88	1	38.5	0	9.5	9.1
В	27	89	2	39.4	0	9.6	9
A	28	86	2	38.6	0	9.2	8.4
В	20	78	2	39.6	1	10.6	8.6
A	23	88	2	38.5	1	10.4	9.4
В	29	86	2	36.6	1	9.8	9.4
A	28	78	1	39.4	0	9.8	7.8
В	20	88	1	38.4	0	9.5	8.2
A	32	78	1	40.1	0	9.6	8.6
В	25	82	1	40.2	0	10.2	8.6
A	26	78	1	38.4	0	10.4	9.8
В	27	86	1	38.4	0	9.8	9.4
A	27	78	1	37.6	0	9.6	9
В	29	80	1	38.4	0	10.4	9.4

PCV PREOP	PLT PREOP(LAKH S)	PLT POSTOP	PCV POSTOP	BP- PRE ,SYST	BP SYST POST	BP- DIAST,PR E	BP- DIAST,POS T
35.4	2.17	2.19	33.4	118	124	86	84
25.2	2.18	1.98	26.6	124	116	82	78
86.4	2.19	2.11	84.4	118	126	86	80
36.7	1.9	2.01	36.4	120	122	84	88
26.7	2.18	1.89	28.4	116	122	78	80
36.7	2.09	1.78	36.4	112	120	74	88
33.5	2.18	1.67	30	116	118	74	86
33	2.11	1.67	32	110	114	78	78
32	3.13	1.89	30.4	124	112	80	76
34.1	1.9	1.9	34	122	123	84	78
28.8	1.89	1.78	28.4	112	126	82	88
28.6	1.78	1.578	28.4	114	126	86	78
28.6	1.45	1.89	28.5	116	128	82	76
28.4	1.99	1.67	28.2	112	118	80	78
28.6	1.89	1.89	28.5	110	124	88	70
28.4	2.09	1.78	27.8	108	120	84	78
30	2.12	1.67	30.2	102	112	82	88
37.1	2.3	1.87	31.7	110	114	88	80
34.1	2.45	1.98	29.2	114	118	82	78
35.9	2.34	1.56	31.7	130	122	88	66
38	2.33	1.78	31.9	132	120	86	78
30	3.01	1.87	26.4	124	124	88	70
34.8	2.19	1.98	31.7	122	123	84	80
30.8	3.12	1.67	31.4	124	113	84	78
37.4	2.89	1.88	36.8	118	114	88	88
33.3	3.12	1.7	32.7	124	118	84	78
36.6	2.88	1.99	38.1	118	116	82	77
29.3	1.78	1.67	29.8	110	121	84	76
35.4	2.13	1.76	32	124	125	86	86
35.3	2.12	1.88	34.1	126	126	78	70
35.3	2.19	1.78	34.1	116	124	80	78
39.9	2.34	1.78	38.7	118	116	88	76
36.4	2.56	1.87	36.2	122	118	84	86
32.6	1.98	1.9	32.4	132	126	88	88
36.2	2.01	1.78	38.8	130	124	84	80
37	2.12	1.65	38	118	120	84	82
37.3	1.98	1.56	35.5	114	124	86	72
35	2.01	1.89	37	112	125	88	74
41.9	2.12	1.67	46	110	126	80	76
38.5	2.67	1.66	41.6	108	124	82	78
33.6	2.12	1.86	31.5	106	120	84	86
28.8	2.01	1.78	37.5	112	126	82	82

