

Health Services Research- Outcomes

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Aim

- recently completed HSR study done in outpatient newborns at a polyclinic
- the position of this study in a systematic program of HSR in newborns conducted in the University Department of Paediatrics over a period of 50 years that has succeeded in practically eliminating a common cause of death and or disability and at the same time, steadily refined the management methods to make it more safe, acceptable and affordable.
- unintended outcomes, which if anticipated can make the research administration process more efficient.

1. This study

Reducing invasive serum bilirubin tests for neonatal jaundice in Polyclinics through screening with Transcutaneous Bilirubinometry

HSRG 11NOV11

NHG DSRB2013/99

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Background and Aim

- Previously shown that using transcutaneous bilirubin (TCB) values that are 90% of the age specific SB value(SBPh) for phototherapy can markedly reduce (50%) the need for invasive SB in Day 1-3 babies in the hospital setting
- Determine if the same principle can be applied to older babies in the outpatient setting
- Hypothesis: There exists a TCB value that is at least 95% sensitive and 80% specific in identifying the need to do a SB(as indicated by age specific SG based thresholds for phototherapy).

Methods

- Three to 14 day olds with Jaundice at the CCK Polyclinic enrolled after obtaining written informed consent; excluded if phototherapy within 2 days.
- TCB level measured on the chest with the Minolta JM103; instrument set to display mean of 3 determinations
- Correlations (Spearman's) and Bias (Blant Altman) were determined
- Using the following test evaluation statistics: Sensitivity, Specificity, False negative and accuracy rates and positive and negative likelihood ratios, the TCB values that best identified the need for a an SB were determined
- Sample size of 940 paired SB and TCB measurments required to determine a TCB threshold with sensitivity of 95% and 80% specificity

Results

- 587 screened
 - 91 (15.5%) not eligible
 - 79 not between 3 and 14 days
 - 12 received phototherapy within 2 days
 - 496 Eligible
 - 12 (2.5%) declined
 - 484 (97.5%) recruited
-
- 1072 paired SB and TCB values obtained from 484 babies

Results

- 484 subjects , Males-245(50.6%), BW - mean, [SD]-3065,408;
- Racial distribution (%) Chinese(39), Malay(35), Indian(14), Others (12);
- Feeding(%): BF (36), FF(6), MF(58)
- Number of visits
 - 1:175
 - 2:134
 - 3:104
 - 4:42
 - >4:29

