Evidence tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Biradar, 2021

Bibliographic Reference	Biradar, Aruna M.; Yaliwal, Rajasri G.; Kori, Shreedevi S.; Mathapati, Sangamesh S.; Shiragur, Shobha S.; Mudanur, Subhashchandra R.; Randomised control trial of 3 iu intravenous oxytocin bolus with 7 iu oxytocin infusion versus 10 iu intramuscular oxytocin in the third stage of labour in the prevention of postpartum hemorrhage; International Journal of Women's Health and Reproduction Sciences; 2021; vol. 9 (no. 3); 171-175

Study details

Country/ies where study was carried out	India
Study type	Randomised controlled trial (RCT)
Study dates	25th February - 25th May 2020
Inclusion criteria	women with singleton pregnancy gestational age 37-42 weeks vaginal delivery
Exclusion criteria	history of uterine surgery (c-section, myomectomy) severe diseases: anemia; coagulopathies; associated cardiac, hepatic and renal diseases known conditions predisposing to atonic PPH: hydramnios; multiple gestations; severe pre-clampsia; eclampsia women undergoing vacuum delivery via forceps cervical lacerations

Patient characteristics	No differences at baseline Proportion of women receiving oxytocin in 1st stage of labour not reported
Intervention(s)/control	Group 1 (n= 160): received 3 IU IV oxytocin bolus and 7 IU oxytocin IV infusion Group 2 (n= 160): received 10 IU IM oxytocin
Duration of follow-up	60 min
Sources of funding	n/a
Sample size	N= 320 women randomised Group 1: n= 160 (included in analysis) Group 2: n= 160 (included in analysis)
Other information	

Outcomes

Outcome	**Group 1 , , N = 160**	**Group 2, , N = 160**
Additional Uterotonics (n (%)) No of events	n = 0	n = 3

Critical appraisal

Section	**Question**	**Answer**
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Allocation was random. No information on allocation*

Section	Question	Answer
		concealment, but no differences in baseline characteristics to suggest a concern.)
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Carers administering intervention and participants not blinded, but no evidence that assignment to intervention affected implementation. No evidence that ITT protocol not followed.)*
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Low *(Carers administering intervention and participants not blinded, but low risk of bias due to non-adherence as intervention administered once.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(No evidence of missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Low risk of bias for the objective outcome 'need for additional uterotonics' (assumed to be determined by blood loss).)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(A pre-specified protocol was not available to determine selective reporting bias)*
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	Not applicable

Oladapo, 2020

Bibliographic Reference	Oladapo, Olufemi T.; Okusanya, Babasola O.; Abalos, Edgardo; Gallos, Ioannis D.; Papadopoulou, Argyro; Intravenous versus intramuscular prophylactic oxytocin for reducing blood loss in the third stage of labour; Cochrane Database of Systematic Reviews; 2020; vol. 2020 (no. 12); cd009332

Study details

Country/ies where study was carried out	Ireland, Egypt, Turkey, Argentina, Mexico, Thailand,
Study type	Cochrane systematic review of randomised controlled trials (RCT)
Study dates	Adnan 2018 January 2016 - December 2017 Charles 2019 April 2014 - September 2015 Dagdeviren 2016 February 2014 - March 2015 Durocher 2019 December 2016 - September 2017 Neri-Mejia 2016 August 2015 - December 2015 Oguz 2014 January 2010 - October 2010 Sangkhomkhamhang 2015 February 2012 - June 2012

Inclusion criteria	Women with planned vaginal birth regardless of other aspects of third stage management Study specific inclusion criteria: Adnan 2018 • 18+ years • Singleton term pregnancy (>37 weeks) • Aiming for a vaginal birth Charles 2019 • No pre-delivery oxytocin (for induction or augmentation of labour) • Live vaginal birth • Dagdeviren 2016 • 18-45 years • Singleton term pregnancy (37-42 weeks) • Cephalic presentation, • Normal blood pressure (< 140/90 mmHg) • Intending to have vaginal birth Durocher 2019 • Active labour with a live fetus • Vaginal delivery Neri-Mejia 2016 • Singleton term pregnancy • Cephalic presentation • No evident cephalopelvic disproportion • Spontaneous labour • Induced onset of labour • Vaginal delivery

