SYSTEMATIC REVIEW PROTOCOL:

Interventions for the treatment of twin-twin transfusion syndrome

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Twin Pregnancies

Prevalence: 1.5-2%

• Zygosity
  – **Monozygotic**: splitting of single fertilized ovum
  – **Dizygotic**: fertilization and development from separate ovum
Monozygotic twins

- Monozygotic
  - 0-3 days:
    Dichorionic/
    Diamniotic (1/3)
  - 4-8 days:
    Monochorionic/ Diamniotic
  - 8-15 days:
    Monochorionic/ Monoamniotic (1%)
  - >15 days:
    Conjoined

March 28, 2006-Geneva
Chorionicity

- More important determinant of prognosis than zygosity

- Monozygotic, dichorionic prognosis similar to dizygotic, dichorionic
Complications of twin pregnancies

- Preterm Delivery
- Low Birth-weight
- Intrauterine Growth Restriction (IUGR)
- Preeclampsia
- Gestational Diabetes
- Placental Abruption
- Fetal Demise/Loss
- Cesarean rates
### Perinatal Outcome of Twin Pregnancies

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<thead>
<tr>
<th>Condition</th>
<th>DC</th>
<th>MC</th>
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<tbody>
<tr>
<td><strong>MISCARRIAGE</strong></td>
<td></td>
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<tr>
<td>12-24 wks</td>
<td>1.8%</td>
<td>12.2%</td>
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<thead>
<tr>
<th>Condition</th>
<th>DC</th>
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<tr>
<td><strong>PERINATAL DEATH</strong></td>
<td></td>
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<tr>
<td>&gt;24 wks</td>
<td>1.6%</td>
<td>2.8%</td>
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<tr>
<th>Condition</th>
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<tr>
<td><strong>GROWTH RESTRICTION</strong></td>
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<tr>
<td>Total fetuses</td>
<td>12%</td>
<td>21%</td>
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<th>Condition</th>
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<tr>
<td><strong>PRETERM DELIVERY</strong></td>
<td></td>
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<tr>
<td>Gestation &lt;32 wks</td>
<td>5.5%</td>
<td>9.2%</td>
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Monochorionic 20%
Dichorionic 80%
Problems associated with chorionicity

• Dichorionic:
  – Crowding problems

• Monochorionic:
  – Crowding:
    • talipes, congenital hip dislocation
  – Twinning:
    • conjoined twins, sirenomelia, NTD
  – Vascular exchange:
    • TTTS, acardia, embolization-microcephaly, limb amputation
Twin-Twin Transfusion Syndrome (TTTS)

• Unbalanced inter twin transfusions through placental anatomoses
  – Arterial- venous unidirectional anatomoses

• Donor twin
  – anemic, growth restricted
  – oligohydramnios, contractures, pulmonary hypoplasia

• Recipient twin
  – polycythemic, circulatory overload and hydrops
  – polyhydramnios, PPROM, heart failure
Twin-Twin Transfusion Syndrome – Diagnosis:

- Monochorionic pregnancy
- Acute 2nd trimester polyhydramnios
- Normal fetal anatomy
Twin-Twin Transfusion Syndrome

• Occurs in 10% to 15% of identical twins
  » Sebire 2000; Jain 2004

• The prognosis for both fetuses is extremely poor
  – mortality 60% - 100%
  – one third of survivors presenting with severe neurologic complications after birth
    » Ung 1990; Skupski 1998; Cincotta 2000; Berghella 2001; Mari 2001
Treatment options

• Repeated serial amnioreduction
• Endoscopic laser ablation of anastomoses
• Amniotic septostomy
• Selective feticide
Amnioreduction

- Reduces uterine distension & PTL
- Correct hemodynamic inequalities in intra-amniotic pressure
- May lead to better uteroplacental perfusion
- May reverse TTTS
  - 60% survival, 20% neurological morbidity

