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Comparison of the Effectiveness of 5 Iu Oxytocin Bolus and 20 Iu Infusion on Uterine Contraction and Hemodynamic Response in Caesarean Section

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ABSTRACT

Uterine atonic can result in postpartum hemorrhage, gravid hysterectomy and maternal mortality. Oxytocin is the most commonly used agent for the prevention and treatment of atonic uterine during cesarean section. However, the provision of rapid and increasing the dose may result in hemodynamic instability, cardiovascular collapse, and death. This study aimed to compare the effectiveness of oxytocin bolus 5 IU and oxytocin infusion 20 IU to contractions of the uterus and the hemodynamic response in cesarean section with spinal anesthesia.

An experimental study, Randomized Controlled Trial (RCT) was conducted in the operating room Mohammad Hoesin Hospital Palembang from July to August 2016. It was obtained a 44 pregnant at term women who will do a cesarean section that meet the inclusion and exclusion criteria. The frequency and distribution of data are described in tables and comparisons between the two groups were analyzed using SPSS.

Of the 44 pregnant women at term, 22 women in the group of oxytocin bolus 5 IU and 22 women in the group of oxytocin infusion 20 IU. By statistical analysis, there was no significant hemodynamic changes after bolus administration of oxytocin 5 IU or oxytocin infusion 20 IU ($p > 0.05$) and there were no significant hemodynamic differences between oxytocin bolus 5 IU and infusion of 20 IU oxytocin ($p > 0.05$). In addition, there are significant changes in uterine contractions after bolus administration of oxytocin 5 IU or oxytocin infusion 20 IU ($p < 0.05$) and there were significant differences in uterine contraction in the 3rd minute ($p = 0.006$), 6th minute ($p = 0.010$) and 9th minute ($p = 0.008$) between oxytocin bolus 5 IU and infusion of oxytocin 20 IU.

It can be concluded that there is no significant hemodynamic changes after administration of oxytocin 5 IU bolus and oxytocin infusion 20 IU and there are differences in uterine contractions significantly in the 3rd minute, 6th minute and 9th minute between oxytocin bolus 5 IU and oxytocin infusion 20 IU.

1. Introduction

Uterine atony can result in postpartum hemorrhage, gravid hysterectomy, and maternal death. Oxytocin is the agent most frequently used for the prevention and treatment of uterine atony during cesarean section; However, rapid administration and increasing doses can result in hemodynamic instability, cardiovascular collapse, and death. Although there is a demonstration of adequate uterine tone after cesarean section with low-dose oxytocin (<3 International Units (IU)), the current and frequent practice is to use continuous infusions of doses greater than 20-40 IU. Recommendations for dosage, timing, and speed of administration of oxytocin, as well as alternative second-line uterotonic agents, from books of obstetrics and professional obstetric associations are unclear or non-existent. Administration of oxytocin and additional uterotonic agents have been associated with significant maternal, fetal, and neonatal side effects.

These side effects, particularly those associated with oxytocin, may be related to dose and speed of administration.[1,3]

There are several guidelines and studies that support slow intravenous bolus of oxytocin 5 IU. Among them, the Royal College of Obstetricians and Gynecologists (RCOG) Guideline on Caesarean section recommends giving a slow intravenous 5 IU bolus dose of oxytocin after the birth of the baby. This dose is a lower dose than previously used, which is 10-20 IU and is based on concerns about the side effects of oxytocin, such as maternal hypotension.[12]

The British National Formulary also recommends that oxytocin should be given in a dose of 5 IU by slow intravenous injection after delivery in cesarean section. Jonsson et al., In 2009 also studied 103 pregnant women who underwent cesarean section under spinal anesthesia. All patients who were included in the inclusion criteria were divided into 2 groups, group I received oxytocin 5 IU and group II received oxytocin 10 IU. The results of this study indicated that the hemodynamic response (decreased MAP) was more stable in the 5 IU oxytocin group compared to the 10 IU oxytocin group.[13,14]

King et al, in 2010 reported that administration of 5 IU IV bolus of oxytocin for 30 seconds followed by 40 IU of oxytocin in 500 ml of normal saline resulted in stronger uterine contractions than administration of normal saline IV for 30 seconds followed by 40 IU of oxytocin in 500 ml of normal saline.[15]

A study by Sartain et al., In 2008, which studied 80 patients undergoing cesarean section with combined spinal-epidural anesthesia who received 5 IU bolus oxytocin revealed good uterine tone and at least (17.5%) demand for additional uterotonic drugs.[11]

Research in South Korea in 2011 by Kim, et al also revealed that 5 IU bolus of oxytocin followed by a continuous infusion of oxytocin resulted in stronger uterine contractions than with only continuous oxytocin infusion.[16]

