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Effect of Multisensory Stimulation on Pain of Eye Examination in Preterm Infants

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Abstract

Background: Eye examination as one of the painful procedures for retinopathy of prematurity screening can cause some pain-related physiological and behavioral changes in preterm infants. Multisensory stimulation is an analgesic non-pharmacological method that has analgesic effects on infants during painful procedures.
Objectives: This study aimed to determine the effect of multisensory stimulation on induced pain during eye examination for retinopathy of prematurity screening in preterm infants.
Methods: In this double-blind clinical trial, 80 preterm infants were randomly divided into two groups. In the intervention group, multisensory stimulation program was performed for 15 minutes before the beginning of examination while the control group received the routine care. Pain score for each infant was recorded by premature infant pain profile. Data were analyzed using independent t-test, Mann-Whitney, and ANOVA with repeated measures by SPSS software (version 16).
Results: The mean gestational age was 30.4 ± 1.7 weeks in the multisensory stimulation group and 30.6 ± 1.8 weeks in the control group. Based on ANOVA with repeated measures, the pain score was significantly different between two groups during the assessment process ($P < 0.001$). The changes in pain severity during the examination were also significant between the two groups ($P < 0.001$); so that the pain was more intensive in the control group than the intervention group.
Conclusions: Multisensory stimulation program as a safe and easy method can reduce pain in neonates and may be used as a way to reduce pain during eye examination in infants.

Keywords: Multisensory Stimulation, Pain, Retinopathy of Prematurity, Preterm Infant

1. Background

According to the definition of world health organization, the infants who are born earlier than 37 weeks from the first day of the last menstrual period are considered premature. The incidence of prematurity in developing countries is estimated to be about 19% (1). Infants admitted to neonatal intensive care units undergo painful procedures due to numerous diagnostic and therapeutic interventions (2).

One of the painful procedures that the preterm infants experience during hospitalization in the neonatal unit is eye examination to screen retinopathy of prematurity (3). Now, according to the statistics of American academy of pediatrics, about 450000 retinopathy of prematurity examinations are performed each year in NICU in the United States of America (4).

Although the examination of retinopathy in premature infants is essential for identifying and improving visual acuity in a small percentage but significant number of infants, the available evidence indicates that the screening examination of ROP is usually a painful, uncomfortable, and dangerous method in the NICU (5, 6).

America academy of pediatrics recognizes the pain caused by ROP screening and recommends to perform additional steps to reduce pain during examination: "efforts must be made to minimize pain, discomfort, and systemic effects of this examination using a topical numbing agent like proparacaine or non-pharmacological techniques" (7-9).

However, the evidence shows that pain management during ROP examination is inadequate. Although currently there are recommendations and guidelines for ROP examination, no standard protocol has been developed for pain management by pharmacological and non-pharmacological methods during ROP examination (7).

We should always be looking for a way to reduce pain in infants during eye examination for ROP screening (8, 9). The clearest and most effective strategy to reduce pain in infants is limiting the number of painful procedures and then, conducting the pharmaceutical and non-pharmaceutical methods (10).

Today, many non-pharmacological techniques are available to relieve and control pain (11). Sensory saturation or multisensory stimulation is a non-pharmacological analgesic method to prevent pain and physiological changes caused by pain in infants during the painful procedure; it is now a part of national guidelines for pain relief in infants (12).

In December 2011, the international association for the study of pain reported that in the case of multisensory stimulation, the simultaneous use of different non-pharmacological techniques has more clinical effectiveness than using each of these methods alone (13). Anand and Hall (2011) (14) wrote: "multisensory stimulation is a non-pharmacological method which is used in preterm infants undergoing painful procedures". Gitto and colleagues (2002) (15) showed that multisensory stimulation is a non-pharmacological alternative to fentanyl to reduce pain in preterm infants.

Bellini showed in a study that multisensory stimulation is an effective analgesic method (16, 17).

