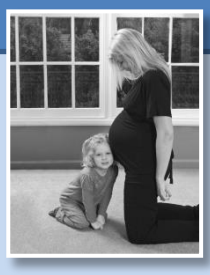
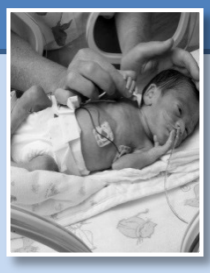
The ON TRACK Network

August 2016

Newsletter Edition 2



ON TRACK NETWORK
BETTER HEALTH FOR MOTHERS AND BABIES

What's In This Issue?

Welcome to the August edition of the On Track Network Newsletter! With winter well and truly upon us, we hope you can find a warm place to sit down and read about the latest happenings in maternal and perinatal health research.

ON TRACK NEWS

- Welcome to **Belinda Chapman** who has been appointed the Site Network Leader for Taranaki DHB! It's great to have you involved and we are looking forward to working with you and your colleagues in Taranaki.
- Plans are underway for an ON TRACK Network Website - Stay tuned for more!
- August has seen the GEMS study gain their 500th recruit! Congratulations to all those involved! Please contact the team at GEMs for any info on this trial- gems@auckland.ac.nz

MAGENTA Recruitment to date: 1237 babies- Only 439 babies remaining!

MAGENTA is one of the multicentre RCTs currently recruiting at 8 sites around NZ! We thought you might be interested to find out a bit more about it!

Keen to get involved with MAGENTA? Contact the team at contact the team at magenta@adelaide.edu.au

Congratulations to these sites already recruiting for MAGENTA: Auckland City, Middlemore, Tauranga, Whakatane, Wellington, Christchurch, Invercargill, Dunedin!

This Month's Feature Trial MAGENTA

Cerebral Palsy (CP) is one of the most frequent causes of severe motor disability in childhood, and babies born between 30 & 33 completed weeks' gestation are up to 8x more likely to have CP than babies born at term (Petrini & Dias et al., 2009). Magnesium Sulphate (MgSO4) for the neuroprotection of preterm infants is currently recommended for women at risk of preterm birth, less than 30 weeks' gestation, based on high quality evidence of benefit (AMSNGDP, 2010). There remains uncertainty as to whether these benefits apply at higher gestational ages. MAGENTA aims to assess whether giving MgSO4 (compared with placebo) to women immediately prior to preterm birth between 30 and 34 weeks' gestation, reduces the risk of death or CP in their children at two years' corrected age.

MAGENTA is a multicentre, double-blind, placebo-controlled randomised clinical trial.

Inclusion Criteria: Women at risk of preterm birth between 30-34 weeks' gestation, where birth is planned or definitely expected within 24 hours, with singleton or twin pregnancy and no contraindications to MgSO4.

Treatment Groups: Treatment group- 50mL of 100mL infusion bag containing 8g magnesium sulphate heptahydrate (16mmol magnesium ions). Placebo group - receive 50mL of 100mL infusion bag containing isotonic sodium chloride solution (0.9%). Both IV administrations over 30 minutes.

Primary Outcome: Death or CP measured at two years' corrected age. **Sample Size:** 1676 children are required to detect a decrease in combined outcome of death or CP from 9.6% with placebo to 5.4% with MgSO4.

Why MAGENTA? As discussed above, there are still some unanswered questions about the benefits of Magnesium Sulphate for neuroprotection at higher gestations. The magnitude of the protective effect in the systematic review, the ongoing uncertainty about benefits at later gestations & the serious health & cost consequences of CP, make this trial both important & relevant for practice globally.

Petrini, J. R., Dias, T. et al. (2009). Increased risk of adverse neurological development for late preterm infants. J Pediatrics 154(2): 169-176.The Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel (AMSNGDP, 2010). *Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus, infant and child: National clinical practice guidelines.* Adelaide: The University of Adelaide. https://www.adelaide.edu.au/arch/MagnesiumSulphate2010.pdf

ontracknetwork@auckland.ac.nz

The ON TRACK Network

See attached table for more details

Multicentre Clinical Trials Recruiting Now!

APTS | GEMS | hPOD | HINT2 | MAGENTA | MAGNUM | My Baby's Movements | PAEAN | PINTO | PROVIDE | STRIDER NZAus | TARGET

We thought you might be interested to read about the OPPTIMUM Study! While there are many studies related to progesterone and preterm birth, this is the largest trial, so it might be useful to consider when planning care for women who have had a previous baby born preterm or who have other risk factors.

Update Your Practice!

The OPPTIMUM Study

dOes Progesterone Prophylaxis To prevent preterm labour IMProve oUtcoMe?