Infusion of oxytocin in cesarean section is given at a wide and varied dose and time of administration (before or after delivery of the placenta). Use of an oxytocin infusion at a rate of 200 mU / minute (20 IU / L in infused fluid at a rate of 10 ml / min) within a few minutes until the uterus contracts well and controlled bleeding is recommended.[17]

In Indonesia, infusion of oxytocin is carried out by giving 20-40 IU which is dissolved in 500 ml of intravenous fluid and given without the correct dose, only monitored based on comments from a specialist obstetrician who states that uterine contractions are good or not.[18]

At RSUP dr. Mohammad Hoesin Palembang, a woman who underwent cesarean section with spinal anesthesia was given 20 IU of oxytocin infusion in 500 ml of intravenous fluid and was monitored based on the evaluation of a specialist obstetrician regarding good or not uterine contractions.

2. Research methods

This research is an experimental study with a randomized controlled trial (RCT), double blind, add on. The research was conducted in the operating room of the RSUP. dr. Moh. Hoesin Palembang from July 2016 to August 2016. Inclusion criteria: pregnant women at term who will undergo caesarean section, ASA II physical status, aged 18-40 years, willing to take part in the research and sign an informed consent. Exclusion criteria: patients with term pregnancy with: uterine over-distension (polyhydramnios, multiple pregnancies, macrosomia), patients at risk of uterine atony / bleeding, patients with cardiovascular disorders, patients with failure of induction, hypertension in pregnancy, preeclampsia, eclampsia, abnormal pregnancy (uterine myoma , placental abnormalities)

After obtaining approval from the Research Ethics Committee of dr. Moh. Hoesin / Faculty of Medicine, University of Sriwijaya, patients who have met the inclusion criteria and excluded and agree to the information on the concentration, were carried out simple randomization using a random number table. Patients were divided into two groups: Group I (slow bolus oxytocin) and Group II (infused oxytocin). Performed a vein line with venous canula no. 18, do

prehydration with crystalloid fluid 20 ml / kgBB for 10-15 minutes. The infusion set used is the blood administration set. Then installed a noninvasive blood pressure monitor, ECG, and peripheral O2 saturation and measurements of blood pressure, mean arterial pressure, pulse rate, breath rate, SpO2, and ECG observations were carried out. Spinal anesthesia was performed in a sitting patient position with a G27 spinal needle puncture in the lumbar (L3-4 or L4-5) median approach and administration of the local anesthetic drug bupivacaine 0.5% hyperbaric 10 mg plus fentanyl 25 µg. After the spinal anesthesia is complete, the patient is positioned to sleep on his back with a pillow on the head and the operating table tilted slightly to the left ± 150, and given a nasal oxygen cannula 2 liters / minute. The sensory block height is expected to reach the Th 6 dermatome, evaluated by the pinprick method on the midclavicular line with a G23 needle. If hypotension occurs, ephedrine 5 mg intravenously, can be repeated until normal blood pressure is reached. After it is confirmed that the spinal is successful, surgery can be performed. After the baby was born and the umbilical cord was clamped, group I was given a slow bolus of 5 IU of oxytocin dissolved into 5 ml with 0.9% NaCL at a rate of 15 seconds followed by infusion of 20 IU of oxytocin in 500 ml of RL at a rate of 40 drops / minute. Group II was given 5 ml of 0.9% NaCl at a rate of 15 seconds followed by administration of 20 IU of oxytocin in 500 ml of Ringers lactate and given at a rate of 40 drops per minute which was used as an infusion.

Systolic blood pressure, diastolic, mean, pulse rate, respiratory rate, SpO_2 were measured at the time after birth, before umbilical cord clamping (before being given oxytocin) as baseline data, and every three minutes after oxytocin administration until 15 minutes later. Uterine contractions as measured by the Linear analog scale (LAS) were measured every 3 minutes to 15 minutes after oxytocin administration. If the LAS is less than 6, given methergin 0.2 mg intravenously within 1 minute. If the LAS after 3 minutes and the administration of methergin remains less than 6 after the administration of methergin, 1000 µg of prostaglandin (PGF2α) can be given rectally.

Post partum, patients were followed up for 6 hours and after 24 hours after cesarean section for any signs of uterine atony or bleeding.

Statistical analysis of the research data was tested by normalizing the data. The results of the study were considered significant if $p < 0.05$. Data were analyzed using SPSS for windows no 22.

