Abstract

Aims and objectives This study aimed to investigate the feasibility and effect of swaddling to control procedural pain among preterm infants.

Background Swaddling has been recommended for controlling neonatal pain. However, feasibility for use is uncertain. Insufficient evidence is available among preterm infants.

Design A two-arm randomized controlled trial with repeated measures.

Method The study was conducted in a 21-bed neonatal intensive care unit of a regional hospital in Hong Kong. Ethical approvals were sought. Written informed consents were obtained prior to data collection. Preterm infants who required heelstick procedure were eligible. 54 preterm infants between 30–36 6/7 gestation age were randomly assigned to swaddling (n=27) and control (standard care, n=27) groups. Pain assessment was performed pre, during, immediate, two, four, six, and eight minutes after heelstick procedure using the Premature Infant Pain Profile.

Results The mean Premature Infant Pain Profile scores were significantly reduced in the intervention compared to the control group during, immediate, two, four, and six minutes after heelstick procedure. The mean changes of heart rate and oxygen saturation in the intervention group were significantly lower than that of the control group at all measured time points. Notably, the swaddled infants quickly resumed to the baseline level at two minutes whereas the control group reached the stable state at an extended period of six minutes.

Conclusion Swaddling seemed to be feasible. The findings provide evidence for the use of swaddling in controlling pain for heelstick procedure among preterm infants. No adverse effects were observed.

Relevance to clinical practice

This article presents the feasibility and effectiveness of swaddling as a non-pharmacological intervention to relieve pain during heelstick procedures among preterm infants. Swaddling can contribute to control minor procedural pain in neonates as one of the simple, safe and low-cost analgesia alternatives.

Keywords: preterm infant, neonate, pain, swaddling, heelstick, analgesia

Summary: What does this paper contribute to the wider global clinical community

- This article contributes to the field of non-pharmacological treatments for neonatal acute pain by providing research evidence to support the use of swaddling for control of minor procedural pain among preterm infants.
- It may contribute to future development of evidence-based clinical practice guideline for non-pharmacological treatments to control neonatal acute pain.

Introduction

For the past three decades, increasing evidence has shown that infants are capable of experiencing pain despite their immature neurodevelopment (Pillai Riddell *et al.* 2011). However, 8.5 million neonates still experience untreated procedural pain per annum (Carbajal *et al.* 2008). In neonatal intensive care unit (NICU), 40-90% of preterm infants have been subjected to at least 10 painful invasive procedures per day with inadequate or no pain control (Cong *et al.* 2009, Cong *et al.* 2012). Uncontrolled and poorly controlled pain not only cause unnecessary suffering but might also lead to short-term and even long-term impairment in the neurobehavioral development associated with neonatal pain experiences (Anand 2000, Grunau *et al.* 2009, Brummelte *et al.* 2012).

Background

Neonatal pain has been managed by pharmacological and non-pharmacological approaches. Non-pharmacological interventions are often preferred for painful minor procedures such as heelstick procedure, owing to the concerns of serious adverse side effect of analgesics (Akman *et al.* 2002, Cong *et al.* 2012). Reviews have shown the efficacies of at least 13 different types of non-pharmacological interventions to manage acute pain for preterms, neonates, and older infants during six different types of minor procedures (Cignacco *et al.* 2007, Pillai Riddell *et al.* 2011). Among these, swaddling is described as one of the most frequently used interventions for pain relief (Cignacco *et al.* 2007).

Only several studies have investigated into the use of swaddling among infants. Previous studies have examined swaddling among full term infants for controlling procedural pain (Campos 1989, Morrow *et al.* 2010), and for soothing effects (Ohgi *et al.* 2004, Richardson *et al.* 2009, Richardson *et al.* 2010). However, less attention has been paid to preterm infants (Fearon *et al.* 1997, Huang *et al.* 2004). Despite International guidelines have recommended various non-pharmacological approaches to be used routinely for managing acute neonatal pain (American Academy of Pediatrics 2006, International Association for the Study of Pain (IASP) 2011), these non-pharmacologic methods are not always implemented in the practice. The reasons may be relating to a lack of facility protocols, resistance to change, knowledge deficit regarding evidence-based non-pharmacologic practices among nurses and physicians, or organizational barriers (Morrow *et al.* 2010). In the local clinical setting, feasibility in the use of non-pharmacologic pain control interventions is perhaps one of the major challenges due to insufficient manpower.