Despite that eye examination in preterm infants is a painful procedure (5-9) and multisensory stimulation is a simple, safe analgesic technique (12-15), no study has specifically examined the effect of multisensory stimulation on pain caused by eye examination to screen retinopathy of prematurity in preterm infants. Therefore, we decided to evaluate the effects of multisensory stimulation on pain caused by eye examination in preterm infants.

2. Objectives

This study aimed to determine the effect of multisensory stimulation on induced pain by eye examination for retinopathy of prematurity screening in preterm infants.

3. Methods

This two-group double-blind randomized clinical trial was conducted from July to August 2014. The study population was preterm infants admitted to Mashhad Khatamolanbia ophthalmology Hospital who were selected based on their recorded information.

3.1. Study Population

Inclusion criteria included: 1. The preterm infants with gestational age $\leq$ 32 weeks according to the records, or the infants with birth weight < 1500 g, or the infants with birth weight of 1500 to 2000 g with severe systemic disease who aged at least 4 weeks. 2. The infants who first time underwent eye examination to screen for retinopathy of prematurity. 3. The infant whose mother was present. 4. The infants who were not fed in the past one hour. 5. The infants who were quiet and alert. 6. The infants with no history of cardiopulmonary resuscitation. 7. The infants with no history of surgery. 8. The infants with 5-minute Apgar scores above 6. 9. The infants with no history of intra ventricular hemorrhage grade 2 or more. 10. The infants not using narcotics and sleeping drugs in the past 24 hours. 11. The infants who had no need for ventilation with positive pressure and those were not connected to the endotracheal tube. 12. The infants with no major congenital malformations. 13. The infants without problems and defects in the central nervous system.

Exclusion criteria included: 1. The infants who needed CPR during the examination. 2. The infants experiencing apnea during the examination.

The study tools included an infant's demographic form, a checklist for recording physiological variables, a checklist for recording time durations of the first and second eye examinations and Premature Infant Pain Profile for measuring pain intensity.

The sample size of 80 preterm infants was calculated through a pilot study using formula of mean comparison with 95% test power. The sample attrition was not occurred in this study. Therefore, 80 preterm infants were selected through non-randomized convenience sampling method and then were divided into intervention and control groups (40 infants in each group) as simple randomization.

3.2. Interventions

All the infants were placed under almost similar conditions in terms of environmental status (light, temperature, and sound) and attached to the pulse oximetry. The location of pulse oximetry probe was on the right foot between the thumb and second finger for all the infants.

In the intervention group, according to the study of Bellieni (2002) (16), after stabilization of infant's condition, the intervention including a multisensory stimulation program (visual, taste, tactile, and smell stimulations) was performed. At first, the infant was placed at supine position, and the hands and legs were bent as the fetal position, so that the infant could move freely.

For tactile stimulation, face, upper and lower limbs of infant were gently touched by the mother. The intervention was performed from 15 minutes before the beginning of examination until the time of examination (17).

For visual stimulation, the infant's mother was asked to look at her baby from near and try for eye communication in order to attract the infant's attention. The intervention was performed from 15 minutes before the beginning of examination until the time of examination (16).

For hearing stimulation, the infant's mother was asked to speak with her baby gently and continuously. The intervention was performed from 15 minutes before the beginning of examination until the time of examination (16).

Vanilla solution was used for smell stimulation. The researcher stained a piece of sterile gauze with 0.64 g vanilla 99% diluted in 100 mL distilled water and closed to the infant's nose without any contact and kept it at an average distance of 1 to 2 millimeters. The intervention was performed from 15 minutes before the beginning of examination until the time of examination.

1 mL of 33% glucose solution was used for taste stimulation. In this test, glucose solution was drawn into a syringe by the researcher. The syringe mouth without needle was placed into the infant's mouth and the solution was injected into the infant's mouth with gentle movements along with infant's sucking for 30 seconds. This intervention started 2 minutes before the examination (16).