Table 1. Characteristics of Research Subjects

Characteristics	Group		Score p
	Bolus	Infusion	
Age (Year), n (%)			
• > 30 Year	8 (36,4%)	9 (40,9%)	1,000*
• ≤ 30 Year	14 (63,6%)	13 (59,1%)	
Gestational age (week), n (%)			
• > 38 week	15 (68,2%)	14 (63,6%)	1,000*
• ≤ 38 week	7 (31,8%)	8 (36,4%)	
Parity, n (%)			
• > 2	17 (77,3%)	11 (50%)	0,147*
• ≤ 2	5 (22,7%)	11 (50%)	
Height (cm)	153,9±4,05	153,9±3,78	0,689**
Weight (kg)	60,60±11,34	61,36±12,76	1,000**
IMT (kg/m²)	25,21±3,59	25,54±4,33	0,785***
Systolic Blood Pressure (mmHg)	122,1±17,98	126,5±10,80	0,325***
Diastolic Blood Pressure (mmHg)	75,23±9,63	77,18±6,77	0,114**
Average Arterial Pressure (mmHg)	89,53±12,59	93,62±7,19	0,195***

Pulse rate (x/ minute)	85,14±14,29	88,18±14,42	0,486***
Breath rate	21,20±2,45	21,68±2,10	0,289**
SpO_2	99±0	99±0	-
Hemoglobin levels (g/dl)	10,13±1,16	10,21±1,51	0,841***

*** X2 test**

**** Mann_Whitney test, ¬p = 0.05**

***** Unpaired T test, p = 0.05**

3. Research result

General Characteristics of Research Subjects

The characteristics of the research subjects are shown in table 4.1. Based on the proportion of age groups given slow bolus oxytocin intervention of 5 IU, it shows that 8 people aged> 30 years (36.4%) and ≤ 30 years old are 14 people (63.6%) while those given oxytocin infusion of 20 IU shows that age> 30 years amounted to 9 people (40.9%) and aged ≤ 30 years amounted to 13 people (59.1%). With the Chi Square test, the value of p = 1,000 (p> 0.005) was obtained, which means that there was no significant difference in age groups between the two groups.

Most of the gestational age in the slow bolus oxytocin group of 5 IU and oxytocin infusion of 20 IU was> 38 weeks, respectively 15 people (68.2%) and 14 people (63.6%). With the Chi Square test, the value of p = 1,000 (p> 0.005) was obtained, which means that there was no significant difference in gestational age between the two groups.

The highest parity of both the 5 IU slow bolus oxytocin group and the 20 IU infusion of oxytocin was> 2, where each parity> 2 was 17 people (77.3%) and 11 people (50%). With the Chi Square test, the p value was obtained = 0.147 (p> 0.005), which means that there was no significant difference in parity between the two groups.

The mean ± SD height of the 5 IU slow bolus oxytocin group was 153.9 ± 4.05, while the 20 IU infusion oxytocin group was 153.9 ± 3.78. Because the data distribution was not normal (p = 0.017), the Mann Whitney test was used to compare the two groups. With the Mann Whitney test, the p value was obtained = 0.689 (p> 0.005), which means that there was no significant difference in height between the two groups.

The mean ± SD body mass index of the 5 IU slow bolus oxytocin group was 25.21 ± 3.59, while the 20 IU infusion oxytocin group was 25.54 ± 4.33. Because the data distribution was normal (p = 0.071), unpaired T test was used to compare the two groups. With the unpaired T test, the value of p = 0.785 (p> 0.005) was obtained, which means that there was no significant difference in body mass index between the two groups.

The mean ± SD systolic blood pressure of the 5 IU slow bolus oxytocin group was 122.1 ± 17.98, while the 20 IU infusion oxytocin group was 126.5 ± 10.80. Because the data distribution was normal (p = 0.127), unpaired T test was used to compare the two groups. With the unpaired T test, the value of p = 0.325 (p> 0.005) was obtained, which means that there was no significant difference in systolic blood pressure between the two groups.

The mean ± SD diastolic blood pressure of the 5 IU slow bolus oxytocin group was 75.23 ± 9.63, while the 20 IU infusion oxytocin group was 77.18 ± 6.77. Because the data distribution was not normal (p = 0.027), the Mann Whitney test was used to compare the two groups. With the Mann Whitney test, the p value was found to be 0.114 (p> 0.005), which means that there was no significant difference in diastolic blood pressure between the two groups.

The mean ± SD mean arterial pressure of the 5 IU slow bolus oxytocin group was 89.53 ± 12.59, while the 20 IU infusion oxytocin group was 93.62 ± 7.19. Because the data distribution was normal (p = 0.106), unpaired T test was used to compare the two groups. With the unpaired T test, the p value was 0.195 (p> 0.005), which means that there was no significant difference in mean arterial pressure between the two groups.

The mean ± SD pulse rate of the 5 IU slow bolus oxytocin group was 85.14 ± 14.29, while the 20 IU infusion oxytocin group was 88.18 ± 14.42. Because the data distribution was normal (p = 0.153), unpaired T test

was used to compare the two groups. With the unpaired T test, the p value was 0.486 (p> 0.005), which means that there was no significant difference in pulse rates between the two groups.