This RCT aims to investigate the feasibility of swaddling in the current clinical setting and to provide the preliminary findings on the effect of swaddling on pain reduction in preterm infants using premature infant pain profile (PIPP) before, during, and after heelstick procedure compared to the standard incubator care. Heelstick is the most common painful invasive procedure in NICU. This study will contribute to the future planning of a larger scale main study. In the long term perspective, it is hoped that the valuable insights gained in this study will provide an important step forward in the development of clinical protocols for the implementation of nonpharmacological pain management strategies to bring about change in practice.

Methods

Research Setting

The study was conducted in a 21-bed NICU of a large university-based regional hospital in Hong Kong. The average admission rate is 250 premature infants per year with the youngest age of 22 weeks of gestation. Ethical approvals were sought from the university and the institution and written informed consent was gained by one of the parents of the infants.

Study Design and Sample

This was a 2-arm randomized controlled trial with repeated measures. Preterm infants of both genders were eligible for inclusion if they were between 30-36$^{6/7}$ gestational weeks and required blood samples by heelstick procedure. The rationales for selecting gestational age 30 weeks or above are: firstly, most of the younger preterm infants (gestational week below 30 weeks) in NICU required intubation and sedation for which would mask and affect pain responses. Secondly, older preterm infants in terms of gestational age exhibit very different pain responses to younger preterm infants as significant development in physiological and behavioral responses to sensory stimulation occurs between gestational age between 28 and 32 weeks (Fearon *et al.* 1997, Cong *et al.* 2012). In this study, older preterm infants refer to their gestational age of 28 weeks or above. To control extraneous variable of external environmental variations, only preterm infants who were taken care of in the incubators were recruited. Exclusion criteria were preterm infants who had major congenital abnormalities, severe cardiovascular diseases, neurological impairment, and required ventilation support, sedatives and analgesics. The required sample size was calculated based on the primary outcome measure PIPP score. Based on a previous study, a reduction of 3 points in PIPP scores during painful procedures were considered as clinically significant (Axelin *et al.* 2009). Assuming a pooled SD of 3.35, a sample size of 27 preterm infants in each group was required to achieve a power of 90% to detect a mean difference on 3 points in PIPP in a two-sided independent t-test at a significance level of 0.05. The eligible preterm infants were randomly assigned to intervention group (swaddling, n=27) and control group (standard care, n=27) using a computer-generated random table (Figure 1).

The Intervention and Control Groups

The intervention group received swaddling by a soft cotton hospital blanket (Campos 1989, Fearon *et al.* 1997). The infants were in a supine position while their arms were flexed and placed cross-over and close to the chest. The end of the one side of the blanket was folded over the neonate's chest and arms to the opposite side, then tucked under the trunk. This folding procedure continued for the end of the other side of the blanket to be folded over the infants and tucked under the opposite side of the trunk. To ensure that the blanket was not over-restrictive, the blanket was checked by sliding a finger between the wrap and the neonate. The lower portion of the blanket was folded up the belly with one of neonate's feet uncovered as the heel was exposed for heelstick procedure. This allowed for the blanket to hold the neonate firmly but gently in a flexed position. The swaddling procedure took about one minute. Then, the neonate was placed in a lateral position. The control group received standard care which was lying in supine position, wearing diapers only and without any clothes.

Outcome Measure

The primary outcome was pain response of infants as measured by Premature Infant Pain Profile (PIPP), a multidimensional pain assessment tool. PIPP has been widely used in pain studies especially in premature infants (Stevens *et al.* 1996) and has high clinical utility (Duhn & Medves 2004). It has been demonstrated to have good construct validity, inter-rater reliability (0.93-0.96) and intra-rater reliability (0.94-0.98) (Ballantyne *et al.* 1999). PIPP composes of seven indicators including physiological data and behavioral states. They are (1) gestational age, (2) heart rate (HR) and (3) transcutaneous oxygen saturation (SaO_2), (4) behavioral state (state of sleep), and cry facial expressions including (5) brow bulge, (6) eye squeeze and (7) nasolabial furrow. The indicators were measured on a 4-point scale from 0-3. Scores for 7 indicators were summed to calculate of the total pain score which ranged between 0 and 21; with 0 being considered as no pain, <6 as minimal pain, 7-12 as moderate pain, and >12 as severe pain (Stevens *et al.* 1996). The HR and SaO_2 were measured on a continuous basis by a bedside pulse oximeter and electrocardiography monitor (Philips

IntelliVue Patient Monitor, Germany) as the NICU standard protocol. The equipment used underwent regular quality control check and calibration to ensure accuracy of readings. The physiological scores calculation was based on the changes of maximum heart rate changes and the changes of minimum oxygen saturation compared to the baseline.