Before engaging in stimulations, the mother was trained by the researcher on the correct method of performing the intervention. No intervention was carried out in the control group. Eye examination for ROP screening was performed by a same skilled operator through an indirect method (using the Ret Cam) in all infants. This person was blind to the groups.

3.3. Measurements

Assessment tools were Premature Infant Pain Profile (PIPP), pulse oximeter, and Chronometer. The content validity method was used to determine the scientific validity of the data collection tool. The reliability of the chronometer monitor was confirmed by using reputable brands cited by experts.

The PIPP is a 7-indicator scale (comprising gestational age, behavioral state, heart rate, O_2 saturation, brow bulge, eye squeeze, and nasolabial furrow). Each parameter is scored from zero to 3 and totally measures acute pain in preterm and term neonates.

The PIPP in this study was assessed by inter-assessor reliability method. To follow this method, two trained colleagues were asked to record pain scores simultaneously in 10 cases in separated questionnaires. The correlation coefficient of 91% was obtained in this test. An equivalent validity method was used to assess the validity of monitoring devices. To this end, the device accuracy was compared with that of another device each time before the intervention.

The pain was assessed at 7 stages of 30 seconds, as follows:

1- 30 seconds before the beginning of the eye examination;

2- Since the start of the first eye examination for 30 seconds (usually each eye examination lasts about 30 to 45 seconds; if the eye examination lasted more than 30 seconds, to standardize the data, the evaluation was performed in the first 30 seconds);

3- Since the beginning of the second eye examination for 30 seconds;

4- At the end of the eye examination for 30 seconds;

5- 30 seconds after the end of the eye examination for 30 seconds;

6- 1 minute after the end of the eye examination for 30 seconds;

7- 1 minute and 30 seconds after the end of the eye examination for 30 seconds.

For single blinding of the study, watching videos, evaluation and scoring of sub-criteria of behavioral status, the status of infant's face, and recording PIPP pain severity were performed by a person other than the researcher after watching the videos.

Also, the sub-criteria of heart rate and oxygen saturation as well as PIPP pain severity scores were recorded by a different person at three times of before, during, and after the eye examination by using the checklist for recording physiological criteria .Also, the time duration of each eye examination was recorded using a chronometer.

3.4. Statistical Analyses

Data were analyzed using SPSS software version 16. To evaluate the normal distribution of quantitative data, Kolmogorov-Smirnov and Shapiro-Wilk tests were used. In order to compare variables between the two groups, independent t-test was used in the case of normally distributed data; otherwise, Mann-Whitney test was employed. To compare between-group dependent variables at different stages, variance analysis with repeated measures was used, while Friedman test was used in case of abnormal distribution. $P < 0.05$ was considered significant.

4. Results

The results of this study showed that there were 25 girls (62%) and 15 boys (38%) in the intervention group, while 18 girls (45%) and 22 boys (55%) were enrolled in the control group. The mean gestational age was 30.4 ± 1.7 weeks in the intervention group and 30.6 ± 1.8 weeks in the control group. The results showed that the two groups were homogeneous in terms of sex, age, modified age, birth weight, weight at the time of examination, and time duration of examination of the first and second eyes (Table 1).

Table 2 shows that during the first and second eye examinations, an increasing trend in the mean pain score

Table 1. Demographic Characteristics of the Subjects

Variable	Group	N	Mean ± SD	Result of Independent t-Test
Gestational age	Intervention	40	30.4 ± 1.7	t = 0.49
	Control	40	30.6 ± 1.8	P = 0.62
Calendar age	Intervention	40	35.1 ± 1.9	t = 0.36
	Control	40	34.9 ± 1.8	P = 0.72
Birth weight	Intervention	40	1385.8 249.4	t = 0.53
	Control	40	1355.8 ± 254.0	P = 0.60
weight at examination	Intervention	40	1995.0 ± 205.6	t = 1.11
	Control	40	1944.0 ± 205.1	P = 0.27
time duration of examination of the first eye	Intervention	40	37.5 ± 4.1	t = 0.56
	Control	40	38.2 ± 3.8	P = 0.55
time duration of examination of the second eye	Intervention	40	36.9 ± 3.9	t = 0.50
	Control	40	37.6 ± 4.3	P = 0.67

was obtained in two groups. However, independent t-test showed a significant difference between the two groups in terms of PIPP scores in the first and second eye examinations ($P < 0.001$).