39.9	2.19	1.66	38.8	116	112	84	90
36.2	2.23	1.68	35.6	114	118	88	82
32.4	2.32	1.65	33.6	118	116	84	80
36.9	2.23	1.85	38	112	124	78	84
41.2	2.19	1.67	33.9	120	126	88	86
31.5	2.12	1.88	29.5	112	124	86	88
36.3	2.11	1.68	38	130	128	88	84
36.1	2.19	1.98	27.3	114	124	88	86
40.4	2.18	1.45	37.5	124	125	86	88
30.3	1.98	1.89	28.1	114	118	86	84
37.2	2.01	1.77	32.5	116	114	84	84
34.5	2.12	2.01	34	118	117	78	86
42.4	2.11	2.01	33	110	118	80	88
28.7	2.01	1.99	30.7	120	121	84	80
43	2.23	1.88	42	132	120	78	82
28.7	2.12	1.66	26.4	134	116	80	84
38.5	2.23	1.88	38.2	130	124	88	88
26.4	2.18	1.66	28.6	122	116	98	84
36.4	2.12	1.66	36.1	126	118	94	86
30.4	2.19	1.87	28.5	124	120	92	88
36.1	1.78	1.98	34.6	114	124	94	85
32	1.22	1.68	31.4	118	124	94	86
32	1.33	1.87	31	102	126	90	87
32	1.78	1.89	29.8	112	112	94	88
31	1.55	1.77	29.8	108	128	88	80
32	1.78	1.98	31	106	124	84	78
34	1.45.	2.01	33.8	126	126	88	78
30.8	2.11	2.11	28.8	122	124	86	77
34.2	2.1	2.11	33	124	122	84	74
32.6	2.11	1.89	31	128	124	88	78
34.2	2.18	1.78	33	130	116	84	84
36.3	1.98	1.87	34.4	122	118	78	78
32.2	2.1	1.9	30.2	108	124	76	76
36.9	2.19	1.77	34.2	106	112	78	78
30.8	2.1	1.98	27.6	104	124	80	79
32.4	2.11	1.78	31.9	124	126	88	68
28.6	2.32	1.88	23.6	114	128	84	88
35.5	2.67	2.01	29.9	124	124	80	87
34.4	2.12	2.11	28.6	120	122	88	79
38.3	1.98	1.67	35.5	126	120	78	78
34.8	2.01	1.98	19.5	122	126	84	89
32.4	2.11	1.78	35.6	120	124	80	86
35.2	1.98	1.77	34.5	112	122	84	85
34.5	1.78	1.66	31.1	118	120	88	84
31.4	2.01	1.98	33.5	118	124	90	78
35.1	2.12	1.77	35	120	126	78	56

33.6	2.01	1.78	35.4	126	122	88	78
38.5	1.98	1.77	34.8	108	124	80	89
34.7	2.11	1.98	37	124	120	88	80
29	2.87	2.11	29.3	120	124	80	88
34.2	1.78	1.75	35	126	124	86	85
40.5	2.01	1.67	37.2	122	116	86	84
34	2.22	1.89	32.6	128	118	88	82
37.4	1.98	1.87	32	124	116	78	80
36.8	2.12	1.86	35.2	124	124	86	84
28.6	1.98	1.68	32.2	126	122	84	82
31.7	2.01	2	27.6	128	120	80	88
31	2.12	1.78	23.1	126	124	84	84
28	1.98	1.78	23.8	124	126	88	80
37.7	1.82	1.88	37.5	120	124	86	84
34	1.89	1.96	30.2	122	112	88	86
38	2.12	1.78	36.3	126	118	80	84
34.9	2.01	1.78	34.2	122	120	84	82
36.6	1.98	1.99	34.5	122	124	78	80
32.6	1.88	1.78	29.8	120	112	70	84
36.5	2.12	1.88	34.4	108	126	78	88
34	1.98	1.98	31.7	112	118	76	86
36.6	2.12	1.78	34.9	112	120	80	84
38	2.11	2.11	36.4	132	124	88	78
27.7	2.01	2.12	35.3	124	126	86	80
36.3	2.22	1.98	36.6	136	120	84	86
36	1.98	2.12	28.8	122	124	80	78
33.2	1.89	2.22	35.7	120	126	84	80
38.8	1.77	3.12	34.3	124	122	86	84
34.9	1.67	1.55	35.4	126	124	80	80
28.2	2.12	1.98	27.3	128	118	84	88
34.4	1.98	1.88	23.8	124	112	78	80
29.7	2.12	1.89	23.4	114	115	70	86
31.1	2.01	1.99	30.6	116	112	74	88
34.6	2.22	2.1	30.7	118	98	78	86
28.9	1.98	1.78	27.2	120	116	80	88
36.9	2.11	1.77	36.2	124	118	84	78
34	2.1	1.89	32.8	122	98	78	80
35.6	1.99	1.9	31.7	120	108	78	80
33.7	1.78	1.77	30.1	126	118	74	78
37.1	1.78	1.66	34.5	124	108	78	80
41.1	1.8	1.66	39.4	122	114	80	88
35.1	1.67	1.55	35.2	120	112	84	84
39.1	2.1	1.89	34.4	114	123	86	88
36.9	2.22	1.98	36.1	116	124	94	80
29.9	2.2	1.78	30.4	112	126	78	86
39.4	2.32	2.11	34.1	108	112	80	80
37.T	2.52	2,11	J-T.1	100	112	00	00