	• Provided written informed consent • Haemoglobin measured during labour Oguz 2014 • Singleton pregnancy > 37 weeks • cephalic presentation • In active phase of labour • Normal vaginal birth Sangkhomkhamhang 2015 • Singleton pregnancy • Attending hospital for a vaginal birth
Exclusion criteria	Not specified Study specific exclusion criteria: Adnan 2018 • Women at an increased risk of PPH • Women whose caregiver had pre-decided to administer an additional oxytocin infusion • Women with a history of atonic PPH, fibroids and coagulopathy • Women receiving anticoagulant treatment • Women with thrombocytopenia. • Women with pre-existing cardiovascular disease, • Women who did not understand English Charles 2019 • Women who received pre-delivery oxytocin • Women who had a caesarean section • Women who could not provide written informed consent Dagdeviren 2016

	• Grand multiparity (not clearly defined, parity ranged from 1-6 in women recruited) • Hb < 7 g/dL • Prolonged 1st stage of labour • Induction (oxytocin for ≥12hours), • Previous caesarean birth or uterine surgery • Uterine myoma or serious obstetric or other comorbidity • Previous PPH • History of coagulopathies and anticoagulant treatment around the time of delivery • Haemorrhage during current pregnancy, • History of placental abruption, macrosomia or polyhydramnios. Durocher 2019 • Women who had a caesarean delivery • Women who could not provide informed consent. Neri-Mejia 2016 • Not clearly specified Oguz 2014 • Fetal death • Multiple pregnancy • Coagulation disorder • Placental pathology • Liver disease • Thrombocytopenia • Hypertension or taking anticoagulants • Caesarean or operative birth • Deep vaginal tear • Chorioamnionitis • HELLP syndrome • Disseminated intravascular coagulation before delivery

	Sangkhomkhamhang 2015 • Women with obstetric complications or medical problems. • Women with a history of curettage, manual removal of the placenta, cardiovascular instability or oxytocin hypersensitivity

Patient characteristics	Adnan 2018
	no differences at baseline
	Charles 2019
	• Episiotomy, n (%)
	  ○ IV infusion group: 930 (44.1)
	  ○ IV bolus injection group: 312 (44.5)
	  ○ IM injection group: 826 39.3
	  ▪ P-value =0.002
	Dagdeviren 2016
	no differences at baseline
	• Augmentation with oxytocin, n (%)
	  ○ IV infusion group: 28 (21.9)
	  ○ IM injection group: 18 (14.1)
	  ▪ P-value= 0.104
	Durocher 2019
	• Labour induced with uterotonics, n (%):
	  ○ IV infusion group: 16 (6.7)
	  ○ IM injection group: 25 (10.4)
	• Labour augmented with uterotonics, n (%)
	  ○ IV infusion group: 40 (16.7)
	  ○ IM injection group: 27 (11.2)
	Neri-Mejia 2016

	no differences at baseline
	
	Oguz 2014
	
	• Augmentation of labour, n (%)
	  ○ IV bolus injection group: 140 (46.7)
	  ○ IM injection group: 107 (35.7)
	
	Sangkhomkhamhang 2015
	
	no differences at baseline
	
	• Proportion of women receiving oxytocin in 1st stage of labour not reported

Intervention(s)/control	Adnan 2018 Intervention: IV oxytocin 10 IU in 1 mL over 1 minute and 1 mL 0.9% normal saline as placebo intramuscularly immediately after the delivery of the baby Control: IM oxytocin 10 IU in 1 mL and 1 mL 0.9% normal saline as placebo intravenously over 1 minute immediately after the delivery of the baby Charles 2019 Intervention group 1: IV oxytocin 10 IU in 500 mL saline through gravity-driven infusion with the roller clamp fully open after the delivery of the baby Intervention group 2: IV oxytocin 10 IU oxytocin over 1 minute after the delivery of the baby Control: IM oxytocin 10 IU after the delivery of the baby Dagdeviren 2016 Intervention: IV oxytocin 10 IU in 1000 mL saline at a rate of 1 mL/minute after delivery of the anterior shoulder Control: IM oxytocin 10 IU after delivery of the anterior shoulder Durocher 2019