At all stages conducted after ending the eye examination, the obtained results showed that there was a significant difference in the two groups in terms of pain severity (Table 2).

The results of variance analysis with repeated measurements showed that PIPP score significantly changed in the intervention group at 7 different assessment stages ($P < 0.001$). This change was also significant in the control group ($P < 0.001$). But, the changes in PIPP scores were significantly different at all the evaluation stages between the two groups ($P < 0.001$)

Covariance analysis was performed to determine the effect of gender, birth weight, and gestational age on the dependent variable of pain score during the examination of the eyes. The results of this analysis showed that only the effect of the intervention of the present study (implementation of multisensory stimulation) was significant on pain score during eye examination ($P < 0.001$) (Table 3).

5. Discussion

In the present study, the results indicated that in the stage before eye examination, pain score was not significantly different between the intervention and control groups. In both groups, infant's pain score during "the first eye examination" and "the second eye examination" increased, but this increase was greater in the control group than the intervention group. In the next stages (30 seconds, 1 minute, 1.5 minute, and 2 minutes after eye examination) the pain declined. The difference in pain score between the two groups was significant at all the stages.

In Bellini et al.'s study (2002) (16) entitled "effect of the multisensory stimulation on analgesia in term infants", the results showed that in the stage of blood sampling from the heel, there was no significant difference in pain scores of the second group (glucose) and sixth group (multisensory stimulation without receiving glucose) than that of the control group. The mean pain score was approximately 9.5 and 8.5 in the second and sixth groups, respectively, and 9.0 in the control group. The mean pain score was approximately 6.5 in the third group (sucking) and 4.0 in the fourth group (sucking along with glucose) that these values were significantly different from the pain score in the control group. The fifth group (multisensory stimulation) had a significant difference from the control group in terms of pain scores; the mean pain score in this group was approximately 1. The multisensory stimulation showed the most reduction in pain among the other pain control methods.

The study of Seifi et al. (2013) (18) entitled "comparison of the effect of oral acetaminophen with glucose on pain caused by eye examination to screen for retinopathy of prematurity", the results showed that in the first 45 seconds of eye examination, the mean pain score in the first group (Acetaminophen group) was 12.9 ± 2.4, in the second group (oral glucose) 9 ± 2.1, and in the third group (control) 13.7 ± 1.6. Statistical tests showed that the difference in the mean pain score was significant among the three groups. During the last 45 seconds of eye examination, the difference

Table 2. Comparison of the Mean Score of Pain Severity in Two Studied Groups

Pain severity	Group	Mean ± SD	Results of Independent-t and Mann-Whitney Between-Groups Test
Evaluation stage			
Before eye examination	Multisensory stimulation	3.6 ± 1.6	t = 0.75; P = 0.45
	Routine care	3.8 ± 1.9	
During examination of the first eye	Multisensory stimulation	6.4 ±1.7	t = 9.34; P = 0.001
	Routine care	10.0 ± 1.7	
During examination of the second eye	Multisensory stimulation	9.2 ± 1.6	t = 14.30; P = 0.001
	Routine care	14.2 ± 1.5	
30 seconds after the end of examination	Multisensory stimulation	7.1 1.8	t = 9.30; P = 0.001
	Routine care	10.6 ± 1.7	
1 minute after the end of examination	Multisensory stimulation	5.5 ± 1.5	t = 5.04; P = 0.001
	Routine care	7.2 ± 1.6	
1.5 minute after the end of examination	Multisensory stimulation	4.5 ± 1.3	Z = 2.93; P = 0.003
	Routine care	5.2 1.2	
2 minutes after the end of examination	Multisensory stimulation	3.8 ± 1.1	Z = 2.86; P = 0.004
	Routine care	4.4 0.9	
The results of variance analysis with repeated measurements	Between-groups multisensory stimulation	P < 0.001	F = 349.26
	Between-groups routine care	P < 0.001	F = 606.41
	Comparison of two groups in terms of the changes of pain within stages	P < 0.001	F = 56.58

