The history and current state of our oxytocic agents

Dr Victoria Eley
Royal Brisbane and Women’s Hospital
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Summary

• 3 Classes all have a role

• Practice concerning oxytocin has evolved

• Ideal agent depend on practice setting and patient characteristics
• Prevention of PPH

• Treatment of PPH
Signal transduction of smooth muscle contraction (2)
• ergometrine and friends
• oxytocin and friends
• prostaglandins (several)

All increase intracellular calcium and cause myosin phosphorylation
Haemorrhage

• 4th leading cause of death 2003-2005

Swanston St from the Bridge, 1861 Oil on Canvas by Henry Burn
1863 Melbourne Lying-in hospital

- Irish, 44 years old
- Twelfth pregnancy
- Twins (8 pounds each)
- Long labour

McCalman J Sex and Suffering: Women’s Health and a Women’s Hospital Melbourne University Press, Melbourne, Victoria 1998

Figure 10: Australian maternal mortality 1875-1990.
Milestones in PPH management

- 1900
- 1930 Maternal mortality begins to fall
- 1932 Ergometrine isolated
- 1937 Oxytocin synthesised
- 1940 Active management of third stage
- 1940 Isolation of prostaglandins
- 1953
- 1960 Isolation of prostaglandins
- 2000

1929 First Blood transfusion service, Victoria
Ergot Alkaloids
Ergot alkaloids

• Claviceps purpurea

• “almost incessant action on the uterus”

• spurs = 500mcg
• 5HT receptors

• Dopamine receptors

• alpha receptor
Oxytocin

• Henry Dale 1909

• Du Vigneaud 1953
Oxytocin receptor

• G protein coupled receptor

• Desensitisation

• Down regulation
• ED 95% not found – very low and zero dose very effective

• suggest 0.5-3 units sufficient
but for failure to progress..

• ED 90 = 2.99 units

looking for the lowest dose...

- CVS effects
- headache, flushing, nausea and vomiting
- worse in hypovolaemia or CVS compromise
- ST depression dose-related

M. Jonsson, U. Hanson, C. Lidell, S. Nordén-Lindeberg ST depression at caesarean section and the relation to oxytocin dose. A randomised controlled trial. BJOG, 117 (2010), pp. 76–83
Original Article

Impact of dose-finding studies on administration of oxytocin during caesarean section in the UK

R. West, S. West, R. Simons and A. McGlennan

• UK survey

• 10 Units is gone

• 5.3% departments using < 5 units at elective
In Australia?

- Survey of obstetricians 2010 (Australia and NZ)
- N=686
- 67% 10 units
- 32% 5 units
- 0.3% 2-3 units


2% reported that the anaesthetist decided
Carbetocin 100mcg

• onset 2 mins

• duration 60 mins

• Accepted as at least equivalent to oxytocin 5 units plus infusion

Su LL et al Cochrane review 2012 Carbetocin for preventing post partum haemorrhage
Carbetocin

• Variation in studies

• International variation
Prostaglandins
Misoprostol

- Rectal or sublingual or PV
- probably later peak effect
- Does not need the fridge, or injecting apparatus
F2 alpha

• Pulmonary hypertension
• Bronchospasm
• VQ mismatch and hypoxemia
• Hyperthermia
• GIT effects
• Hypotension

5mg in 1ml
Dilute to 20ml
250mcg/ml
Maximum 3mg
*needle*
Prophylaxis for Vaginal Delivery

• Active versus expectant management

• Cochrane review

Prendiville WJP et al Active versus expectant management in the third stage of labour (A Cochrane Review) 2000
Active Management

• give an oxytocic

• early cord clamping

• controlled cord traction
• give an oxytocic

• early cord clamping

• controlled cord traction

Reduce neonatal iron stores
↑ IVH
↑ Transfusion

CCT little effect on PPH
(nb retained placenta)

Aflaifel N, Weeks D. Editorial Active management of the third stage BMJ 2012 345
Which uterotonic?

• ergometrine and friends

• oxytocin and friends

• prostaglandins (several)
• Syntometrine benefit over oxytocin?

( WHO recommendations for the prevention and treatment of postpartum haemorrhage: Evidence base WHO/RHR/12.29)

• Rectal misoprostol – less effective

• Carbetocin- not licensed

Boucher M et al. JOGC May 2004/ Leung SW et al BJOG 2006;113: 1459
Melbourne Lying-in hospital

- Irish, 44 years old
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Ultrasound
Risk assessment - IV
Active management of third stage
Blood transfusion
Rapid access to surgery

McCalman J Sex and Suffering: Women’s Health and a Women’s Hospital Melbourne University Press, Melbourne, Victoria 1998
Routine management

- Uterine compression
- Cold packs
- Breast-feeding
- Discharged day 6

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