	Intervention: IV oxytocin 10 IU in 500 mL saline solution at a rate of 12 mL/minute and 1 ampoule intramuscularly immediately after delivery of the baby Control: IM oxytocin 10 IU and 1 ampoule in 500 mL saline solution as placebo intravenously at a rate of 12 mL/minute immediately after the delivery of the baby Neri-Mejia 2016 Intervention group 1: IV oxytocin 10 IU over 1 minute after the delivery of the anterior shoulder Intervention group 2: IV oxytocin 20 IU in 1000 mL 5% glucose solution at a rate of 150 mL/hour after the delivery of the placenta (group not eligible for inclusion in this review) Control group: IM oxytocin 10 IU after the delivery of the anterior shoulder. Oguz 2014 Intervention group 1: 10 IU IV oxytocin at 1 mL/minute, this was given after delivery of the baby and cord clamping, Intervention group 2: 10 IU IV oxytocin at 1 mL/minute, this was given at the point of delivery of the anterior shoulder. Control group 1: 10 IU IM oxytocin, this was given after delivery of the baby and cord clamping Control group 2: 10 IU IM oxytocin, this was given at the point of delivery of the anterior shoulder. Sangkhomkhamhang 2015 Intervention: IV 10 IU of oxytocin in 10 mL normal saline administered over 2 minute after delivery of the anterior shoulder Control: IM 10 IU of oxytocin after delivery of the anterior shoulder
Duration of follow-up	N/A
Sources of funding	Adnan 2018 Trinity College, University of Dublin

	Coombe Women and Infants University Hospital Charles 2019 The Bill & Melinda Gates Foundation Dagdeviren 2016 Source of funding not reported Durocher 2019 The Bill & Melinda Gates Foundation Neri-Mejia 2016 Source of funding not reported Oguz 2014 Source of funding not reported Sangkhomkhamhang 2015 Source of funding not reported
Sample size	Adnan 2018 N= 1075 randomised IV bolus oxytocin n= 517 IM oxytocin n= 518 Charles 2019 N= 4913 randomised IV infusion oxytocin 10 IU in 500 mL saline n= 2108 IV bolus oxytocin 10 IU oxytocin over 1 minute n= 701

	IM oxytocin n= 2104 Dagdeviren 2016 N= 256 randomised IV oxytocin n=128 IM oxytocin n=128 Durocher 2019 N= 480 randomised IV infusion oxytocin n= 239 IM oxytocin n= 241 Neri-Mejia 2016 N= 66 randomised (23 excluded from the review) IV bolus oxytocin n= 23 IM oxytocin n= 22 Oguz 2014 N= 600 randomised IV bolus oxytocin after the delivery of the baby n= 150 IV bolus oxytocin at the point of delivery of the anterior shoulder n=150 IM oxytocin after the delivery of the baby n= 150 IM oxytocin at the point of delivery of the anterior shoulder n=150 Sangkhomkhamhang 2015 N= 450 randomised

	IV bolus oxytocin n= 225 IM oxytocin n=225
Other information	Setting: Adnan 2018 University affiliated maternity unit Charles 2019 1 teaching hospital and 1 university hospital Dagdeviren 2016 Teaching hospital Durocher 2019 Tertiary- level hospital Neri-Mejia 2016 Regional Hospital Oguz 2014 Teaching hospital Sangkhomkhamhang 2015 Hospital

Outcomes

Adnan 2018

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 517	Intramuscular oxytocin during third stage of labour, , N = 518	Intravenous oxytocin infusion during third stage of labour, , N =
Side effects after oxytocin Nausea, vomiting, hypotension, tachycardia, headaches, shivering No of events	n = 21	n = 27	*N/A*
Primary PPH (≥ 500 mL) No of events	n = 97	n = 120	*N/A*
Severe PPH (≥ 1000 mL) No of events	n = 24	n = 42	*N/A*
Need for additional uterotonics No of events	n = 128	n = 140	*N/A*
Admission to a high dependency unit No of events	n = 9	n = 19	*N/A*

Charles 2019

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 701	Intramuscular oxytocin during third stage of labour, , N = 2104	Intravenous oxytocin infusion during third stage of labour, , N = 2108
Primary PPH No of events	n = 5	n = 21	n = 11