Table 3. The Role of Interventional Variables in Pain Score Changes During Examination of the Eyes

Interventional Variables	The Results of Covariance Analysis	
Infant's gender	Effect of group	P < 0.001
	Simple effect of intervention	P = 0.83
	Interaction effect	P = 0.68
Gestational age	Effect of group	P < 0.001
	Simple effect of intervention	P = 0.59
	Interaction effect	P = 0.74
Birth weight	Effect of group	P < 0.001
	Simple effect of intervention	P = 0.25
	Interaction effect	P = 0.85

in the mean pain scores was not significant among three groups, so that the mean pain scores in this stage were 12.3 ± 2.4 in the first group, 11.2 ± 3 in the second group, and 12.1 ± 2.6 in the control group.

In the study of Costa et al. (2013) (19) that investigated the effect of 25% oral glucose 2 minutes before the eye examination for ROP screening, the results indicated that in the stage before examination, the mean pain score was not significantly different between two groups. The mean pain score was 0.8 ± 0.8 in the intervention group and 1.2 ± 1.2 in the control group. In the stage after eye examination, the mean pain score in the intervention group was 2.6 ± 1.1 and in control group 4.5 ± 1.3. There was a significant difference in the mean pain score between the two groups at this stage of eye examination.

The study of Boyle et al. (20) showed that eye examina-

tion for ROP screening is a painful procedure and the obtained results confirm the results of this study indicating increased pain score during the eye examination. Pain assessment tool in the study of Boyle was similar to the tool employed in the present study.

Marsh et al. (2005) in a study evaluated "the effects of local anesthesia on pain of eye examination for ROP screening", and the results showed that mean score of pain was not significantly different between intervention and control groups at the stages of 1 minute and 5 minutes before the eye examination. At the stage of initial examination and putting speculum in the first eye, the mean pain score had an increased trend, so that the mean pain score at this stage was 11.0 $\pm$ 3.2 in the intervention group and 13.5 $\pm$ 3.5 in the control group. Indeed, the rate of increase in the mean pain score was higher in the control group than the intervention group. The difference in the mean pain scores was significant between the two groups.

After the end of examination, a decrease was recorded in the mean pain scores in infants, so that the mean pain scores at the stages of 1 minute and 5 minutes after the examination were 9.3 $\pm$ 3.7 and 4.5 $\pm$ 2.5, respectively, in the intervention group and 10.5 $\pm$ 3.5 and 5.8 $\pm$ 3.2, respectively, in the control group. The difference in the mean pain scores was not significant between two groups at these stages (21).

In all above studies, the pain score was not high at the stage before examination, and almost in all studies the pain scores were not significantly different at the stage before examination. By starting the eye examination and putting the speculum in the eye, the pain score increased that this increase was usually higher in the control group than the other groups. By ending the eye examination, the trend stopped increasing and start to decline. However, the method used to control pain, duration of eye examination, type of eye examination, and pain assessment tools were different in various studies.

5.1. Conclusion

The overall objective of this study was to determine the effects of multisensory stimulation on pain caused by eye examination to screen retinopathy of prematurity in preterm infants. Given that premature infants undergo many painful procedures and multisensory stimulation is an effective non-pharmacological method of pain relief during painful procedures, and according to the results of the present study, implementation of multisensory stimulation program can lead to less increase in the pain severity. Therefore, the implementation of this program as a standard of care is recommended to reduce stress and pain in premature infants. It is recommended also to perform more studies about the effect of multisensory stimulation on physiological indices during eye examination in preterm infants and comparison of multisensory stimulation with other non-drug methods in pain control during the eye examination for ROP screening.

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