EFFECTS OF AGE, GENDER AND HOLDING ON PAIN RESPONSE DURING INFANT IMMUNIZATION

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ABSTRACT

Determinants of infant pain responses are important when assessing the efficacy of analgesics. In a randomized controlled trial, 106 infants aged 2 to 6 months were positioned either supine (SUP) on the examination table or held (HLD) by a parent during routine immunization in a community pediatric office. There was no difference between the SUP and HLD infants in duration of crying, facial grimacing or visual analogue scale (VAS) pain scores. Similarly gender did not affect pain response. In contrast, 2-month-old infants displayed more pain during immunization than did 4 or 6-month-old infants.

Immunizations are among the most aversive medical procedures for healthy infants and children and are the most common source of childhood iatrogenic pain.[1,2] The unpleasant sensory and emotional responses that result from the pain of immunization may induce a fear of needle sticks for these children. Efforts to eliminate pain and distress at the time of painful procedures have been directed to the use of pharmacological[3] and non-pharmacological techniques with some success.[4] Swaddling and providing a pacifier alone[5] and with sucrose,[6,7] have been reported to decrease pain but these interventions have been found to be less effective in infants beyond the newborn period. While clinicians do believe that pharmacological and non-pharmacological comfort measures should be provided for painful procedures, the use of these measures is uniformly low.[8]

The ability to provide adequate pain relief for infants and children depends on an understanding of the unique features of each of the numerous painful events they experience, to accurately assess their pain responses and to develop therapeutic interventions most effective for each condition. Little is known about holding infants as a comfort measure to eliminate pain at the time of immunization. The routine in most clinics is to vaccinate infants while lying on an examination table. In primates, the role of the mother as a source of safety and security through contact comfort and clinging has been studied[9] and recently the analgesic effect of skin-to-skin contact in neonates has been shown to be effective in pain relief.[10] While pain responses in the newborn infant of varying gestational age have been studied,[11] the influence of postnatal age on pain responses in developing infants beyond the neonatal period has not received much attention.[12,13]

This study was designed to evaluate the effect of holding and postnatal age, on infant response to the pain of routine immunization. Such data are important in analyzing the effectiveness of pharmacological and non-pharmacological interventions in diminishing immunization pain.

METHODS

This study was a randomized controlled study. Healthy infants between 2 months and 6 months of age, seen for routine well childcare in a community pediatric office, and scheduled for their routine immunizations were enrolled in the study. They were

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excluded if they were born prematurely, had any underlying chronic disorder or required neonatal intensive care unit admission or required hospitalization after the newborn period. Prior participation was not an exclusion criterion, however this only occurred in <10% of cases. Infant characteristics including gender, type of birth (vaginal or cesarean), type of feeding and weight at the time of the study were recorded. The infants were randomly allocated to one of two positions, held (HLD) by their mothers or placed unrestrained on the examination table (SUP) while receiving their immunization. Randomization was performed by drawing a card that indicated infant position assignment (holding or supine) after each infant was enrolled in the study, and immediately before immunization.

The mothers of infants in the HLD group were instructed to stand during the immunization procedure and to hold their infants in the manner they were accustomed to and which felt most comfortable for them. No specific instructions were given as to how firmly to hold their infants, whether to cradle the infant or hold the infant up on their shoulder, or whether to talk to or pat their infant. They were asked however to hold their infant to avoid interference with the view of the video camera on their infant's face. The infants in the SUP group were placed unrestricted on a clean paper towel on the examination table. The mothers were instructed to interact with their infants in the way they were used to and which felt most comfortable and familiar to them. No specific instructions were given as to talking to or touching the infant while on the examining table other than to avoid interference with the view of the video camera on the infant's face. If mothers wanted to pick up their crying infant after immunization (deemed an appropriate parental response), they were not discouraged, but no specific instructions were given to the mother in this regard. For each infant enrolled in the study, the anterolateral aspect of the thigh was exposed so that easy access to immunization was permitted. A standard noxious stimulus was administered (routine Diphtheria-Pertussis-Tetanus-Polio [DPTP] immunization, Connaught Laboratories, Canada) using standard equipment (3 milliliter syringe, 25 gauge needle, and 5/8th inch needle) at 2, 4 or 6 months of age.