25	0.45	2.1	24.4	110	110	70	0.0
35	2.45	2.1	34.4	110	118	78	88
32.4	1.78	1.67	31.8	124	108	84	86
34.2	1.98	1.78	30.4	126	126	80	88
36.5	2.23	2.12	31.7	130	112	84	84
33.1	3.2	2.19	34.3	128	114	82	78
38.5	3.1	2.88	35.4	112	116	78	70
38.8	3.22	3.1	37.1	112	112	80	78
32.1	2.89	2.7	29.9	116	118	80	76
42.1	2.78	2.67	37.3	128	113	84	78
31.3	2.45	2.12	30.4	114	116	78	80
31.3	2.12	2.1	30.7	124	132	76	88
37.4	2.34	2.12	33.8	112	112	78	86
36.6	2.12	2	29.1	114	118	80	84
32	1.98	1.87	26.4	116	116	84	80
35.5	2.1	1.89	30.5	124	106	78	82
32.8	1.78	1.67	29.8	120	116	80	80
32.8	2.34	1.89	30.4	126	114	84	88
34.2	2.12	2.1	30.4	124	112	82	84
34.1	1.98	1.78	34.6	122	108	78	86
36.8	2.1	1.98	32	120	126	76	88
41	1.98	1.78	40	112	122	76	84
33.8	1.45	1.4	27.7	108	112	74	88
34	1.78	1.88	33.2	116	116	78	86
38.4	1.66	1.6	35.8	124	114	80	76
30.7	2.1	1.98	31.1	112	104	84	78
43.1	2.22	2.1	42.6	114	108	88	88
43.2	1.89	1.77	36	118	106	84	80
34.6	1.9	1.78	34.4	106	116	78	84
39.7	1.92	1.88	37	112	118	80	88
36	1.48	1.4	32.5	126	124	84	85
35.4	1.89	1.78	30.9	112	122	78	86
25	2.01	1.89	30.9	114	126	80	78
36.5	2.11	1.79	31.6	118	122	84	84
35.4	2.14	2.1	28.3	120	124	88	88
30.5	2.22	2.11	25.9	122	122	86	80
39	2.23	2.12	33.3	124	126	78	86
37.2	2.34	2.12	35.1	126	124	80	78
34.3	2.56	1.98	29.8	112	112	82	80
37.5	2.78	1.78	35.5	118	116	70	88
37.4	2.85	2.1	32	116	108	74	80
35.6	2.18	1.78	34.7	124	106	78	88
34.7	1.78	1.67	27.4	126	106	78	86
33.3	1.88	1.98	29.4	116	108	80	78
32.3	1.68	1.78	25.8	118	118	88	78
34	1.98	1.78	32.3	124	112	84	88
32.8	2.1	1.68	30.9	122	116	80	68