This was a multicentre randomised double-blind placebo controlled trial to determine whether vaginal progesterone prophylaxis given to reduce the risk of preterm birth (PTB) affects neonatal and childhood outcomes.

Women were screened at 18-24 weeks and eligible if they had risk factors for PTB including- History of previous PTB or second trimester loss or PPROM or cervical procedure to treat cervical abnormality and a positive fFN at 22-24 weeks OR History of previous PTB <34 weeks or cervical length <25mm (regardless of prior history) and fFN negative at 22-24 weeks.

Intervention groups: Treatment commenced at 22-24 weeks and continued until 34 weeks or delivery, whichever occurred first. Treatment- 200mg vaginal progesterone capsules (Utrogestan) nocte. Control- Identical appearing placebo capsules.

Primary outcomes: Three primary outcomes were selected- 1. Fetal death or delivery <34+0 weeks (**obstetric outcome**) 2. Composite of death, bronchopulmonary dysplasia and brain injury on USS (**neonatal outcome**), 3. Bayley-III cognitive composite score at 22-26 months (**childhood outcome**)

Results: Women were screened (n=15132) and recruited (n= 1228) at 65 UK NHS hospitals and one Swedish hospital. Data was available in 97% for obstetric outcomes, 96% for neonatal outcomes and 71% for childhood outcomes.

Point estimate of the odds ratio was in the direction of benefit for progesterone use (although non-significant) for obstetric and neonatal outcomes but with no effect on childhood outcome at two years of age.

	Placebo group	Progesterone group	Unadjusted odds ratio (95% CI) or difference in means (95% CI)	p value (unadjusted)	Adjusted odds ratio (95% CI)* or difference in means (95% CI)	p value (adjusted*)
Fetal death or delivery <34 weeks of gestation	108/597 (18%)	96/600 (16%)	0·86 (0·64 to 1·17)	0·34	0·86 (0·61 to 1·22)	0·67
Neonatal morbidity or death	60/587 (10%)	39/589 (7%)	0·62 (0·41 to 0·94)	0·02	0·62 (0·38 to 1·03)	0·072
Cognitive composite score at 2 years†‡	97·7 (17·5)	97·3 (17·9)	−0·48 (−2·77 to 1·81)§	0·68	−0·48 (−2·77 to 1·81)§	0·68

Neonatal deaths were less common with progesterone use and the proportion with observed brain injury was lower (but with no resultant improvement in two year cognitive score). There was, however, a trend towards an increase in moderate/severe neurodevelopmental impairment at two years in those treated with progesterone 8.7% vs 12.4%. No significant interactions were seen in subgroup analysis for women with a positive fetal fibronectin or short cervix (i.e. it does not suggest the therapy was more or less effective in particular subgroups).

What does this mean? OPPTIMUM is the largest RCT of vaginal progesterone for the prevention of PTB in women at high risk. The direction of effect on obstetric & neonatal outcomes suggests some possible short term benefit which needs to be explored further in meta-analyses including other trials using the same preparations of progesterone. This is not seen to translate into demonstrable benefit on two year developmental outcomes and even a suggestion of possible harm (also needing further exploration). **At present, the results of the OPPTIMUM study do not support routinely using vaginal progesterone in women at high risk of PTB, however, may be considered as part of a shared decision making process between clinician and patient following discussion of the risks & benefits.**

Norman et al Lancet 2016 Feb 23. pii: S0140-6736(16)00350-0. doi: 10.1016/S0140-6736(16)00350-0

We're Coming To Your Place!

The OTN would like to hear more about you in our Feature Site! You'll hear from a different district each month about their service, research interests and top research tips! Our first Site will be Tauranga Hospital! Stay tuned to meet them in September!

Who's Your Site Network Leader?

Northland- David Bailey

Waitemata- Jutta van den Boom

Auckland- Melissa Brown

Middlemore- Michael Meyer

Waikato- Phil Weston

Tauranga- Chris Thurnell

Whakatane- Maggie Sadlier

Taranaki- Belinda Chapman

Rotorua- Anne Jaquiery

Gisborne- Sean Pocock

Whanganui- TBC

Palmerston North- TBC

Nelson- Flora Gastrell

Grey Base- Sherif Mehrez

Hastings- Kirsten Gaerty

Wellington- Max Berry

Christchurch- Nicola Austin

Timaru- TBC

Hutt Valley & Wairarapa- Chris Mallon

Dunedin- Pauline Dawson

Southland- Meggan Zsemlye

Have you thought about implementing research projects in your area but barriers in the way?

Perhaps you want to complete research of your own but don't know where to start?

Contact us at ontracknetwork@auckland.ac.nz and maybe we can help you!

ontracknetwork@auckland.ac.nz