The mean ± SD breath rate of the 5 IU slow bolus oxytocin group was 21.20 ± 2.45 while the 20 IU infusion oxytocin group was 21.68 ± 2.10. Because the data distribution was not normal (p = 0.004), the Mann Whitney test was used to compare the two groups. With the Mann Whitney test, the p value was 0.289 (p> 0.005), which means that there was no significant difference in the respiratory rate between the two groups.

The mean ± SD hemoglobin level of the 5 IU slow bolus oxytocin group was 10.13 ± 1.16, while the 20 IU infusion oxytocin group was 10.21 ± 1.51. Because the data distribution was normal (p = 0.200), unpaired T test was used to compare the two groups. With the unpaired T test, the p value was 0.841 (p> 0.005), which means that there was no significant difference in hemoglobin levels between the two groups.

Hemodynamics and uterine contractions of bolus and infusion oxytocin groups before and after treatment

Hemodynamic variables (systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate, oxygen saturation) and uterine contractions were examined before and after oxytocin administration. With the Kolmogorov Smirnov normality test, the probability of each hemodynamic variable and uterine contraction was 0.200 (p> 0.05); 0.200 (p> 0.05); 0.200 (p> 0.05); 0.200 (p> 0.05); 0.014 (p <0.05); 0,000 (p <0.05) and 0.001 (p <0.05), while for the oxytocin infusion group the probability values were 0.200 (p> 0.05); 0.200 (p> 0.05); 0.061 (p> 0.05); 0.119 (p> 0.05); 0.000 (p <0.05); 0.000 (p <0.05) and 0.000 (p <0.05), which means that the data for systolic blood pressure, diastolic blood pressure, mean arterial pressure and pulse rate for both groups were normally distributed (p> 0.05), because the data distribution was normal. so that to see the difference in systolic blood pressure, diastolic blood pressure, mean arterial pressure and pulse rate before and after treatment, a paired T test was used, while the data on breath rate, oxygen saturation and uterine contraction of the two groups were not normally distributed (p <0.05). To see the difference in breath rate, oxygen saturation and uterine contraction before and after treatment, the Wilcoxon test was used.

Oxytocin Bolus 5 IU

Oxytocin Bolus 5 IU minutes 0 & 15 minutes

In the 5 IU bolus oxytocin group, systolic blood pressure increased by 0.91 mmHg (0.82%), diastolic blood pressure decreased 0.14 mmHg (0.21%), mean arterial pressure decreased 0.46 (0.57%), pulse rate decreased 7.23 x / minute (8.24%), respiratory rate decreased 0.19 x / minute (0.91%), oxygen saturation increased by 0.09% and contraction uterus increased by 3.36 (58.63%).

From the paired T test, it was found that there was no significant difference in systolic blood pressure, diastolic blood pressure, mean arterial pressure and pulse rate before and after 5 IU bolus oxytocin administration with probability values respectively 0.760 (p> 0.05), 0.958 (p> 0.05), 0.933 (p> 0.05) and 0.054 (p> 0.05).

In addition, the Wilcoxon test showed no significant difference (p> 0.05) in breath rate and oxygen saturation, but there were significant differences (p <0.05) in uterine contractions before and after 5 IU bolus oxytocin administration with probability values respectively. 0.874 (p> 0.05), 0.157 (p> 0.05) and 0.000 (p <0.05).

Table 2 Differences in hemodynamics and uterine contractions of the 5 IU 5 IU bolus oxytocin groups 0 and 15 minutes

Variable	5 IU slow bolus oxytocin		
	Minute -0	Minute -15	P
Systolic blood pressure	111,64±18,06	112,55±13,37	0,760*
Diastolic blood pressure	64,73±16,29	64,59±6,38	0,958*
Average arterial pressure	80,36±16,04	80,58±7,07	0,933*
Pulse rate	88,73±19,29	80,50±16,06	0,054*

Breath Rate	20,82±2,68	20,63±2,65	0,874**
SpO_2	99,09±0,53	99,18±0,39	0,157**
Uterine contractions	5,73±1,28	9,09±0,68	**0,000****

*** Paired T test, P = 0.05**

**** Wilcoxon test, P = 0.05**

In the 20 IU infusion of oxytocin group, systolic blood pressure decreased by 2.27 mmHg (1.91%), diastolic blood pressure decreased by 3.36 mmHg (4.7%), mean arterial pressure decreased by 3.91 (4.87%), pulse rate increased 0.23 x / minute (0.26%), breath rate increased 0.41 x / minute (1.93%), oxygen saturation increased by 0.09% and contraction uterus increased by 2.77 (46.87%).

The paired T test showed no significant difference in systolic blood pressure, diastolic blood pressure, mean arterial pressure and pulse rate before and after 20 IU of oxytocin infusion with probability values respectively 0.320 (p> 0.05), 0.097 (p> 0.05), 0.112 (p> 0.05) and 0.902 (p> 0.05).