37.6	2.22	1.98	37.7	126	112	84	78
37.6	1.98	1.67	31.6	124	118	78	86
30.9	2.01	1.98	35.4	118	102	80	84
33.3	2.22	1.78	30.4	120	108	84	74
36.8	2.34	1.66	35.6	124	118	88	77
39.6	2.34	1.9	38.4	122	112	78	78
35.6	2.44	1.78	34.4	112	108	80	76
35.9	2.12	1.67	32.8	114	118	84	80
35.7	2.34	1.66	34.8	124	102	80	88
32.6	1.98	1.87	30.8	126	118	84	85
35.2	2.11	1.97	32.5	114	112	78	78
38.4	2.34	1.88	37.2	126	108	80	75
42.4	1.98	1.89	36	128	112	88	76
38.6	2.1	1.98	29.4	124	124	84	79
32.2	1.98	1.8	27.9	126	122	88	80
37.2	2.11	1.89	34.8	116	120	80	88
38.3	2.34	1.87	33.9	118	124	84	86
36.1	2.31	1.97	30.5	116	122	88	80
26.6	2.02	1.88	26.8	110	124	88	86
33.1	2.11	1.97	28.4	114	122	80	78
34.2	2.13	1.89	33.2	116	120	86	80
33.8	2.18	1.88	32.4	115	117	82	82
34	2.11	1.99	30.8	123	103	80	78
34.2	1.98	1.78	33.6	112	104	88	80
34	2.12	1.88	32	123	113	80	78
32	2.12	1.9	30.4	112	112	82	84
31.8	2.12	2.1	30.4	132	113	80	68
34.8	2.67	2.22	31.4	132	114	78	70
30.4	2.84	2.12	32	134	112	85	80
33.4	1.98	2.13	28.9	112	102	80	82
32.1	1.56	2.18	31.2	134	108	78	88
30.4	2.01	1.78	29.4	113	110	80	80
31.8	2.23	1.89	30.4	114	112	80	78
30.4	1.98	1.78	29.7	109	132	82	84
31.8	2.45	1.67	30.8	110	112	82	78
34.8	1.86	1.88	33.2	112	102	84	80
33.4	1.98	1.78	29.5	114	108	84	82
30.4	2.12	1.87	29.8	114	104	88	80
31.8	1.8	1.67	29.8	113	112	80	78
32.8	1.78	1.7	31.7	114	104	84	78
34.4	1.89	1.67	33.4	123	104	80	80
30.2	1.78	1.56	29.8	132	104	82	82
34.6	1.68	1.6	32	129	108	80	78
33.4	1.88	1.7	31.2	118	113	82	80
33.5	1.78	1.67	32.3	116	112	84	78
34.5	1.78	1.66	32.8	113	123	86	80

