Pain Behaviours in Extremely Low Gestational Age (ELGA) Infants

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Outline

• Definition of pain
  – Limitations
• Traditional Pain responses
• Assessment & Measurement
  – What measures
  – What populations
• Evidence for ELGA infants
• Implications & Future direction

Pain

“Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” IASP

• Pain has been defined further as a subjective experience that is best understood through self-reports

Challenges to the Pain Definition

Infants do not speak...need surrogates

• Physiological
• Hormonal
• Biochemical

“Efforts should be directed towards increasing recognition of pain and developing broader sources of information to infer the subjective experience of pain in nonverbal neonates”
Summary of Pain Responses

<table>
<thead>
<tr>
<th>PHYSIOLOGICAL INDICATORS</th>
<th>BEHAVIOURAL INDICATORS</th>
<th>BIOCHEMICAL/HORMONAL INDICATORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Heart Rate</td>
<td>Increased Facial Actions</td>
<td>Increased Cortisol</td>
</tr>
<tr>
<td>Changes in Respiratory rate</td>
<td>Cry</td>
<td>Increased Epinephrine</td>
</tr>
<tr>
<td>Increased Intracranial Pressure</td>
<td>Increased Body Movements</td>
<td>Increased Norepinephrine</td>
</tr>
<tr>
<td>Fluctuations in Blood Pressure</td>
<td>Changes in State</td>
<td>Increased Growth Hormones</td>
</tr>
<tr>
<td>Decreased Oxygen Saturation</td>
<td>Function/Sleeplessness</td>
<td>Decreased Prolactin</td>
</tr>
<tr>
<td>Changes in Heart Rate Variability</td>
<td>Moro Reflex</td>
<td>Decreased Insulin</td>
</tr>
<tr>
<td>Dilated Pupils</td>
<td>Consolability/sleep patterns</td>
<td>Prostaglandin</td>
</tr>
<tr>
<td>Patellar Dorsal Reflex</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Difficulties with Interpretation of Individual Pain Responses

- Behavioral but not physiological indicators are predominant during painful procedures in preterm infants

- Unpredictability of biomarkers

- Biological Factors
  - gender differences

- Responses are influenced by gestational age, behavioral state, neurological integrity and severity of illness

Difficulties with Interpretation of Individual Pain Responses

- Repeated pain affects pain response
  - preterm infants who were born at 28 weeks gestation and hospitalized in a NICU for 4 weeks (early preterm group) had significantly higher heart rates and lower oxygen saturation levels during heel lances than preterm infants born at 32 weeks (late preterm group)
  - the more recently a preterm infant had experienced a painful procedure, the less likely he/she would demonstrate behavioral pain responses to subsequent painful procedures

Psychometric Properties of Procedural Pain Measures

<table>
<thead>
<tr>
<th>Measure &amp; Author</th>
<th>Gestational Age</th>
<th>Pain Indicators</th>
<th>Pain Stressors</th>
<th>Reliability</th>
<th>Validity</th>
<th>Clinical Utility &amp; Feasibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNIPS (Blauer &amp; Stein, 1998)</td>
<td>27 weeks GA to term</td>
<td>Increased heart rate, respiratory rate</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>MAPI (Craig, 1992)</td>
<td>&gt; 25 weeks GA</td>
<td>Increased heart rate, respiratory rate, sleeplessness</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>Premature Infant Pain Profile (PIPP) (Stevens, 1996)</td>
<td>33 weeks GA to term</td>
<td>Increased heart rate, respiratory rate</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>Infant Body Coding System (IBCS) (Craig, 1984)</td>
<td>&gt; 25 weeks GA</td>
<td>Increased heart rate, respiratory rate</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>Neonatal Facial Coding System (NFCS) (Grunau &amp; Craig, 1990)</td>
<td>32 weeks GA to term</td>
<td>Increased heart rate, respiratory rate, sleeplessness</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>NIPS (Lawrence, 1993)</td>
<td>32-36 weeks GA</td>
<td>Increased heart rate, respiratory rate, sleeplessness</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>CRIES (Krechel &amp; Bildner, 1995)</td>
<td>&gt; 25 weeks GA</td>
<td>Increased heart rate, respiratory rate, sleeplessness</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
<tr>
<td>N-PASS (Hummel &amp; Puchalski, 2003)</td>
<td>0-100 days</td>
<td>Increased heart rate, respiratory rate, sleeplessness</td>
<td>Increased pain</td>
<td>High</td>
<td>Constructive</td>
<td>Constructive</td>
</tr>
</tbody>
</table>
 limit of infant pain measures

- Limited psychometric analyses of existing pain measures

- Certain high-risk populations excluded
  - ELBW (<1000g) (Grunau et al., 2000; Holsti et al., 2005; Morison et al., 2003)

- Certain situations excluded
  - Chronic vs. Procedural vs. Disease related

Background of the Problem

- Increased survival of ELGA infants
- Frequent exposure to painful and stressful procedures
- Immediate and long-term consequences of pain
- Focus on quality of life
- Plethora of pain measures
  - Not specific for ELGA infants
  - Extrapolation from more mature infants
  - Potential for error