In addition, the Wilcoxon test showed no significant difference (p> 0.05) in breath rate and oxygen saturation, but there were significant differences (p <0.05) in uterine contractions before and after 20 IU of oxytocin infusion with probability values respectively. 0.738 (p> 0.05), 0.157 (p> 0.05) and 0.000 (p <0.05).

Table 3 Differences in hemodynamics & uterine contractions of the 20 IU group of 20 IU infusion of oxytocin in the 0th minute and 15th minute

Variable	Oxytocin infusion of 20 IU		
	Minute -0	Minute -15	P
Systolic blood pressure	118,82±10,29	116,55±9,75	0,320*
Diastolic blood pressure	71,5±9,27	68,14±10,77	0,097*
Average arterial pressure	80,36±16,05	84,27±9,20	0,112*
Pulse rate	86,82±15,51	87,05±12,16	0,902*
Breath Rate	21,27±1,55	21,68±2,57	0,738**
SpO_2	98,91±0,43	99,0±0,31	0,157**
Uterine contractions	5,91±0,97	8,68±0,84	**0,000****

*** Paired T test, P = 0.05**

**** Wilcoxon test, P = 0.05**

Hemodynamic Characteristics and Uterine Contractions of the Infusion & Bolus Oxytocin Group

Systolic Blood Pressure

The systolic blood pressure of the two groups was checked at minutes 0, 3, 6, 9, 12 and 15 then performed a statistical test to see the difference between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes except for the 9th minute> 0.05 means that the data is normally distributed except at the 9th minute so that the statistical test used is the unpaired T test while for the 9th minute using the Mann-Whitney. From the statistical test, it was found that there was no difference in systolic blood pressure at 0, 3, 6, 9, 12 and 15 minutes between groups of 5 IU bolus oxytocin and 20 IU infusion of oxytocin (p. > 0.05).

Table 4 Systolic blood pressure (mmHg) of bolus and infusion oxytocin groups

Minutes to	Group		Score p
	Bolus	Infusion	
0	111,64±18,06	118,82±10,29	0,114*
3	111,59±15,56	116,18±9,25	0,242**
6	112,14±14,11	119,09±15,81	0,131*
9	104 (93-156)	118 (112-146)	0,378**
12	111,36±13,33	117,45±9,12	0,084*
15	112,55±13,37	116,55±9,75	0,263*

*** Unpaired T test, P = 0.05**

**** Mann-Whitney test, ¬p = 0.05**

Diastolic Blood Pressure

Diastolic blood pressure of both groups was checked at minutes 0, 3, 6, 9, 12 and 15 then performed a statistical test to see the difference between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes is obtained> 0.05, which means that the data is normally distributed, so the statistical test used is the unpaired T test. From the statistical test, it was found that there was no difference in diastolic blood pressure at 0, 3, 6, 9, 12 and 15 minutes between groups of 5 IU bolus oxytocin and 20 IU infusion of oxytocin (p. > 0.05).

Table 5 Diastolic blood pressure (mmHg) of bolus and infusion oxytocin groups

Minutes to	Group		Score p*
	Bolus	Infusion	
0	64,73±16,29	71,5±9,27	0,098
3	63,36±13,15	67,23±11,01	0,297
6	64,77±10,59	67,77±11,82	0,380
9	63,82±8,75	67,32±9,99	0,223
12	62,64±8,46	69,14±10,50	0,059
15	64,59±6,38	68,14±10,77	0,191

*** Unpaired T test, P = 0.05**

Average Arterial Pressure

The mean arterial pressure of the two groups was checked at minutes 0, 3, 6, 9, 12 and 15 then performed a statistical test to see the difference between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes is obtained> 0.05, which means that the data is normally distributed, so the statistical test used is the unpaired T test. From the statistical test, it was found that there was no difference in mean arterial pressure at 0, 3, 6, 9, 12 and 15 minutes between groups of 5 IU bolus oxytocin and 20 IU infusion of oxytocin (p. > 0.05).

Table 6 Mean arterial pressure (mmHg) of bolus and infusion oxytocin groups

Minutes to	Group		Score p*
	Bolus	Infusion	
0	80,36±16,05	87,27±8,67	0,083
3	79,44±13,38	83,55±9,89	0,254
6	80,56±11,15	84,88±12,23	0,228
9	78,82±11,22	82,17±11,93	0,343
12	78,88±9,34	85,24±8,95	0,056
15	80,58±7,07	84,27±9,20	0,143

*** Unpaired T test, P = 0.05**

Pulse rate

The pulse rates of the two groups were checked at 0, 3, 6, 9, 12 and 15 minutes then a statistical test was performed to see the difference between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes is obtained> 0.05, which means that the data is normally distributed, so the statistical test used is the unpaired T test. From the statistical test, it was found that there was no difference in the pulse rate at 0, 3, 6, 9, 12 and 15 minutes between the 5 IU bolus of oxytocin and 20 IU infusion of oxytocin (p> 0.05).