Data Collection Procedure

The demographic data included gestational age, birth weight, postnatal age, gender, Apgar score which were collected from the hospital chart. All recruited infants were subjected to routine standardized heelstick blood sampling procedure which was performed by experienced phlebotomists to obtain 0.1-0.2ml of blood into a capillary tube. An advanced practice nurse with over 20 years of clinical working experience in the NICU was the researcher for this study. The researcher recruited each subject by first explaining to the parent about the details of the research. After written informed consent was signed, the recruited infants were randomly allocated into either the intervention group or the control group using the series of random numbers on the computer-generated random table. The infants remained inside the incubator throughout the heelstick procedure to decrease the environmental variances. The data were collected by the same researcher by observation at baseline, during the heelstick procedure and immediately after the procedure and then every 2 minutes, until the time needed to resume to normal baseline data. Recommendations from the literature suggest using 2 minutes time interval for measurement because it had higher scoring than the short interval of 30 seconds and one minute, and also it could provide precise and detailed data when compared with a longer interval (Huang *et al.* 2004, Evans *et al.* 2005).

Data Analyses

The analyses were performed using SPSS version 20 by the researcher with assistance from the statistician and the interpretation of the results was done by the research team. The assumptions of normality of the variables were assessed by K-S tests. The baseline characteristics between the two groups were tested by Fisher's exact tests for binary variables, independent t-tests for normally distributed continuous variables, and Mann-Whitney tests for non-normal continuous variables. The overall PIPP scores and the physiological data of SaO_2 and HR were analyzed by repeated measures analysis of variance for 1 between-subject factor (group) and 1 within-factor (time) to assess the effectiveness of swaddling compared to the standard care respectively. For each of the three outcome measures, post-hoc pairwise comparisons were made to examine the differences in the outcome measure at each of the seven time points between the two groups (between-subjects effects). A Bonferroni adjustment for the seven comparisons (α =0.05/7= 0.007) was made to control the overall Type I error to 5% for the post-hoc comparisons. If significant between-group effect was found, a repeated measures ANOVA with 1 within factor (time) was performed to assess the changes in the outcome measure over time. All the 54 subjects were included in the analyses, and the significance level of all the statistical tests was set at 5%.

Results

All the subjects were successfully followed up in the study. As shown in Table 1, no significant differences in the demographics and the baseline clinical variables were found between the intervention and the control groups in terms of gestational age, birth weight, gender, postnatal age, and the Apgar score. Repeated measures ANOVA with a Greenhouse-Geisser correction showed that the mean PIPP scores differed significantly between time points ($F(4.052, 210.726) = 283.145$, $P < .001$) and a statistical significant interaction effect between time and treatment group (time X group) ($F(4.052, 210.726) = 34.580$, $P < .001$) (Table 2 and Figure 2). Post-hoc pair-wise comparisons showed significant differences in the PIPP mean scores were observed during heelstick (10.4±2.9 vs 14.4±1.9, $P < .001$), immediate after heelstick (7.0±2.7 vs 14.7±2.9, P < .001), and at 2-min (3.3±1.8 vs 10.5±3.5, *P* < .001), 4-min (1.7±1.4 vs 6.5±3.4, *P* < .001) and 6-min (1.2±1.2 vs 3.8±2.7, *P* < .001) after heelstick, and the PIPP mean scores at these five time points were lower in the swaddling group when compared with the control group (Table 2). Similar patterns were observed for the mean HR and SaO_2. For HR, there were significant differences in the mean scores between time points (F(3.963, 206.086) = 146.30, *P* < .001) and a statistical significant time X group interaction effect (F(3.963, 206.086) = 26.685, *P* < .001), and the corresponding statistical results for SaO_2 on time effect and time X group interaction effect were (F(2.771, 144.074) = 85.482, *P* < .001) and (F(2.771, 144.074) = 17.043, *P* < .001) respectively. The mean SaO_2 values in the swaddled infants were significantly higher than that of the control group at all measured time points except before heelstick (*Ps* < .004) while the mean HR values in the swaddled infants were signigicantly lower than that of the control group immediately and 2-min after heelstick (*P*s < .001) (Table 3 and Figure 3).