Endoscopic laser ablation of anastomoses

Survival 76%
periventricular leukomalacia 6%
Senat MV, 2004
Septostomy

- Equilibrates the fluid
- Donor can swallow some fluid
- TTTS rare in mono/mono twins
  - Survival rate 83%, but no figures for neurological outcome
    » (Saade, Belfort et al. 1998; Moise, Dorman et al. 2005).
  - Cord entanglement
    » (Gilbert, Davis et al. 1991).
Selective Feticide

• In the event of the death of one twin, approximately 25 to 50% of surviving twins will experience mortality or neurological handicap
  » van Heteren 1998

• Techniques such as fetoscopic cord ligation and ultrasound guided vascular embolisation have been described
  » Crombleholme 1996; Quintero 1996; Deprest 1998; Robyr 2005; Spadola 2005
Reason for this review

• The last systematic Cochrane review:
  – in 2001
  – found no evidence from randomized trials to influence practice

• There are some new studies
  Quintero 2003; Senat 2004; Moise 2005
Criteria for selecting studies for this review

• Types of studies:
  - Randomised controlled trials
  - Quasi-randomised trials
  - Randomised studies

Comparisons of one treatment versus another will be considered.
Criteria for selecting studies for this review

• Types of participants:
  
  – Twin-twin transfusion syndrome diagnosed by ultrasound before 26 weeks:

    • confirmation of monochorionicity
    • oligohydramnios in one sac and hydramnios in the other
    • normal anatomy of both fetuses
Types of interventions:

• Any intervention performed as a therapy for twin-twin transfusion syndrome to improve
  - fetal, neonatal and childhood outcome
  - maternal symptoms
  - and prolonging pregnancy

will be reviewed
Types of outcome measures:

• Primary outcomes:
  - overall fetal survival
  - perinatal death
  - neuro-motor disorders
    » intraventricular haemorrhage
    » ventriculomegaly
    » cystic periventricular leukomalacia
    » seizures within 28 days of delivery/anticonvulsant therapy
    » developmental delay at 2 years of age
Types of outcome measures:

• Secondary outcomes
  – Procedure related events
    » number of interventions per pregnancy
    » first intervention to delivery time
    » need for a combination of therapies
    » type of anaesthesia
  – Pregnancy outcome
    » gestational age at birth
    » preterm prelabour rupture of membranes (within 48 hours of procedure)
    » preterm labour (within 48 hours of procedure)
    » preterm labour/prelabour rupture of membranes prior to 32 weeks gestation.
    » Neonatal outcome
    » fetal haemoglobin discordance at birth
    » need for blood transfusion within 48 hours of delivery
    » use of mechanical ventilation
    » admitted to neonatal intensive care unit
    » length of stay on neonatal intensive care unit
  – Maternal outcome
    » maternal death
    » amniotic fluid embolism
    » placental abruption
    » chorioamnionitis
    » intraperitoneal bleeding
Search strategy for identification of studies:

• The electronic sources of medical databases

  - MEDLINE/Pubmed
  - BioMed Central
  - ScienceDirect
  - Scitation
  - Pubmed Central
  - Cochrane Controlled Trials Register

will be used to identify relevant trials
Search terms used will be:

- Twin twin
- Fetofetal Transfusion
- Twin AND twin OR (transfusion) AND ("transfusion syndrome")
- OR Amnioreduction
- OR Amniodrainage
- OR Septostomy
- OR Laser coagulation
- OR Laser ablation
- OR Fetoscopic laser ablation
Methods of the review:

- Not blind: author's name, institution and the source of publication will be known by reviewer.

- Trials will be assessed for methodological quality and appropriateness for inclusion without consideration of results.

- The reason for excluding any trial will be stated.

- Data extraction will be performed by the contact reviewer and processed as described by Clarke in Cochrane Reviewers' Handbook, 1999.

- Statistical analysis will be performed using the Review Manager software (RevMan 1999).

- Relative risks and 95% confidence intervals will be calculated.
Eligible studies