Table 7 Pulse rate (x / minute) of bolus and infusion oxytocin groups

Minutes to	Group		Score p*
	Bolus	Infusion	
0	88,73±19,29	86,82±15,51	0,719
3	86,50±18,08	87,0±13,61	0,918
6	83,91±17,38	87,77±14,39	0,426
9	81,82±18,05	86,05±12,76	0,375
12	81,91±15,94	85,64±12,46	0,393
15	80,50±16,06	87,05±12,16	0,135

*** Unpaired T test, P = 0.05**

Breath Rate

The breath rates of the two groups were checked at 0, 3, 6, 9, 12 and 15 minutes then a statistical test was performed to see the difference between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes was obtained <0.05, which means that the data were not normally distributed, so the Mann-Whitney statistical test was used. From the statistical test, it was found that there was no difference in the respiratory rate at 0, 3, 6, 9, 12 and 15 minutes between groups of 5 IU bolus oxytocin and 20 IU infusion of oxytocin (p> 0, 05).

Table 8 Respiration rate (x / minute) of bolus and infusion oxytocin groups

Minutes to	Group		Score p*
	Bolus	Infusion	
0	21,5 (12-25)	22 (18-24)	0,495
3	21 (12-24)	22 (15-24)	0,291
6	21,5 (12-26)	22 (16-26)	0,865
9	21,5 (12-23)	21 (15-28)	0,905
12	20,5 (12-24)	22 (16-26)	0,550
15	20,5 (12-24)	22 (18-29)	0,097

***Uji Mann-Whitney, ¬p = 0,05**

Oxygen Saturation

Oxygen saturation of both groups was checked at 0, 3, 6, 9, 12 and 15 minutes then statistical tests were performed to see the difference between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes is obtained <0.05, which means that the data is not normally distributed, so the statistical test used is the Mann-Whitney test. From the statistical test, it was found that there was no difference in oxygen saturation at 0, 3, 6, 9, 12 and 15 minutes between groups of 5 IU bolus oxytocin and 20 IU infusion of oxytocin (p> 0.05).

Table 9 Oxygen saturation of bolus and infusion oxytocin groups

Minutes to	Group		Score p*
	Bolus	Infusion	
0	99 (98-100)	99 (98-100)	0,215
3	99 (98-100)	99 (98-100)	0,709
6	99 (99-100)	99 (97-100)	0,134
9	99 (99-100)	99 (98-100)	0,411
12	99 (99-100)	99 (98-100)	0,247
15	99 (99-100)	99 (98-100)	0,097

*** Mann-Whitney test, ¬p = 0.05**

Uterine contractions

The uterine contractions of the two groups were examined at 0, 3, 6, 9, 12 and 15 minutes then a statistical test was performed to see the difference

between the two groups. With the Kolmogorov-Smirnov normality test, the probability of all minutes is obtained <0.05, which means that the data is not normally distributed, so the statistical test used is the Mann-Whitney test. From the statistical test, it was found that there was no difference in uterine contractions at 0, 12 and 15 minutes between the 5 IU bolus of oxytocin and 20 IU of oxytocin infusion (p> 0.05) and there was a significant difference after oxytocin administration. bolus 5 IU and oxytocin infusion of 20 IU in the 3rd, 6th and 9th minutes, where uterine contractions after 5 IU bolus oxytocin administration were greater than the 20 IU infusion of oxytocin.

Table 10 Uterine Contraction (LAS) bolus and infusion oxytocin groups

Minutes to	Group		Score p*
	Bolus	Infusion	
0	5 (4-8)	6 (4-8)	0,598
3	8 (7-10)	7,5 (5-8)	**0,006**
6	8.5 (7-10)	8 (6-9)	**0,010**
9	9 (8-10)	8 (7-9)	**0,008**
12	9 (8-10)	8,5 (7-10)	0,058
15	9 (8-10)	9 (7-10)	0,083

*** Mann-Whitney test, ¬p = 0.05**

Side effects

The incidence of hypotension (systolic blood pressure <90 mmHg or a decrease in blood pressure> 30% from baseline in the 5 IU slow bolus oxytocin group was 4 people (18%) and in the 20 IU infusion oxytocin group was 1 person (4.5%).

The average use of ephedrine in the 5 IU slow bolus oxytocin group was 12.5 ± 14.29, while the 20 IU infusion oxytocin group was 7.73 ± 19.50. Because the data distribution was not normal (p = 0.000), the Mann Whitney test was used to compare the two groups. With the Mann Whitney test, the p value was 0.053 (p> 0.005), which means that there was no significant difference in the use of ephedrine between the two groups.

