DOSING GUIDELINES FOR THE OFF-LABEL USE OF DRUGS IN OBSTETRICS AND GYNAECOLOGY

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Obstetrics And Gynaecology
Therapeutic Drug Working Committee
MINISTRY OF HEALTH, MALAYSIA

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1. DOSING GUIDELINES FOR THE OFF-LABEL USE OF TOCOLYTIC AGENTS IN PRETERM LABOUR

1.1. Aim of tocolysis

i. To allow time for completion of antenatal steroid therapy
ii. In-utero transfer to another hospital for the benefit of the fetus (ventilator)

1.2. Contraindications of tocolysis

i. Chorioamnionitis
ii. Intrauterine death
iii. Fetal abnormality/fetal distress
iv. Maternal cardiac disease
v. Hyperthyroidism
vi. Advanced labour (os >5cm)
vii. Antepartum haemorrhage
viii. Hypertension
ix. Diabetes mellitus

} To discuss with specialist

1.3. Prerequisites for starting tocolysis

i. Normal viable fetus
ii. No maternal contradindications for labour suppression
iii. Normal maternal ECG
iv. Baseline random blood sugar level (RBS)
v. Baseline serum electrolytes (BUSE)
vi. CTG if gestation > 32 weeks

1.4. Tocolytic agent/regimen

1.4.1. Terbutaline Sulphate Infusion Regimen (Terbutaline Sulphate Injection 0.5mg/ml)

- Increase infusion every 15 minutes
- Maximum infusion rate 80 drops per minute (240ml/hr)

Terbutaline Dosage (mcg/min)	**Infusion syringe pump** 2.5mg (5ml) + 45ml Dextrose 5% or Normal Saline		**Dropmat** 2.5mg (5ml) + 500ml Dextrose 5% or Normal Saline	
	Drop per minute (dpm)	**ml/hr**	**Drop per minute (dpm)**	**ml/hr**
2.5	1	3	10	30
5	2	6	20	60
7.5	3	9	30	90
10	4	12	40	120

Terbutaline Dosage (mcg/min)	Infusion syringe pump 2.5mg (5ml) + 45ml Dextrose 5% or Normal Saline		Dropmat 2.5mg (5ml) + 500ml Dextrose 5% or Normal Saline	
	Drop per minute (dpm)	ml/hr	Drop per minute (dpm)	ml/hr
12.5	5	15	50	150
15	6	18	60	180
17.5	7	21	70	210
20	8	24	80	240

1.4.2. Salbutamol Infusion Regimen (Salbutamol Injection 5mg/5ml)

- At the rate of 10-45mcg/min increase at intervals of 10 minutes until evidence of patient response as shown by reduction of strength, frequency or duration of contractions: maintain rate for 1 hour after contractions stopped, then gradually reduce by 50% every 6 hours (Available in MOH Drug Formulary).

Salbutamol Dosage (mcg/min)	Infusion syringe pump 5mg (5ml) + 45ml Dextrose 5% or Normal Saline		Dropmat 5mg (5ml) + 500ml Dextrose 5% or Normal Saline	
	Drop per minute (dpm)	ml/hr	Drop per minute (dpm)	ml/hr
10	2	6	20	60
15	3	9	30	90
20	4	12	40	120
25	5	15	50	150
30	6	18	60	180
35	7	21	70	210
40	8	24	80	240
45	9	27	90	270

1.4.2.1.Monitoring for Beta-Agonist Infusion Regimen

- Maternal blood pressure every 10 minutes (Salbutamol) or 15 minutes (Terbutaline), inform doctor is $\leq$ 90/60mmHg
- Pulse rate (every 10-15 minutes), inform doctor is >120bpm
- Maternal temperature every 4 hourly
- Contraction every ½ hourly
- Auscultation of lungs every 4 hourly
- Continuous cardiac monitoring
- Random blood sugar.glucometer 4-6 hourly
- BUSE 4-6 hourly
- Fetal heart rate monitoring
- Input/Output charting

1.4.2.2.Complications

- Fetal tachycardia
- Palpitation
- Headache
- Maternal tachycardia
- Maternal Hypotension
- Maternal Pulmonary Edema
- Hypokalaemia
- Hyperglycaemia

1.4.2.3.Cessation of tocolysis

- Symptoms of intolerance (e.g palpitation, severe tremors, chest pain, vomiting, severe headache and restlessness)
- Maternal heart rate >120 bpm
- Maternal SBP <90mmHg or DBP <60mmHg
- Signs & Symptoms of pulmonary edema
- FHR > 160bpm
- Maternal Hypokalaemia
- Uterine contractions persist despite maximum infusion for 6-8 hours

1.4.3. Nifedipine 10mg Tablet

- Oral: 20mg given as a stat dose followed by another 20mg in 30 minutes if contractions persist (max 40mg in the first hour).
- Maintenance; Oral: 20mg 6-8 hourly, 6-8 hours of the last dose for 72 hours.

1.5. Maintenance treatment after threatened preterm labour

Maintenance tocolysis is not recommended for routine practice.

1.6. Care after tocolysis

i. Bed rest for 24-48 hours after infusion and discharged after 72 hours, if no contractions.
ii. Vital signs/FHR and uterine activity are done hourly for 6-12 hours
iii. If patient goes into labour, to discuss with neonatologist regarding possibility of delivery.

2. DOSING GUIDELINES FOR THE USE OF MISOPROSTOL 200MCG TABLET IN THE MANAGEMENT OF STABLE FIRST TRIMESTER MISCARRIAGES < 13 WEEKS

STABLE FIRST TRIMESTER MISCARRIAGE < 13 WEEKS
Missed Miscarriage Crown-rump Length (CRL) 5-40mm/
Anembryonic Pregnancy Gestational Sac (GS) 20-45mm

Surgical Evacuation
preferably on elective date

Non-Surgical Management
-Can be considered in patients:

1. Who are able to UNDERSTAND; as well as able and agreeable to COMPLY with instructions and follow-up;
2. Who have been COUNSELLED about
   -success/failure rate
   -risk of unplanned hospitalization and curettage
   -low risk of infection
   -lack of histology, and
3. Who have given INFORMED CONSENT

EXCLUSION CRITERIA
- bleedimg disorders/haemolytic disease/anemia Hb<9g/dl
-on anticoagulation/ systemic steroids
-multiple pregnancies
-smoker, >35 years of age
-severe asthmatics

MEDICAL (recommended for missed/anembryonic miscarriage)

-Rhogam if RhD negative

Day 1: Vaginal misoprostol 800mcg

Day 3: Repeat vaginal misoprostol 800mcg if incomplete/no expulsion

Day 8: Transvaginal Ultrasound (TVUS). If complete abortion, reassure and discharge wiyh follow up at 2 weeks. If incomplete or no expulsion, for Evacuation of Retained Products of Conception (ERPOC)

6 weeks: Urine Pregnancy test (UPT) if no resumption of normal menses

3. REFERENCES

i. Guidelines and Protocols, Department of Obstetrics and Gynaecology, Hospital Kuala Lumpur

ii. MIMS Malaysia

iii. MOH Drug Formulary 2014

iv. Zhang et al. A Comparison of Medical Management with Misoprostol and Surgical Management for Early Pregnancy Failure, NEJM, 2005, vol 353 no.8.

v. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College Statement C-Obs 12. The use of Misoprostol in Obstetrics and Gynaecology, Current: Nov 2010.