33.5	1.68	1.6	32	112	102	84	82
33.8	1.66	1.56	32.4	132	100	88	78
33.4	1.69	1.57	32.6	112	112	80	80
32.5	1.8	1.78	31.8	109	110	85	80
36.3	2.1	1.89	35.4	107	102	86	87
36.3	2.11	1.9	35.5	123	110	80	78
34.5	2.08	1.99	33.6	112	102	78	80
34.2	1.78	1.76	33.5	113	104	80	89
36.3	2.12	1.98	35.3	114	120	82	98
34.2	1.78	1.88	33.4	108	110	80	80
34.8	1.88	1.76	33.2	106	102	84	78
34.5	1.67	1.56	33.6	104	104	78	68
36.4	1.78	1.66	35.5	112	110	80	80
35.3	1.88	1.78	34.8	108	103	80	89
35.2	1.9	1.8	34.3	118	110	86	80
34	2.1	1.89	33.2	102	102	84	85
34.8	2.11	1.89	33.5	114	104	86	78
33.4	1.98	1.8	32.8	102	112	80	88
34.2	2.1	1.98	33.5	110	102	78	78
35.5	1.98	1.8	34.4	103	103	80	76
34.6	1.78	1.67	33.4	102	102	84	78
33.2	1.8	1.78	32.8	104	102	78	68
35.8	1.78	1.67	34.5	110	104	76	70
32.8	1.77	1.67	31.3	112	103	74	74
33.4	1.78	1.66	32.4	103	102	76	74
34.2	1.6	1.56	33.4	104	112	78	72
34.7	1.66	1.58	33.2	104	104	80	74
33.4	2.1	1.98	32.4	110	103	78	72
29.9	1.98	1.88	28.4	110	112	80	70
34.3	2.1	1.98	30.3	112	104	84	74
33.5	2.11	1.86	32	110	105	68	72
33.6	1.98	1.76	32.9	102	112	78	70
34.2	1.88	1.78	33	103	104	78	76
36.4	2.1	1.98	32.4	104	102	70	74
34.7	1.78	1.67	33.4	112	132	72	70
34.5	1.88	1.78	33.2	104	112	76	78
33.8	1.78	1.66	32.3	104	102	78	76
32.8	1.88	1.8	31	103	112	88	74
34.2	1.98	1.9	32	102	102	80	70
33.8	2.01	1.99	32	110	104	80	76
35.3	2.11	1.98	34.3	102	112	86	75
34.2	2.22	1.78	33.3	104	112	78	74
33.4	3.12	1.99	32	112	103	80	80
35.6	3.12	2.11	34.2	114	102	88	86
33.6	2.18	2.01	32	117	104	80	84
33	2.19	2.11	32.1	103	102	82	78
- 55	2.1)	2,11	34.1	105	102	02	70

32.9	2.11	2.01	31	102	103	78	68
36.8	2.19	2.01	34.8	110	104	80	78
37.4	2.88	2.11	36.8	112	103	88	67
33.2	2.77	2.33	32.1	102	102	80	78
30.5	2.67	2.44	29.3	110	110	78	80
34.4	2.56	2.33	33.3	103	110	80	88
35.2	2.68	2.44	34.4	102	112	84	84
32.5	2.76	2.45	31.3	110	104	78	86
34.6	2.45	2.22	32.3	103	102	78	78
36.8	2.44	2.33	31.3	121	104	70	80
34.2	1.98	1.89	32.3	102	112	80	85
33.6	1.89	1.78	32.2	112	105	83	78
36.3	2.1	1.98	34.3	102	110	78	90
34.6	1.98	1.88	33.2	103	120	77	78
28.8	1.88	1.78	27.4	103	121	76	80
29.9	1.76	1.67	28.4	112	122	78	84
28.6	1.78	1.66	27.4	112	102	79	78
27.8	2.1	1.98	27.3	102	104	80	80
36.2	1.98	1.89	34.4	105	103	82	84
35.3	1.78	1.67	34.2	121	112	78	78
35.4	1.68	1.56	34.4	124	104	76	80
37.3	1.66	1.6	36.4	124	112	78	84
32.9	1.78	1.7	31.9	122	108	70	78
33	2.1	1.89	32.4	121	118	78	88
34.2	2.01	1.98	33.3	123	113	88	80
36.2	2.22	1.99	35.4	124	112	80	78
32.8	3.21	1.89	31.9	124	120	86	80
33.8	3.21	2.12	32.1	123	120	78	84
34.2	3.01	2.19	33.2	121	112	80	78
33.4	3	2.1	32.8	123	108	82	88
34.2	2.12	1.89	32.3	124	119	78	78
33.8	2.18	2.1	32.2	121	120	70	80
36.4	3.12	2.19	34.2	120	118	80	86
34.6	2.18	1.78	33.2	123	108	86	78
35.8	3.12	2.19	34.2	127	119	70	80
33.4	2.18	2.19	32.8	124	112	78	76
32.4	3.12	2.19	30.4	120	108	80	80
33.2	2.18	1.78	32.3	128	112	84	85
31.9	2.13	1.98	30.8	114	102	86	86
31.8	2.12	2.12	30.4	112	108	84	84
30.8	2.18	1.98	31.3	113	102	78	88
31.4	3.12	2.18	30.8	110	110	80	78
32.4	3.11	2.78	30.3	113	108	80	88
35.5	3.19	2.12	34.4	118	102	78	78
34.4	3.01	2.78	30.3	132	104	76	80
30.8	2.18	1.98	32.3	127	110	78	78

