South Thames Sickle Cell and Thalassaemia Network
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Adult Network Meeting 27 January 2012

Peri-operative Management of Sickle Cell Disease

How does practice change following the TAPS trial?

Does pre-operative transfusion in HbSS/Sβ⁰thal increase or decrease the overall incidence of significant peri-operative complications?

Trial Design

- Multicentre phase III RCT, unblinded to treatment
- Group sequential design: analysis every 40 patients
- Stratification: Age, surgery, history of complications

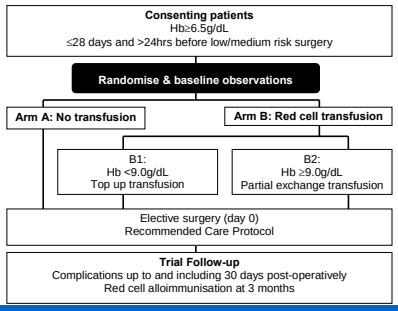
Primary Outcome

- Patients with clinically significant complications between randomisation and 30 days post surgery

Secondary Outcomes

- Complications included in primary outcome plus alloimmunisation at 3 months
- Total hospital days (pre and post-op) up to 30 days
- Number of RBC units (intra & post-op)
- Re-admission/failure to discharge by day 30

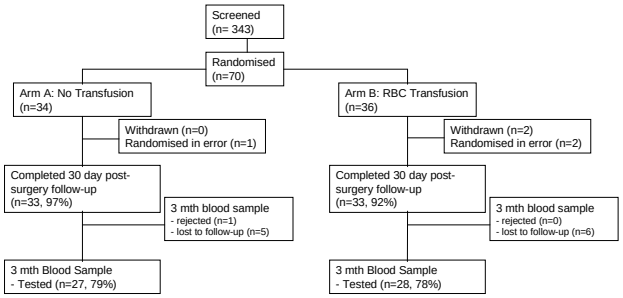
Trial methods



Trial progress

- Nov 2007: Trial opened
- Sep 2010: 1st interim analysis (n = 40)
  - An imbalance in patients with SAEs was noted
- Feb 2011: (n = 70 enrolled)
  - Imbalance in patients with SAEs more marked
  - IDMC request unscheduled interim analysis (n = 61)
  - No significant difference in primary outcome
  - Majority of SAEs were Acute Chest Syndrome
- March 2011: Trial closure

Consort diagram



Baseline Characteristics- Patients in ITT Analysis

	Arm A – No pre-operative blood transfusion	Arm B – Pre-operative blood transfusion	Overall
No. of Patients	**33**	**34**	**67**
Gender (N, %): Male	17 (51.5)	16 (47.1)	33 (49.3)
Sickle Diagnosis (N, %): HbSS	33 (100)	32 (94.1)	65 (97.0)
Age at Randomisation (Median, IQR)	13.3 (6.4-21.4)	15.1 (7.6-37.4)	13.4 (6.4-26.5)
History of sickle cell complications (N, %): Yes	10 (30.3)	15 (44.1)	25 (37.3)
Medium Risk Surgery (N, %)	28 (84.9)	26 (76.5)	54 (80.6)
-Abdominal	13 (39.4)	10 (29.4)	23 (34.3)
-ENT	9 (27.3)	7 (20.6)	16 (23.9)
-Orthopaedic	4 (12.1)	6 (17.7)	10 (14.9)
-Other	2 (6.1)	3 (8.8)	5 (7.5)
Low Risk Surgery (N, %)	5 (15.2)	8 (23.5)	13 (19.4)
Hb on Admission (Median, IQR)	7.7 (7.1-8.4)	8 (7.4-8.6)	7.9 (7.3-8.6)
Pre-op Hb (Median, IQR)	7.7 (7.1-8.2)	9.7 (9.1-10.5)	8.7 (7.5-9.7)

Primary Outcome and Serious Adverse Events (SAEs)

Trial Arm	Arm A – No Pre-operative blood transfusion	Arm B – Pre-operative blood transfusion	Overall
Patients Recruited	**33**	**34**	**67**
Patients with significant complications	13 (39.3%)	5 (14.7%)	18 (26.9%) OR 3.8 (CI 1.2-12.2) p 0.027
Patients with SAEs	10 (30.3%)	1 (2.9%)	11 (16.4%) 27.4% difference (CI 10.6-44.0) P 0.003
Patients with Acute Chest Syndrome	9 (27.3%)	1 (2.9%)	10 (14.9%)