Table 11. Ephedrine (mg) use in the study group

Characteristics	Group		Score p
	Bolus	Infusion	
Use of Ephedrine (mg)	12,5±14,29	7,73±19,50	0,053**

**** Uji Mann_Whitney, ¬p = 0,05**

Other side effects such as nausea, vomiting, headache, and flushing were not found in all samples, both in the 5 IU slow bolus oxytocin group and the 20 IU infusion oxytocin group.

Post partum, patients were followed up for 6 hours and after 24 hours after cesarean section for any signs of uterine atony or bleeding. None of the samples in each of the study groups experienced uterine atony or post partum hemorrhage.

4. Discussion

The demographic characteristics of research subjects were examined statistically, in this study the results showed that there were no differences in age group (p = 1,000), gestational age (p = 1,000), parity (p = 0.147), height (p = 0.689), body weight (p = 1,000) and body mass index (p = 0.785) between the two groups significantly. This confirms that the hemodynamic differences and uterine contractions between the two groups after the intervention were not influenced by demographic characteristics.

From the results of the statistical test for

hemodynamic characteristics, there was also no difference in systolic blood pressure (p = 0.325), diastolic blood pressure (p = 0.141), mean arterial pressure (p = 0.195), pulse rate (p = 0.486) and respiratory rate (p. = 0.289) between the two groups significantly. So that research can be continued with the provision of interventions.

The mean systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse rate, breath rate and oxygen saturation of both groups were checked at 0, 3, 6, 9, 12 and 15 minutes. From the statistical test, it was found that there was no difference in systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse rate, breath rate and oxygen saturation at minutes 0, 3, 6, 9, 12 and 15th group between the 5 IU bolus of oxytocin and 20 IU of oxytocin infusion (p> 0.05). In addition, the results also showed that there was no difference in systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate and oxygen saturation before and after bolus oxytocin intervention. This means that bolus administration of oxytocin does not change the effect on hemodynamics. However, there are differences in diastolic blood pressure, and mean arterial pressure at 3, 9 minutes, and differences in diastolic pressure at 6 minutes. This means that close monitoring should be done at the 3rd, 6th, and 9th minutes of infusion of oxytocin because it can reduce hemodynamics.

Side effects of oxytocin are caused by the effects of ADH, so that water intoxication can occur. After oxytocin administration, mean blood pressure decreased by 30%, peripheral resistance decreased by 50%, pulse rate increased by 30% and cardiac output increased by 50%. These events can lead to hypotension and tachycardia. Bolus doses of oxytocin induce hypotension due to peripheral vasodilation effects. Oxytocin 0.1 IU / kgBW intravenously in first trimester pregnant women, causing increased heart rate, decreased mean arterial pressure 30%, and decreased systemic vascular resistance by 50%. A 5 IU or 10 IU oxytocin bolus increases pulmonary artery pressure in pregnant women. Electrocardiographic changes (ECG) may also occur during oxytocin administration.27-31 However, in the study these side effects did not occur in either the 5 IU bolus ostosin group or the 20 IU infusion. This may be due to the bolus dose of oxytocin given is 5 IU because the administration of bolus oxytocin which can have an effect on blood pressure is when the dose given exceeds 10 IU where the rapid bolus injection can cause hypotension, tachycardia, myocardial arrhythmias, myocardial ischemia, coronary spasm, cardiac arrest and headache and confusion.[27-31]

Apart from hemodynamic characteristics, uterine contractions of the two groups were also examined at 0, 3, 6, 9, 12 and 15 minutes. From the statistical test, it was found that there were differences in uterine contractions before and after the intervention of bolus and infusion oxytocin, where uterine contractions increased significantly.

The results of this study are consistent with several guidelines and studies that support slow intravenous bolus of oxytocin 5 IU. Among them, the Royal College of Obstetricians and Gynecologists (RCOG) Guideline on Caesarean section recommends giving a slow intravenous 5 IU bolus dose of oxytocin after the birth of the baby. This dose is a lower dose than previously used, which is 10-20 IU and is based on concerns about the side effects of oxytocin, such as maternal hypotension.[12]

The British National Formulary also recommends that oxytocin should be given in a dose of 5 IU by slow intravenous injection after delivery in cesarean section. Research by Jonsson et al, in 2009 also showed that the hemodynamic response (decreased MAP) was more stable in the 5 IU oxytocin group compared to 10 IU oxytocin.[13,14]

Oxytocin is a hormone used to help initiate labor or during labor and to control bleeding after childbirth. Oxytocin stimulates uterine smooth muscle, producing rhythmic contractions, especially towards the end of pregnancy, during labor, after labor and the puerperium, when the number of specific oxytocin receptors in the myometrium increases.