31.8	2.19	1.78	30.2	128	102	80	84
34.8	2.11	1.78	32.3	112	104	85	78
33.4	1.78	2.11	30.4	120	110	67	78
34.8	1.76	1.67	33.4	119	102	78	80
33.8	1.67	1.56	30.2	1120	104	89	84
32.8	1.78	1.66	30.2	120	112	80	78
33.7	1.65	1.6	32.4	130	110	87	80
34.6	1.45	1.4	33.4	129	130	78	77
33.6	1.87	1.78	30.4	128	112	76	79
34.8	1.89	1.65	33.3	122	104	68	88
37.3	1.9	1.689	34.4	120	104	78	78
34.2	2.1	1.98	30.4	121	102	80	80
35.2	2.11	2.01	34.4	119	120	84	78
35.3	2.01	1.98	34.8	112	122	86	86
34.2	1.98	1.78	33.7	110	118	68	78
35.4	1.89	1.65	34.3	120	123	78	80
28.5	1.67	1.68	27.4	121	122	80	78
34.9	1.68	1.78	30.3	120	120	78	80
35.9	1.98	1.89	32.4	132	112	79	84
38.4	2.1	2.01	34.4	128	120	70	88
37.4	2.11	1.98	36.4	128	119	86	78
34.7	1.98	1.78	32.9	124	112	78	70
34.3	1.78	1.67	33.3	120	122	70	72
38.9	1.99	1.78	36.4	119	120	76	68
36.3	2.1	1.98	35.5	112	112	74	80
38.3	3.12	2.18	36.5	120	114	70	84
34.4	2.35	2.11	32.3	118	110	76	88
34.2	2.66	2.55	34.2	120	120	68	82
32.9	2.56	2.55	31.4	121	110	70	84
31.8	2.78	2.66	30.4	122	120	80	86
36.4	2.89	2.56	32.3	120	120	82	78
34.2	2.7	2.34	32.4	124	112	84	88
38.4	2.65	2.45	35.3	112	110	84	70
36.8	1.98	1.67	34.2	114	110	80	80

PULSE,PRE	PULSE- POSTOP	IIT 1MIN	UT,3MIN	IIT SMINI	UT,10 MIN
90 90	94	UT,1MIN 4	4	UT,5MIN 4	5
92	98	3	4	4	5
98	88	3	4	4	5
86	80	4	4	5	5
88	86	3	4	5	5
84	86	4	5	5	5
86	88	3	4	4	5
80	90	4	4	5	5
88	94	3	4	4	5
96	94	4	5	5	5
94	96	4	4	5	5
88	88	4	5	5	5
86	80	4	5	5	5
78	78	3	4	4	5
88	80	4	4	4	5
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86	82	4	4	4	5
86	88	4	4	4	5
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88	88	4	4	4	5
82	80	3	3	4	5
78	88	4	4	4	5
70	80	3	4	4	5

80	78	3	4	4	5
82	80	3	4	5	5
86	82	3	4	5	5
68	86	3	4	5	5
78	78	3	4	5	5
76	74	4	4	5	5
70	76	4	4	5	5
72	78	4	4	5	5
74	80	4	4	5	5
72	88	4	4	5	5
70	86	4	4	4	5
74	80	4	4	4	5
72	68	3	4	4	5
74	78	3	4	4	5
78	80	3	4	4	5
76	88	3	4	4	5
76	80	4	4	4	5
74	82	3	4	4	5
72	78	3	4	4	5
70	80	3	4	4	5
74	86	3	4	5	5
72	84	3	4	5	5
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86	86	3	4	5	5
88	78	3	4	5	5
84	80	4	4	5	5
82	90	4	4	5	5
68	94	4	4	5	5
80	78	4	4	5	5
88	80	4	4	5	5
86	90	3	4	5	5
78	94	3	3	5	5
76	96	3	3	5	5
74	98	3	3	5	3
78	78	3	4	5	5
80	80	4	4	5	
	84	4	4	5	5
82	04	4	4	3	3