Notably, the repeated measure ANOVA with 1 within factor on swaddled infants showed that the PIPP scores of the swaddled infants almost resumed to the baseline level (3.3±1.8) at 2-min after heelstick (F(1,26) = 1.189, *P* = 0.29) whereas the corresponding results for the control group recovered (3.8±2.7) at an extended period of 6-min after heelstick (F(1,26) = 3.294, *P* = .08). The physiological variables also resumed at a faster rate in the intervention group than the control group. For HR, the swaddled infants resumed to baseline level (149±12 beats per minute) at 2-min after heelstick (F(1,26) = 0.350, *P* = .56) whereas the control infants took 6-min after heelstick to recover (149±17 beats per minute) (F(1,26) = 0.010, *P* = .92). For SaO_2, the baseline reading (98±2) was reached at 2-min after heelstick (F(1,26) = 2.831, *P* = .10) for the intervention group but the control group did not return to the baseline level (97±2) until 8-min after heelstick (F(1,26) = 20.505, *P* < .001). No adverse effects were observed during the intervention of swaddling.

Discussion

This study was undertaken to assess the feasibility of the use of swaddling and the effect of swaddling on pain responses by comparing the dependent variables of PIPP between the swaddled preterm infants and preterm infants who received standard care. The use of swaddling as the non-pharmacological intervention seemed feasible because it is easy to administer, low-cost and readily available as a nurse-initiated intervention. Although the implementation of non-pharmacological pain interventions may pose challenges to the healthcare team including manpower resources and policy change implications (Morrow *et al.* 2010), the insights gained in this study will contribute towards the pain protocol development for practice change. This is the first study to address the effectiveness of swaddling for reducing pain for heelstick procedure among older preterm infants. Our study found that swaddling seemed effective in controlling procedural pain among preterm infants as indicated by significantly lower PIPP scores compared to the control group. It was also shown that swaddling significantly diminished increase in HR, diminished decrease in SaO_2 level, and induced a faster recovery time. The findings were congruent with a previous RCT by Fearon et al., 1997 which involved 15 preterm infants (group 1: n=7 gestational age of 27-30 weeks, group 2: n= 8 gestational age of >30-36 weeks) during heelstick procedure. The swaddled older preterm infants were reported to recover faster in physiological and behavioral responses than the control group with no treatment.

Similarly, findings were consistent with another RCT conducted by Huang et al. (2004) who compared the effect of containment and swaddling on pain reduction during heelstick in 32 preterm infants (gestational age between 25 and 36 weeks) using PIPP. The PIPP scores were lower in the swaddling group compared to the containment group with significant difference at the 3rd and 7th minute. Both the HR and SaO_2 returned to their baseline quicker in the swaddled infants than the motor containment infants. The pain reduction effect of swaddling in this study is more pronounced compared to the study by Huang et al. (2004) which involved both older and younger preterm infants. This may be attributed by a consistent age-specific sample of older preterm infants in this study. Like term infants, older preterm infants tend to display pain-elicited behavioral and physiological responses concomitantly (Fearon *et al.* 1997, Cong *et al.* 2012). Younger preterm infants are likely to exhibit less and delayed facial expressions during heelstick due to their immature nervous systems (Fearon *et al.* 1997, Cong *et al.* 2012). Thus, concurrent analysis of both samples without age differentiation might have led to the underestimation of the intervention effect.

Other studies involving term infants have also reported that swaddling alleviated pain-elicited distress during heelstick as documented by reduced physiological and behavioral pain responses (Campos 1989, Morrow *et al.* 2010). Physiological changes measured include diminished increase in heart rate and a faster recovery time (return of physiological variables to baseline) (Campos 1989). Behavioral changes reported include decreased crying time, reduced state of arousal (Campos 1989), and less exhibition of behavioral pain responses including facial expressions, breathing pattern, motor behaviors (Morrow *et al.* 2010).

Theories posit that swaddling alleviates pain through sensory or multisensory stimulation (Campos 1989, Stevens *et al.* 2000, Johnston *et al.* 2011). The motor containment using the blanket has been theorized to provide multiple sensory inputs including continuous activation across the tactile, thermal, and proprioceptive sensory systems (Campos 1989, Stevens *et al.* 2000). These simultaneous non-nociceptive stimulations of various sensory systems may cause sensory saturation, whereby the gate-control mechanism becomes activated by closing the gates to nociceptive input to attenuate or suppress the nociceptive transmission (Bellieni *et al*., 2002; IASP, 2011). Another postulation is that neonatal developmental position with flexed and lateral posture could simulate the familiar uterine posture, which may help to promote physiological stability and self-regulatory capacity (Huang *et al.* 2004, Hill *et al.* 2005). However, the exact underlying mechanism of how swaddling produces analgesia is not yet known.