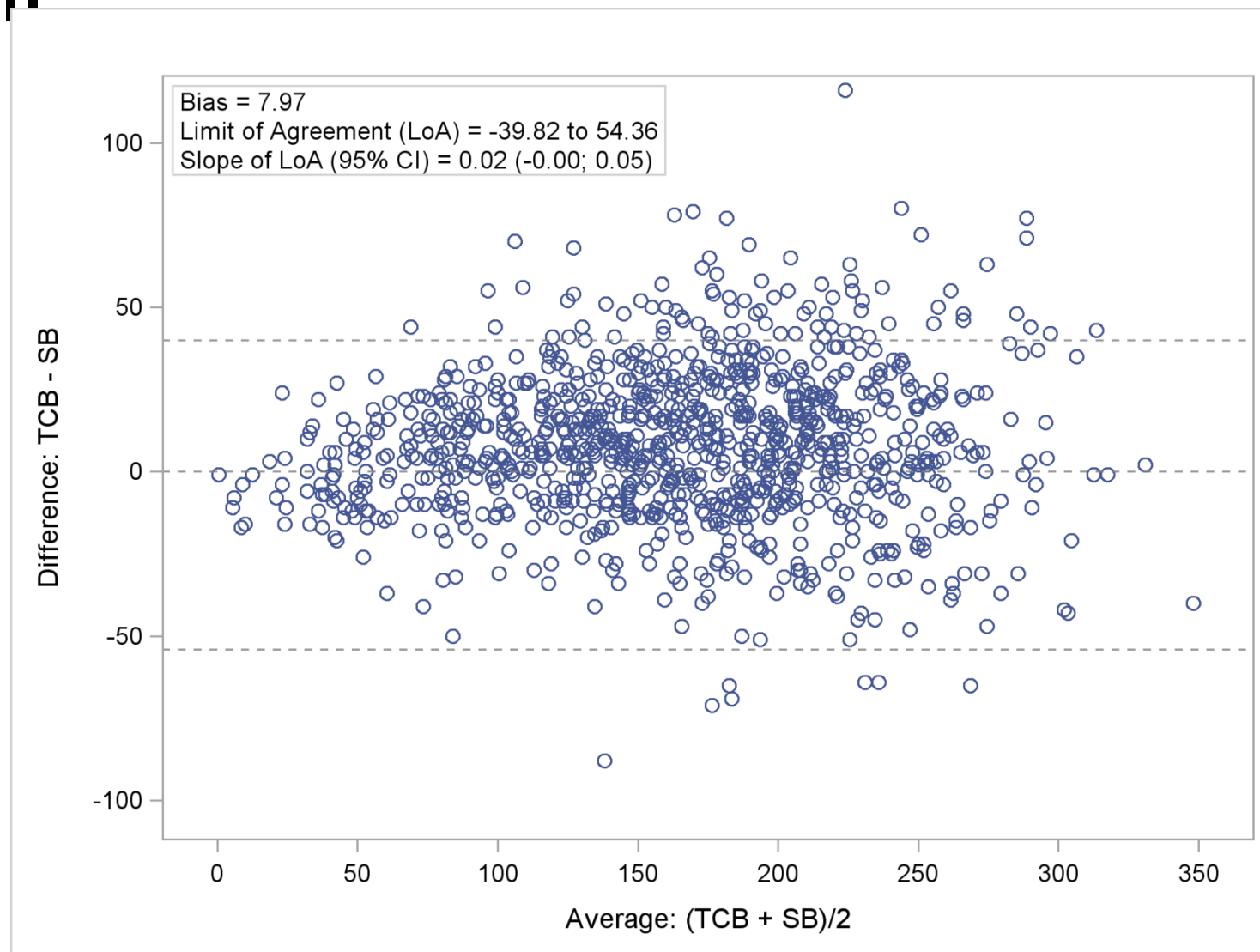
Results-Serum and Transcutaneous Bilirubin distribution by age

| | | Serum | Bili | TCB | | SB | TCB |
|-----|------|-------|------|------|----|-----|-----|
| Age | N | Mean | SD | Mean | SD | P95 | P95 |
| All | 1072 | 159 | 63.6 | 167 | 65 | 261 | 266 |

Results – SB vs TCB Spearman's correlation coefficients

| Age group | Spearman Correlation |
|-----------|----------------------|
| 3-5 days | 0.82260 |
| 6-8 | 0.90842 |
| 9-11 | 0.93005 |
| 12-14 | 0.94652 |
| >14 | 0.95451 |

Overall



Results- Bland-Altman Analysis

| Age Group | Bias | Limits of Agreement |
|------------|------|---------------------|
| Overall | 7.97 | -39.82 to 54.36 |
| < 96 hours | 6.17 | -54.49 to 62.62 |
| >96 hours | 8.18 | -38.29 to 53.22 |

Results – Diagnostic properties- Babies <96 hrs

| | TCB Cutoff (as % of age sp PV) for doing SB | Accuracy | Sensitivity | Specificity | LR(+) | LR(-) | False Neg rate(Harm: % of SB missed) | Efficiency(% of SB avoided) |
|--|--|----------|-------------|-------------|-------|-------|---|------------------------------------|
| | 90 | 89.6 | 100 | 88.9 | 9.00 | 0.0 | 0.0 | 88.89 |

Results – Diagnostic properties- Babies >96 hrs

| | TCB Cutoff (as % of age sp PV) for doing SB | Accuracy | Sensitivity | Specificity | LR(+) | LR(-) | False Neg rate(Harm- % of SB missed) | Efficiency(% of SB avoided) |
|--|---|----------|-------------|-------------|-------|-------|---|------------------------------------|
| | 90 | 96.2 | 83.3 | 96.3 | 22.5 | 0.17 | 0.11 | 96.3 |