Oxytocin has a strong uterotonic effect by increasing the frequency, amplitude and duration of uterine contractions. Oxytocin binds to G-protein on the surface of uterine myocytes, resulting in the generation of 1,2-diacylglycerol and 1,4,5-triphosphate (IP3) inositol through the action of phospholipase C. IP3 triggers the

release of Ca2 + from the sarcoplasmic reticulum. Oxytocin also increases intracellular Ca2 + entry via L-type Ca2 + channels and decreases Ca2 + depletion. Calcium ions bind to calmodulin and activate myosin light chain kinase, which is the core mechanism of uterine smooth muscle contraction. Myometrial oxytocin receptor concentrations increase with increasing pregnancy, and oxytocin has been shown to increase its action potential in pregnant human myometrial tissue with varying degrees of oxytocin sensitivity.[27-30]

The dose of oxytocin is 5 units given a slow bolus or 20-40 IU / 1000 ml of intravenous fluid infused up to 200 ml / hour. In this study, the results showed that there were differences in uterine contractions at 3, 6 and 9 minutes between the two groups, where uterine contractions after 5 IU bolus oxytocin were greater than the 20 IU infusion of oxytocin, where the increase in uterine contractions before and after the intervention in the 5 IU bolus group, respectively 40.3%, 47.64%, 53.9%, 56.4%, and 58.63% at minutes 3, 6, 9, 12th, and 15th while in the 20 IU infusion group 23%, 31.47%, 39.9%, 44.5%, and 46.87% respectively in the 3rd, 3rd minute. 6, 9th, 12th, and 15th. This may be because when given via bolus, oxytocin acts rapidly with a latency period of less than 1 minute. Meanwhile, if oxytocin is given by continuous IV infusion, the uterine response occurs gradually and usually reaches a steady state within 20-40 minutes.[27-30]

The results of this study are also in line with a study conducted by King et al., In 2010, who reported that administration of 5 IU IV bolus of oxytocin for 30 seconds followed by 40 IU of oxytocin in 500 ml of normal saline resulted in stronger uterine contractions than normal administration. 30 s of IV saline followed by 40 IU of oxytocin in 500 ml of normal saline.[15]

A study by Sartain et al., In 2008, which studied 80 patients undergoing cesarean section with a combination of spinal-epidural anesthesia who received 5 IU bolus oxytocin also revealed good uterine tone and at least (17.5%) demand for additional uterotonic drugs.[11]

Finally, a study in South Korea in 2011 by Kim, et al also revealed that 5 IU bolus of oxytocin followed by a continuous infusion of oxytocin resulted in stronger uterine contractions compared to only continuous infusion of oxytocin.[16]

The incidence of hypotension (systolic blood pressure <90 mmHg or a decrease in blood pressure> 30% from baseline in the 5 IU slow bolus oxytocin group was 4 people (18%) and in the 20 IU infusion oxytocin group was 1 person (4.5%).

The average use of ephedrine in the 5 IU slow bolus oxytocin group was 12.5 ± 14.29, while the 20 IU infusion oxytocin group was 7.73 ± 19.50. With the Mann Whitney test, the p value was 0.053 (p> 0.005), which means that there was no statistically significant difference in the use of ephedrine between the two groups significantly.

In spinal anesthesia, sympathetic block causes a drop in blood pressure as a result of decreased systemic vascular resistance and cardiac output, the latter due to reduced venous return and decreased heart rate. To overcome this, and if there is significant hypotension (BP decreased by> 30% from baseline), then given ephedrine starting from a dose of 5 mg IV. Ephedrine is a non-specific adrenergic agonist and increases blood pressure primarily by increasing cardiac output through stimulation of β-1 receptors by vasoconstriction. In this study, the administration of ephedrine was not significant in both groups, as evidenced by a p value of more than 0.05.

Other side effects such as nausea, vomiting, headache, and flushing were not found in all samples, both in the 5 IU slow bolus oxytocin group and the 20 IU infusion oxytocin group.

Post partum, patients were followed up for 6 hours and after 24 hours after cesarean section for any signs of uterine atony or bleeding. None of the samples in each of the study groups experienced uterine atony or post partum hemorrhage. Conclusions

5. Conclusions

There were no significant hemodynamic changes after 5 IU slow bolus oxytocin administration, and there were changes in diastolic blood pressure, and mean arterial pressure at 3, 9 minutes, and changes in diastolic pressure at 6 minutes in the 20 IU infusion of oxytocin group. . There was a significant change in uterine contractions after 5 IU slow bolus oxytocin and 20 IU infusion of oxytocin. There was no significant

hemodynamic difference between 5 IU slow bolus oxytocin and 20 IU infusion of oxytocin. There was a significant difference in uterine contractions at 3, 6 and 9 minutes between 5 IU slow bolus oxytocin and 20 IU infusion of oxytocin.

6. References

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