Baseline Characteristics- Patients with Complications

	Arm A – No pre-operative blood transfusion	Arm B – Pre-operative blood transfusion	Overall
No. of Patients with Significant Complications	**13**	**5**	**18**
Age at Randomisation (N, %)			
1-6 years	4 (30.8)	0 (0.0)	4 (22.2)
7-16 years	4 (30.8)	2 (40.0)	6 (33.3)
17-39 years	5 (38.5)	2 (40.0)	7 (38.9)
40+ years	0 (0.0)	1 (20.0)	1 (5.6)
Medium Risk Surgery (N, %)			
- Abdominal	6 (46.2)	2 (40.0)	8 (44.4)
- ENT	4 (30.8)	0 (0.0)	4 (22.2)
- Orthopaedic	1 (7.7)	2 (40.0)	3 (16.7)
- Other	1 (7.7)	0 (0.0)	1 (5.6)
Low Risk Surgery (N,%)	1 (7.7)	1 (20.0)	2 (11.1)
History of sickle complications (N, %)	3 (23.1)	2 (40)	5 (27.8)

Secondary Outcomes and Transfusion

	Arm A – No pre-operative blood transfusion	Arm B – Pre-operative blood transfusion	Overall	Difference of Proportions
Patients with complications or red cell alloimmunisation at 3 months post surgery (N) - Patients with complications - Patients with alloimmunisation	13 13 0	5 5 1	18 18 1	24.7% (CI 4.2-45.2%)
Patients receiving pre-operative blood transfusion	1	31 Top up 26 Exchange 5	32	
Patients receiving intra-op or post-op blood transfusion	12	3	15	27.5% (CI 8.6-46.5%)
Total number of patients receiving blood transfusion	13	31	44	
Total number of red cell units Received	38	71	109	

Conclusions

NHS Blood and Transplant

- There was an increase in significant complications in un-transfused SCD patients having surgery
- There was a marked increase in Acute Chest Syndrome in the un-transfused group
- The allo-immunisation rate in transfused patients was low
- 38% of patients who were un-transfused pre-operatively received an intra-operative or post-operative transfusion
- Limited by early closure and small numbers in trial
- Pre-operative transfusion should be offered to patients with HbSS having medium risk surgery and be considered in other genotypes and in low risk surgery

Joint protocol on Peri-operative management

- Continues collaborative working across network
- Practical benefits as many patients move between hospitals to have surgery
- Surgical and anaesthetic colleagues rotate between hospitals and would be helpful to have same approach

Peri-operative management

- Pre-operative identification
- Pre-operative investigations
- Pre-operative management
- Intra-operative management
- Post-operative management
- Regional anaesthesia

Pre-operative identification

- All (non-European) patients prior to surgery
- All patients at pre-assessment visit
- Lab tests – HPLC
- If urgent: sickle solubility, fbc and discuss with haematologist

Pre-operative investigations

- Fbc
- U+E
- Blood group (extended phenotype) and antibody screen

Pre-operative management

- Discuss all patients with haematology team
- Avoid
  - Dehydration
  - Hypoxia
  - Cooling
  - Hypovolaemia
  - Acidosis
  - Low cardiac output

Pre-operative management

- Assess previous analgesia requirements
- Assess end-organ damage
- Folic acid
- Assess pre-op hydration
  - Clear fluids until 3 hours pre-op
  - Or iv fluids from NBM
  - ? What fluids

Pre-operative transfusion

- HbSS
  - High risk Surgery (Neuro/cardiac, hips?) – EBT
  - High risk patient – EBT
  - Moderate risk surgery Hb <9 : top up
  - Moderate risk surgery Hb >9: ? EBT - ? Depends on patient
  - Low risk patient - ? Depends on patient – probably top up

Pre-operative transfusion

- HbSC
  - High risk surgery – consider transfusion
  - Moderate risk surgery – transfusion if high risk patient
  - Low risk surgery – supportive care

If unable to transfuse

- Hyperhaemolysis/JW
- Follow JW protocol
  - Epo
  - Iron
  - Consider cell salvage

Emergency operations

- If Hb <9 and there is time – top up
- If Hb >9 – if operation urgent operate and ? top up afterwards. If high risk surgery/patient and operation can be delayed, consider EBT

Intra-operative managment

- No specific anaesthetic technique
- Full monitoring
- Pre-oxygenation
- Positioning to avoid venous stasis
- Measures to avoid heat loss
- NOT Cell salvage routinely

Post-operative management

- Pulse oximetry – if <94% on air call haem
- Iv fluids until drinking
- HDU/ITU if high risk (or if no transfusion)
- Consider IS/CPAP
- Effective analgesia
- Thromboprophylaxis
- Antibiotics

Regional anaesthesia

- Tourniquets – relative contra-indication
- Otherwise no issues

Next steps

- Circulation of STSTN protocol
- Comments from group
- Discuss with local anaesthesic/surgical team
- Feedback at next meeting