Applications

- Using a TCB value that is 90% of the age specific SB value for phototherapy in this cohort would have resulted in a 89% and 96% reduction in the number of SB done in the <96 hours and >96 hours age groups respectively and a corresponding false negative rate of 0% and 0.1% .
- Babies with TCB that is 80% of the PV can be seen the next day
- If a higher degree of certainty is required, then using a TCB value that is 80% of the SB based age specific phototherapy value will yield

| Age Gp | Harm -% of SB missed | Efficiency % of SB avoided |
|---------------|-----------------------------|-----------------------------------|
| <96 hrs | 0 | 68.5 |
| >96hrs | 0 | 87.27 |

2. Position of this study

Bilirubin encephalopathy – common cause of mortality and brain damage

- Third common cause of death (Wong HB, 1957, Tan KH 1968)
- Commonest causes of severe jaundice – G6PD deficiency and liver immaturity (Smith & Vella, 1960, Wong HB, 1966)
- Treatment was exchange transfusion-invasive, dangerous, expensive and labour intensive

Subsequent research

- G6PD deficiency affected 1.62% of newborns (Wong HB, 1966)
- Higher incidence in Males, Chinese and the Malays (Joseph,1999)
- Newborn Screening feasible with a locally developed screening test (Brown & Wong 1968)
- Severe jaundice in the G6PD deficient preventable by protection from exposure to triggers for hemolysis, close observation and education. (Wong HB 1975)

Research on treatment

- severe jaundice is easily controlled with phototherapy (Tan KL , 1974)
- Phototherapy showed dose dependence, was safe and could replace exchange transfusions (Tan KL, 1982, 1986, 1992)
- Multi pronged approach had eliminated the problem (Wong HB, 1980, Joseph 2005)

Parental dislike of measures

- 3 week separation from their newborn
- frequent drawing of blood that measuring serum bilirubin required
- increasing cost over the years, of hospital stay

Review of data and change in management

- only a small proportion of G6PD deficient babies developed severe jaundice after the first week of life (Tan KL 1981, Lim HH, 2003).
- Hospital stay reduced in stages to now about 3-5 days
- Issue of numerous heel stabs remained (almost 6 in the well baby)
- Role of non invasive transcutaneous bilirubin (TCB) investigated

TCB research outcomes

- High correlation (>0.7) between TCB and SB, skin pigmentation caused interference, the limits of agreement between TCB and SB values were wide (about ± 50 $\mu\text{mole/L}$ and that the TCB is not an accurate measure of SB (Yamanouchi 1980, Tan KL, 1996)
- Interference from skin pigmentation was overcome by new technology (Maisels 2004, Thompson 2008)

TCB as a screening tool

- In young babies (ie those < 4 days) in the Department of Neonatology (a sub-speciality department), about 50% of SB measurements could be avoided if the threshold was set at 80% of the age specific SB value that indicated the need for phototherapy. (Chinnadurai and Joseph 2010)

Problem

- However the majority (60%) of babies especially from the subsidized wards were going home within 24-48 hours of birth and given appointments for follow up in the polyclinics a day or two later
- The practice in the polyclinics was to do a SB in every baby presenting with jaundice even before seeing the doctor. This was the only way, the heavy patient load could be efficiently and effectively managed. The doctor could thus decide on the management with the benefit of an actual SB value, a process that gave effectiveness the highest priority.

Hence the need for this study

3. Unintended outcomes

- 6 month delay in starting because
 - Ethics approval from DSRB considered only after grant application was shortlisted
 - Team members had not agreed on practical details, lengthening the DSRB approval process
 - Research assistant appointment took 3 months and could not begin until grant account was opened
- Funds approved for Conference could not be fully utilized
 - Conference date is after the end of the study

Conclusion (1)

- TCB can be used safely and effectively as a screening tool for identifying the newborn who needs a SB
- Cut offs can be a fraction of the age specific phototherapy SB value or any other predetermined value.
- Operational requirements need to be considered when determining what this fraction should be
- Based on this study about 70% reduction in SB determinations can be achieved

Conclusion (2)

- With multi-institutional teams, detailed planning and activities must be agreed on even before grant application is submitted
- Apply for DSRB approval when the grant application is submitted
- Take care when budgeting for remote expenses
- Duration of project should include time needed for administrative activities

Post project activities

- Findings presented and validated at a local and an international conference
- Disseminate findings to polyclinic and wider medical community
- Design a new care process incorporating screening with the TCB
- Collect data on parent response to the new process, changes in turnaround time and real changes in the number of SB's done