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 701	Intramuscular oxytocin during third stage of labour, , N = 2104	Intravenous oxytocin infusion during third stage of labour, , N = 2108
Severe PPH No of events	n = 1	n = 9	n = 4
Need for manual placenta removal No of events	n = 9	n = 60	n = 50
Need for additional uterotonics No of events	n = 7	n = 23	n = 13

Dagdeviren 2016

Outcome	Intravenous oxytocin bolus during third stage of labour, , N =	Intramuscular oxytocin during third stage of labour, , N = 128	Intravenous oxytocin infusion during third stage of labour, , N = 128
Primary PPH No of events	*N/A*	n = 15	n = 15
Severe PPH No of events	*N/A*	n = 0	n = 4
Need for manual removal of placenta No of events	*N/A*	n = 2	n = 2

Outcome	Intravenous oxytocin bolus during third stage of labour, , N =	Intramuscular oxytocin during third stage of labour, , N = 128	Intravenous oxytocin infusion during third stage of labour, , N = 128
Need for additional uterotonics No of events	*N/A*	n = 3	n = 12

Durocher 2019

Outcome	Intravenous oxytocin bolus during third stage of labour, , N =	Intramuscular oxytocin during third stage of labour, , N = 241	Intravenous oxytocin infusion during third stage of labour, , N = 239
Primary PPH Primary PPH No of events	*N/A*	n = 57	n = 49
Severe PPH Severe PPH No of events	*N/A*	n = 18	n = 14
Need for manual removal of placenta No of events	*N/A*	n = 3	n = 0
Need for additional utertonics No of events	*N/A*	n = 30	n = 13

Orguz Orhan 2014

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 300	Intramuscular oxytocin during third stage of labour, , N = 300	Intravenous oxytocin infusion during third stage of labour, , N =
Primary PPH (≥ 500 mL) Reported blood loss > 600 mL No of events	n = 12	n = 18	*N/A*
Need for additional uterotonics No of events	n = 6	n = 9	*N/A*
Retained placenta or manual removal of placenta No of events	n = 2	n = 2	*N/A*

Neri-Meija 2016

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 21	Intramuscular oxytocin during third stage of labour, , N = 22	Intravenous oxytocin infusion during third stage of labour, , N =
Need for additional uterotonics No of events	n = 0	n = 2	*N/A*
Retained placenta or manual removal of placenta No of events	n = 0	n = 0	*N/A*
Side effects Hypotension	n = 1	n = 0	*N/A*

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 21	Intramuscular oxytocin during third stage of labour, , N = 22	Intravenous oxytocin infusion during third stage of labour, , N =
No of events			

Sangkomkamhang 2015

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 225	Intramuscular oxytocin during third stage of labour, , N = 225	Intravenous oxytocin infusion during third stage of labour, , N =
PPH ≥ 500 mL PPH not clearly defined by authors (measured up to 24 hours postpartum) No of events	n = 5	n = 11	*N/A*

Critical Appraisal

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
Oladapo 2020	Total score: 13/16
Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool	
Adnan 2018	Random sequence generation: low Allocation concealment: low Incomplete outcome data: low Selective reporting: low Other bias: low Blinding of participants and personnel: low

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
	Blinding of outcome assessment: low
Charles 2019	Random sequence generation: low Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: low Other bias: some concerns Blinding of participants and personnel: high Blinding of outcome assessment: some concerns
Dagdeviren 2016	Random sequence generation: low Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: low Other bias: low Blinding of participants and personnel: high Blinding of outcome assessment: high
Durocher 2019	Random sequence generation: low Allocation concealment: low Incomplete outcome data: low Selective reporting: low

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
	Other bias: low Blinding of participants and personnel: low Blinding of outcome assessment: low
Neri- Mejia 2016	Random sequence generation: some concerns Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: some concerns Other bias: low Blinding of participants and personnel: some concerns Blinding of outcome assessment: some concerns
Oguz 2014	Random sequence generation: low Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: high Other bias: some concerns Blinding of participants and personnel: high Blinding of outcome assessment: some concerns
Sangkhomkhamhang 2015	Random sequence generation: some concerns Allocation concealment: some concerns

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
	Incomplete outcome data: low Selective reporting: low Other bias: low Blinding of participants and personnel: high Blinding of outcome assessment: high