Comparison of Pain Responses in Infants of Varying gestational ages

Gibbins et al. 2007 Neonatology

Part of a larger study with 149 neonates (25-40 weeks gestation) at high (Cohort A, n=54), moderate (Cohort B, n=45) and low (Cohort C, n=40) risk for neurological impairment

Infants were stratified into 4 mutually exclusive gestational age (GA) strata

Observed 9 facial actions and physiological indicators in response to a standardized heel lance procedure

Demographic Characteristics of Gestational Age (GA) Strata at Baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort A</th>
<th>Cohort B</th>
<th>Cohort C</th>
<th>All n=149</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)*</td>
<td>892 (175)</td>
<td>1298 (322)</td>
<td>2059 (605)</td>
<td>3049 (801)</td>
</tr>
<tr>
<td>Gestational age* (weeks)</td>
<td>26.0 (0.7)</td>
<td>29.4 (1.1)</td>
<td>33.6 (1.1)</td>
<td>38.4 (1.6)</td>
</tr>
<tr>
<td>Apgar score at 1* minute</td>
<td>4.7 (2.2)</td>
<td>5.8 (2.2)</td>
<td>6.5 (2.2)</td>
<td>6.6 (2.6)</td>
</tr>
<tr>
<td>Apgar score at 5 minutes</td>
<td>7.5 (1.7)</td>
<td>7.7 (1.3)</td>
<td>8.4 (1.2)</td>
<td>7.7 (2.1)</td>
</tr>
<tr>
<td>SNAP: PE score*</td>
<td>31.6 (20.1)</td>
<td>17.7 (18.2)</td>
<td>15.8 (15.7)</td>
<td>14.1 (20.9)</td>
</tr>
<tr>
<td>NTIS score*</td>
<td>20.8 (4.2)</td>
<td>16.7 (5.9)</td>
<td>14.1 (7.2)</td>
<td>11.7 (8.2)</td>
</tr>
<tr>
<td>% Male</td>
<td>25 (60%)</td>
<td>32 (64%)</td>
<td>12 (57%)</td>
<td>27 (55%)</td>
</tr>
<tr>
<td>% Multiple birth*</td>
<td>9 (22%)</td>
<td>14 (28%)</td>
<td>6 (28%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>% Cohort A*</td>
<td>11 (27%)</td>
<td>12 (24%)</td>
<td>8 (38%)</td>
<td>26 (53%)</td>
</tr>
<tr>
<td>% Cohort B</td>
<td>16 (39%)</td>
<td>15 (30%)</td>
<td>5 (24%)</td>
<td>12 (24%)</td>
</tr>
<tr>
<td>% Cohort C</td>
<td>14 (34%)</td>
<td>23 (46%)</td>
<td>8 (38%)</td>
<td>11 (22%)</td>
</tr>
</tbody>
</table>
Results

- Significant differences in total facial activities from baseline to lance phase were found with the least mature GA infants having the least amount of change from baseline.
- There were no effects of cohort allocation.
- Only 8 infants (20%) in the least mature GA stratum cried during the lance phase and comparisons between GA were not possible.

Conclusions

- Four facial activities (brow bulge, eye squeeze, nasolabial furrow, vertical mouth stretch) were present in ELGA infants.
- Facial activities increased significantly following painful procedures but the magnitude of responses was proportional to GA.
- Audible cry was not a sensitive indicator in ELGA infants, due to the presence of endotracheal tubes in this high-risk population.
- Future studies should be directed towards evaluation of gross/fine body movements and factors known to dampen pain responses.
Pain Behaviours of Extremely Low Gestational Age Infants

Gibbins et al. 2007 submitted

Following REB approval, 53 infants were examined in random order during a standardized 4-phase diaper change and heel lance procedure.

- Stratification into 2 groups (23-25 weeks GA and 26-27 weeks GA)
- Demographic data, severity of illness, history of painful events collected
- Heart rate, oxygen saturation, 9 facial actions, 6 body actions, salivary cortisol levels were collected within the first week of life

Stratification into 2 groups:
- 23-25 weeks GA
- 26-27 weeks GA

Demographic data, severity of illness, history of painful events collected

Results

- No differences in Total Facial Activity
- Individual Facial Expression during the Procedure Phase

Implications

- Four facial actions (BB, ES, NLF, VMS) are the most sensitive pain indicators
  - Premature Infant Pain Profile
  - Behavioral Indicators of Infant Pain
- Gross body movements (arms, legs, hands, feet, torso, head) are not specific to pain
  - Further studies with specific movements are warranted
- Physiological indicators, in isolation, are not specific
- Salivary cortisol levels for ELGA infants are not specific

Future Direction

- Focused analysis of facial and body movements
- Examination of maturational effects on pain response
- Development of measure for ELGA
  - Further testing of PIPP, BIIP