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78	80	3	3	5	5
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80	80	3	4	4	5
88	84	3	4	5	5
84	78	3	4	5	5
78	80	3	4	5	5
80	84	3	4	5	5
82	78	4	3	5	5
78	88	4	3	4	5
80	84	4	3	4	5
84	78	4	3	4	5
84	84	3	3	4	5
78	86	3	3	4	5
80	78	3	3	4	5
84	80	3	4	5	5
76	84	3	4	5	5
78	78	3	4	5	5
80	88	4	4	5	5

84	90	4	4	5	5
85	94	4	3	4	5
78	88	4	3	4	5
80	80	4	3	4	5
78	78	4	3	4	5
80	80	4	4	5	5
84	84	3	4	5	5
84	78	3	4	5	5
78	80	3	4	5	5
80	78	3	4	5	5
84	84	3	4	4	5
78	78	3	4	4	5
84	80	3	4	4	5
78	78	3	4	4	5
80	80	3	4	5	5
80	84	3	3	5	5
84	78	4	3	5	5
78	80	4	3	5	5
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78	86	3	3	4	5
84	78	3	3	4	5
84	80	4	4	5	5
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80	78	3	3	5	5
84	80	3	3	5	5
78	84	3	3	5	5
70	78	4	3	5	5
76	80	4	4	4	5
80	88	3	4	4	5
78	78	3	4	4	5
80	84	3	4	5	5

ADVERSE	USE OF		
EVENTS	ADDITIONAL	BLOOD	Blood
LIKE PPH	UTEROTONICS	TRANSFUSION	loss
NO	NO	NO	800
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	890
NO	NO	NO	860
NO	NO	NO	900
YES	yes	NO	900
NO	NO	NO	770
NO	NO	NO	740
NO	NO	NO	990
NO	NO	NO	1000
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	890
NO	NO	NO	900
NO	NO	NO	880
NO	NO	NO	800
NO	NO	NO	880
NO	NO	NO	970
NO	NO	NO	800
NO	NO	NO	800
NO	NO	NO	1000
NO	NO	NO	1100
NO	NO	NO	800
NO	NO	NO	900
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	800
NO	NO	NO	940
NO	NO	NO	800
NO	NO	NO	900
NO	NO	NO	800
NO	NO	NO	900
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	900
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	800
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	1000
NO	NO	NO	900
NU	NU	INU	900

NO	NO	NO	940
NO	NO	NO	990
NO	NO	NO	880
NO	NO	NO	1000
NO	NO	NO	940
NO	NO	NO	880
NO	NO	NO	700
NO	NO	NO	880
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	960
NO	NO	NO	1050
NO	NO	NO	880
NO	NO	NO	780
NO	NO	NO	940
NO	NO	NO	900
NO	NO	NO	740
NO	NO	NO	800
NO	NO	NO	800
NO	NO	NO	840
NO	NO	NO	1000
NO	NO	NO	940
NO	NO	NO	900
NO	NO	NO	1000
NO	NO	NO	940
NO	NO	NO	1000
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	840
NO	NO	NO	880
NO	NO	NO	940
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	880
NO	NO	NO	880
NO	NO	NO	800
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	860
YES	YES	NO	780
NO	NO	NO	800
NO	NO	NO	940
NO	NO	NO	900
NO	NO	NO	700
NO	NO	NO	780
NO	NO	NO	800