Steps were taken to standardize the injection procedure by using only one of two trained pediatricians for all immunizations, by standardizing skin cleaning (15 seconds with an alcohol soaked cotton swab), location of the injections (anterolateral thigh), limb side (alternate sides, beginning on the left at age 2 months), pressure of injection and total injection time (rapid penetration of skin and immediate rapid intramuscular injection). The immunization procedures were videotaped with a color camera (Canon E30). A mirror was mounted on the wall behind the examining table so that the videographer could film the infant's reaction both face-on and from the mirror image. The videographer stood approximately 3 feet from the infant and did not interfere with the procedure. The entire immunization procedure was taped until the infant settled down (approximately 180 seconds).

The primary outcome was infant pain response, as assessed using the facial grimacing scoring method. The pain from the immunization was assessed using 3 different methods; "Facial activity " score based on the Neonatal Facial Coding System (NFCS),[14]cry duration and a 0 - 100 mm unmarked visual analogue scale (VAS). The NFCS has been validated for use in infants aged 2 – 6 months of age[15]. A single research assistant trained and experienced in facial coding assessed facial activity using the videotapes. The research assistant could not be blinded to the position of the infant, but was blinded to the objective of the study. Facial activity [brow bulge, nasolabial furrowing, and eyes squeezed shut] was scored on a per second basis as percentage time that each facial activity was observed, and summed together as previously described.[14] Scores ranged from 0-300%. The cry duration, in seconds, was measured from the videotapes using a hand held stopwatch. The VAS was scored by the pediatrician injecting the vaccine and was done within 15 seconds of the injection. On

the VAS, a score of zero denoted no pain and 100-mm denoted maximal possible pain.

From previous studies[3,16] a calculated sample size of 50 subjects in each group was expected to show a 50% difference in pain scores between HLD and SUP groups with power of 80% and alpha of 0.05. Differences between groups were analyzed using the chi-square test or student t test, where appropriate. Univariate analysis of variance (ANOVA) was conducted to determine if there were differences in pain among infants at 2, 4 and 6 months of age.

The protocol was approved by the Hospital for Sick Children Research Ethics Board. Informed written consent was obtained from the parents of each subject enrolled.

RESULTS

There were a total of 106 infants randomly assigned to the two positioning groups. Fifty infants were assessed lying (SUP) and 56 were held (HLD) by their mothers. There were 37 infants aged 2 months, 37 aged 4 months and 32 aged 6 months. The mean age of participants (± SD) was 123 days (51). Infant characteristics did not differ between groups and are presented according to infant age (Table 1). Sixty percent of male infants were circumcised. During immunization, the 3 pain indicators did not differ between infants in the SUP and HLD groups (Table 2). Two-month-old infants had significantly higher facial activity scores and VAS scores compared with 4 and 6-month-old infants (Table 3). Two-month-old infants cried for a significantly longer duration than 4-month-old infants and 6-month-old infants (Table 3). Gender and male circumcision status were not associated with significant effects on immunization pain response ($p>0.05$). Two-month-old infants cried for a significantly longer duration than 4-month-old infants and 6-month-old infants (Table 3).

TABLE 1 INFANT CHARACTERISTICS

	2-month immunization (n=37)	4-month immunization (n=37)	6-month immunization (n=32)
Age (days)*	62.9 (6.7)	126.4 (7.3)	187.9 (14.5)
Weight at study (kg)*	5.4 (0.7)	7.0 (0.6)	7.8 (0.8)
Vaginal delivery (%)	78.4	72.2	86.7
Caucasian (%)	75.7	85.7	90.6
Breast fed (%)	64.9	57.1	53.6
Gender (%)	37.8	48.6	46.9
Position (% supine)	45.9	48.6	48.4

Values indicate mean and standard deviations (in brackets)
**P<0.05 among groups*

TABLE 2 PAIN MEASUREMENT DURING IMMUNIZATION: Lying vs. Holding

Pain	Supine Group n=50	Holding Group n=56	p
Facial activity (NFCS indications)	117 (92)	137 (79)	0.18
Cry duration (sec)	38 (33)	43 (30)	0.26
VAS (mm)	32 (25)	28 (20)	0.07