Due to limited resources, the subjects' faces were not videotaped to avoid assessor bias. This study was limited by no blinding of the outcome assessor. However, it is worth noting that the physiological data provide objective evidence to support the beneficial effect of swaddling. Future research is necessary to confirm the generalizability of findings by fully blinded, multicenter trials. Prospective longitudinal designs are warranted to investigate the long term effect of swaddling on developmental and behavioral outcomes. Replication of studies is recommended to consider using swaddling for full term, older preterm and younger preterm infants as distinctively different groups to determine the age-appropriateness of the non-pharmacological pain control intervention.

Conclusion and Relevance to clinical practice

The use of swaddling compared to the usual care significantly reduced the mean Premature Infant Pain Profile scores during, immediate, two, four, and six minutes after heelstick procedure among older preterm infants. The findings will contribute to developmentally sensitive care in the NICU, which optimize the health and developmental outcomes and enhance the preterm infants' quality of life. Swaddling is a simple, safe, low-cost and non-pharmacological pain intervention that can be used to control minor procedural pain in older preterm infants.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Table 1. Subject Baseline Characteristics

	Control (n=27)	Swaddling (n=27)	P value*
Gender, n(%)			1.00†
Male	16 (59.3)	15 (55.6)	
Female	11 (40.7)	12 (44.4)	
Postnatal age, days	11.2±14.0	9.3±9.1	0.815
Estimated gestation age, weeks	34.5±1.9	34.2±1.5	0.536‡
Birth weight, kg	1.92±0.4	1.94±0.4	0.829‡
Apgar-5 minute	7.9±1.8	8.8±1.0	0.053

Note: Mean±SD.

* Mann-Whitney test.

† Fisher's exact test

‡ Independent samples t-test.

Table 2. Mean PIPP scores over time by treatment group

	Control (n=27)	Swaddling (n=27)	P value*
Baseline (range)	2.7±1.3 (1-5)	2.8±1.7 (0-7)	0.79
During (range)	14.4±1.9 (11-18)	10.4±2.9 (5-17)	< 0.001
Immediate after (range)	14.7±2.9 (7-19)	7.0±2.7 (3-16)	< 0.001
Two minutes (range)	10.5±3.5 (4-17)	3.3±1.8 (0-8)	< 0.001
Four minutes (range)	6.5±3.4 (2-13)	1.7±1.4 (0-4)	< 0.001
Six minutes (range)	3.8±2.7 (0-10)	1.2±1.2 (0-4)	< 0.001
Eight minutes (range)	1.7±1.6 (0-5)	1.2±1.2 (0-4)	0.21

* Repeated ANOVA.

Table 3. Mean readings of oxygen saturation (SaO_2) and heart rate (HR) over time by treatment group

	Control (n=27)	Swaddling (n=27)	P value*
SaO_2			
Baseline	98.6±2.0	98.2±2.0	0.42
During	85.6±5.2	91.8±3.7	< 0.001
Immediate after	86.7±6.6	95.5±4.1	< 0.001
Two minutes	91.2±4.0	97.5±2.4	< 0.001
Four minutes	93.4±3.9	97.6±1.9	< 0.001
Six minutes	95.6±2.8	97.9±2.0	< 0.001
Eight minutes	96.7±2.2	98.5±1.9	0.003
HR			
Baseline	144.9±12.1	149.6±11.2	0.15
During	172.7±16.9	173.3±11.3	0.87
Immediate after	181.8±16.7	161.7±9.7	< 0.001
Two minutes	171.3±19.7	148.7±12.3	< 0.001
Four minutes	157.8±18.1	146.8±9.8	0.008
Six minutes	148.9±16.6	145.2±11.6	0.35
Eight minutes	144.9±12.6	141.7±12.4	0.37

* Repeated ANOVA.

Figure 1.