NO	NO	NO	840
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	1000
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	840
NO	NO	NO	960
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	800
NO	NO	NO	940
NO	NO	NO	900
NO	NO	NO	940
NO	NO	NO	980
NO	NO	NO	940
NO	NO	NO	900
NO	NO	NO	780
NO	NO	NO	800
NO	NO	NO	840
NO	NO	NO	900
NO	NO	NO	940
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NO	NO	NO	960
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NO	NO	NO	940
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NO	NO	NO	1000
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NO	NO	N	940
NO	NO	N	970
110	NO	IN	710

NO	NO	N	1000
NO	NO	N	1100
NO	NO	N	940
NO	NO	N	920
NO	NO	N	880
NO	NO	N	1020
NO	NO	N	1000
NO	NO	N	970
NO	NO	N	890
NO	NO	N	900
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NO	NO	N	960
NO	NO	N	940
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NO	NO	N	940
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NO	NO	N	920
NO	NO	N	940
NO	NN	N	800
NO	NN	N	840
YES	YES	N	800
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NO	NO	N	940
NO	NO	N	1000
NO	NN	N	940
NO	NO	N	960
NO	NN	N	1000
NO	NO	N	1050
NO	NO	N	940
YES	YES	N	960
NO	NO	N	940
YES	YES	N	900
NO	NO	N	920
NO	NO	N	900
NO	NO	N	780
YES	YES	N	820
NO	NO	N	840
NO	NN	N	800
NO	NO	N	840
YES	YES	N	800
YES	YES	N	900
NO	NO	N	840
NO	NO	N	900
NO	NO	N	940
NO	NO	N	1000

NO	NO	N	940
YES	YES	N	1000
NO	NO	N	940
NO	NO	N	920
NO	NO	N	940
NO	NO	N	1000
NO	NO	N	960
NO	NO	N	1000
NO	NO	N	920
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NO	NN	N	940
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NO	NO	N	1040
NO	NO	N	940
NO	NO	N	1000
YES	YES	N	800
NO	NO	N	840
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NO	NO	N	1000
NO	NO	N	940
NO	NO	N	1000
NO	NO	N	960
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NO	NO	N	900
NO	NO	N	1050
NO	NO	N	900

NO	N	850
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NO	N	1050
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NO	N	800
NO	N	840
NO	N	880
NO	N	1000
NO	N	800
		000
NO	N	900
NO	N	800
NO NO	N N	800 880
NO	N	800
	NO N	NO N NO N NO N NO

NO	NO	N	1020
NO	NO	N	980
NO	NO	N	860
NO	NO	N	1000
NO	NO	N	900
NO	NO	N	940
NO	NO	N	940
NO	NO	N	980
NO	NO	N	1000
NO	NO	N	1050
NO	NO	N	1500
NO	NO	N	1020
NO	NO	N	900
NO	NO	N	940
NO	NO	N	1000
NO	NO	N	940
NO	NO	N	880
NO	NO	N	900
NO	NO	N	940
NO	NO	N	960
NO	NO	N	1000
NO	NO	N	940
NO	NO	N	980
NO	NO	N	1000
NO	NO	N	940
NO	NO	N	880
NO	NO	N	900
NO	NO	N	940
NO	NO	N	1050
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NO	NO	N	1000
NO	NO	N	850
NO	NO	N	1500
NO	NO	N	1200
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NO	NO	N	880
NO	NO	N	840
NO	NO	N	850
NO	NO	N	860
NO	NO	N	880
NO	NO	N	900
NO	NO	N	940
NO	NO	N	960

NO	NO	N	1000
NO	NO	N	1050
NO	NO	N	1100
NO	NO	N	1000
NO	NO	N	850
NO	NO	N	900
NO	NO	N	950
NO	NO	N	900
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NO	NO	N	980
NO	NO	N	950
NO	NO	N	1000
NO	NO	N	940
NO	NO	N	940
NO	NO	N	930
NO	NO	N	940
NO	NO	N	880

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