VAS= *Visual Analogue Scale*
Values in brackets are SD

TABLE 3 PAIN DURING IMMUNIZATION FOR INFANTS OF DIFFERENT AGES

Pain Measurement	2 months old	4 months old	6 months old	ANOVA*
Facial activity (%)	186 (70)	104 (82)	90 (73)	P<0.001
Cry duration (seconds)	55 (29)	37 (32)	30 (30)	P=0.003
VAS score (mm)	41 (22)	24 (20)	24 (22)	P=0.001

VAS = *Visual Analogue Scale*
Values in brackets are SD
**P <0.05 for 2-month-old infants compared to 4 and 6-month-old infants*

DISCUSSION

The pain response of infants during routine immunization in this study was not different as a function of infant position. These results are similar to those in a previous report where there was no difference in intensity of crying between infants held or vaccinated lying on the examination table.[4] Both the present study and the previous one allowed mothers to pick their babies up once they began crying, thus all crying measurements from that moment on were as if all babies were being held. This may have made any distinction between groups in both studies difficult to determine.

A more recent study found that skin-to-skin contact while being held was an effective intervention for reducing pain from heel sticks in newborn infants.[10] Very specific standards were used for holding in that study including a period of acclimatization and establishment of a steady state for 10-15 minutes prior to the heel stick. In other reports contact alone was not sufficient to reduce crying, while holding infants in the upright position seemed to only modestly reduce crying.[17,18]

In our study, no steps were taken to standardize the holding style of the mothers, how they interacted with their infants, or whether skin-to-skin contact was made between caregiver and infant. The time of feeding infants prior to immunization was also not standardized, since in a previous study there was no indication that feeding infants had any effect on altering pain responses.[3] Instead, in this study a more "real world" approach was adopted allowing mothers to use the style that they and their infants were most comfortable with and accustomed to. Distraction techniques, which have been shown in other studies to diminish pain[19] and which may influence infant pain responses, were also not assessed systematically in this study.

Significantly higher pain scores in this study were found in two-month-old infants as compared to 4 or 6-month-old infants. The reason for the different responses at different ages is unknown although this observation has been studied before in both newborns and young infants with variable outcomes.[12,13,20,21] Johnston et al.[12] found differences between preterm and older infants and between newborns and 2 and 4 month old infants but showed no differences in pain expression between 2 and 4 month old infants. This may have been accounted for by their small sample size and the fact that responses were only measured during a strict 15-second window, post-stimulus. It is clear that the impact of development on pain responses is complex and needs further characterization. Younger infants may have more urgency and desperation in their behavioral responses to pain, as was seen in our study, and as the infant matures these pain associated behaviors likely become more organized and consistent in tandem with better coping mechanisms.[22] There were no gender differences in terms of pain scores. Other investigators have found that the female sex was associated with lower pain scores but these results have been inconsistent.[3,14,23]

The methods used for measuring infant pain include observation of the infant's behavior, physiologic responses or both. In our study healthy infants' pain responses to DPTP immunization were studied by measuring behavioral responses. Other investigators have used similar approaches.[15,23] The "facial activity" scores, obtained from video analysis by a trained coder were significantly correlated with the VAS pain scores obtained from direct observation suggesting that both scales measured similar responses.[3] The raters of the VAS scores in this study were not blind to group allocation and were also the pediatricians who were administering the injection therefore this could have biased the results.

This study did not demonstrate an effect of infant circumcision on pain response during immunization. These results differ from previous observations demonstrating an increased pain response during immunization in male infants that were circumcised compared to those that were not.[24,25] However, there are several differences between this study and previous studies that prevent direct comparisons from being made.

For instance, this study included infants from 2 to 6 months of age, whereas our previous study only included 4 and 6-month old infants. As observed in this study, pain responses may differ significantly between infants of such wide ages, and this might obscure any differences due to circumcision. Within each age group, the sample sizes were too small for us to be able to look for an effect of circumcision on infant immunization pain response in the present study.

CONCLUSIONS

Infant position and gender were not associated with differences in pain responses during routine immunization. In contrast, 2-month-old infants displayed more pain during immunization than 4 or 6-month-old infants.

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