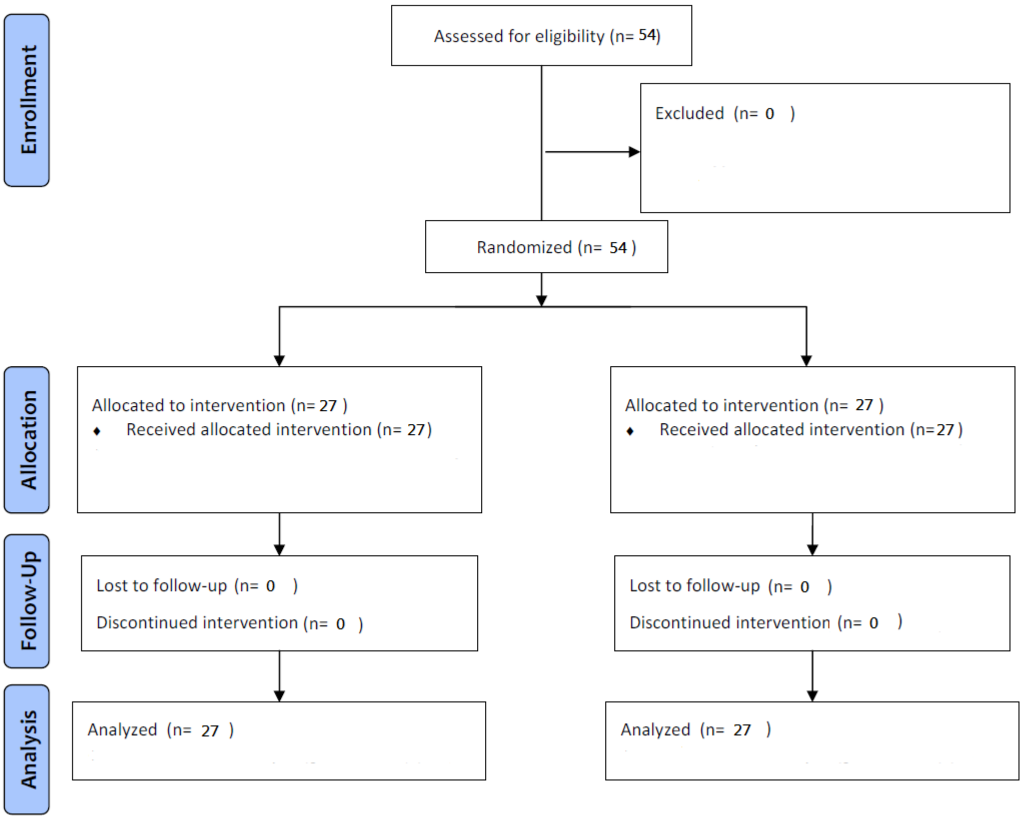
Enrollment
Assessed for eligibility (n= 54)
Excluded (n= 0)
Randomized (n= 54)
Allocation
Allocated to intervention (n= 27)
Received allocated intervention (n= 27)
Allocated to intervention (n= 27)
Received allocated intervention (n=27)
Follow-Up
Lost to follow-up (n= 0)
Discontinued intervention (n= 0)
Lost to follow-up (n= 0)
Discontinued intervention (n= 0)
Analysis
Analyzed (n= 27)
Analyzed (n= 27)

Figure 2. PIPP score

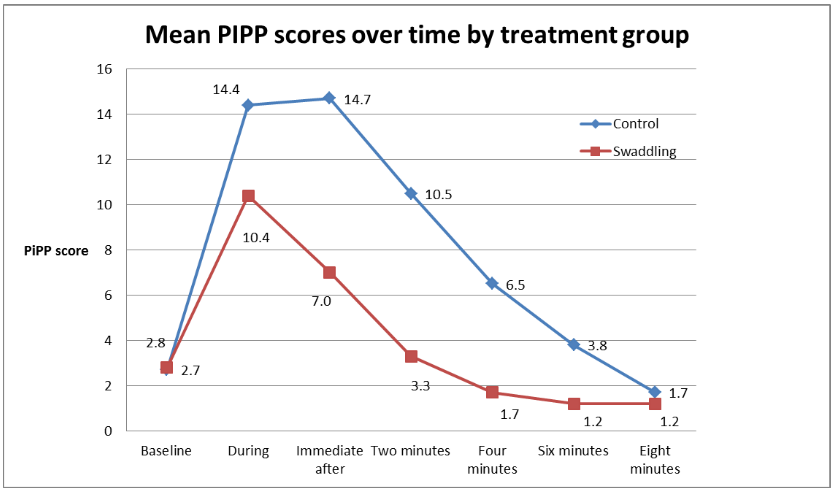

Figure 3. Physiological data