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Comparison of the effect of local anesthetic cream and orally administered glucose solution in reduction of pain in icteric newborns during venipuncture

M Noori-Shadkam[1]*, MH Lotfi[2], H Aarafi[3]

[1]Department of Community Medicine, School of Medicine, [2]Department of Epidemiology, Faculty of Health, [3]Department of Pediatric, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Abstract

Background: A number of studies have shown that orally administered sweet-tasting solutions reduce feeling of pain during invasive procedures. The local anesthetic cream EMLA has recently been shown to be safe for use in neonates. The present study aimed to compare the pain-reducing effect of EMLA cream with that of orally administered glucose during venipuncturing of newborns in Yazd city.

Methods: A randomized, controlled, double blind clinical trial was performed on 220 newborns undergoing venipuncture for clinical reasons. EMLA cream was applied to the skin of 106 of the newborns, along with orally administered sterile water as placebo. In addition, a 30% solution of glucose was administered orally to 114 neonates whose skin was treated with vitamin A+D cream as placebo. Symptoms associated with pain while venipuncturing measured by Neonatal/ Infant pain scale (NIPS) and crying time was compared between the two groups.

Results: There were no differences in background variables between the 2 groups. The results showed that the NIPS scores were significantly lower in the glucose group (Median: 2) compared with the EMLA group (median: 3) ($p<0.001$). The duration of crying in the first 2 minutes was significantly lower ($p<0.01$) in the glucose group (median: 2 sec) than in EMLA group (median: 9 sec). The NIP values higher than 3 were observed in 12.3% and 29.2% of neonates in glucose and EMLA groups respectively, where the difference was found to be statistically significant ($p<0.05$).

Conclusions: Our study showed that compared with EMLA cream, orally administered glucose can be more effective, tolerable and convenient in reducing pain from venipuncturing in neonates.

Keywords: Neonatal/Infant pain score; EMLA cream; Oral glucose

Introduction

There are some unavoidable situations in which invasive procedures are used for neonatal care. Venipuncture is the most common procedure used for both healthy and un-

***Correspondence:** M Noori Shadkam, MD, Department of Community Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Tel: +98-913-353-5419. E-mail: *mahmood 7072005@vahoo.com*

healthy babies. Sufficient experiments have demonstrated anatomic and physiologic potential of babies for feeling pain.[1, 2] Recent investigations suggested that experience of pain during neonatal period would affect the succeeding period of life.[3,4] Venipunture is a method of choice for taking blood from full-term babies[5]. The advantages of venipuncture over ankle sampling are obtaining sufficient volume of blood, lesser pain and more success rate.[6-8] Numerous studies show that oral administration of sweet-tasting solutions relieve signs of pain during invasive procedures.[9-11] This can be due to the release of endorphins as well as to the mechanism involved in pre-absorption of sweet-tasting substances.[12,13] EMLA cream is a local pain reducer consisting of lidocaine and prilocaine. It has been shown that using EMLA cream 60 minutes before venipuncturing can lead to feeling reduced pain in humans.[14] Moreover, the recent investigations have shown that EMLA, which is used in most countries such as Sweden, has no harmful effect on neonates.[15-17] With respect to oral administration of 30% glucose solution, studies indicated that it has no harmful effect and can be easily tolerated.[8]

Whereas, oral glucose exerts its pain reducing effect immediately, that of EMLA cream takes about 60 minutes. Therefore, ELMA cream has its limitations in regard to acute situations.[18-20] The pain reducing effects of EMLA cream and orally glucose solution have been studied separately. However, there are few reports in which their combined effects have been investigated.[21] The present study aimed to compare the pain reducing effects of EMLA cream and orally administered sweet-tasting solution on icteric newborns admitted to Shahid Sadoughi Hospital of Yazd city affiliated to Shahid Sadoughi University of Medical Sciences.

Materials and Methods

This double blind randomized clinical trial (RCCT) was conducted in Shahid Sadoughi Hospital situated in Yazd city, Yazd Province, Iran between October 2004 and June 2005. The study comprised full term neonates (≥38 weeks), aged more than 1 and less than 15 days, who underwent venipuncture for bilirubin measurement. Babies excluded from the study were those with neurolgic symptoms, gestational age<38 weeks, newborns with a history of sedation therapy or pain relieving medication 24 hours before admission as well as the neonates with no consent form. Data from an earlier study[15] was used to estimate the sample size by considering σ_1=7.5 (SD of crying time in EMLA group) and σ_2=6.7 (SD of crying time in glucose group). It was interesting to detect whether orally administered glucose could significantly reduce at least 3 seconds (d=3/sec difference) the mean of crying time, using study power of 0.90 (β=0.10) and (α=0.05). Considering an increase of 25%, a total of 230 subjects were randomly assigned to two different trial groups (115 each). The back of neonates' hands in group 1 were smeared with 0.5 g EMLA cream[14] and covered by dressing which were removed after 60 minutes. To reduce venous contraction and any stress in babies, venipuncture was delayed for 15 minutes. Five minutes before sampling, 1m of sterile water, as placebo, was then poured into each baby's mouth by means of a syringe. Group 2 were orally treated with 1ml of %30 solution of glucose[8] and similarly smeared with 0.5 g placebo ointment. Venipuncture

was done by a 21-gauge needle followed by bandaging the venipuncture site. The neonate was then placed on the nursery bed for 2 minutes, for evaluation under low stress condition. Each neonate had only a single chance of being included in the study. Duration of crying and response to pain were scored by NIPS [21] whereby the scale measured changes in six parameters including face appearance, crying, and respiratory status, movement in upper and lower extremities and alertness within two minutes from venipunturing. The highest and lowest score given to subjects were 7 and zero respectively where the highest value was correlated with the highest response to pain. A score of less than or equal to 3 was considered as painless or mild grade of pain. The tools of enquiry were a pre-coded questionnaire and clinical evaluation. Analysis was done by SPSS software package using appropriate non-parametric statistical tests such as Chi-square for the categorical and Mann-Whitney U Test for the numeric variables.

Results

In this study, a total of 10 neonates, 9 subjects in group I and one in group2, did not meet research criteria because of unsuccessful venipunture and were therefore excluded from the study. In regard to gender, 51 (48%) and 67 (59%) of neonates were females in groups 1 and 2 respectively, and in this connection, no significant difference was observed between the two groups. In addition, using student t-test, no significant difference was found in mean age, weight and level of serum bilirubin between two groups (Table 1). Using non-parametric Mann-Whitney U Test, it was found that the median of NIPS score of group 2 was significantly lower than that of group 1 ($P<0.001$). Moreover, applying the same statistical test to crying time it was shown (Table 2) that median crying time/sec, measured within the first two minutes of venipunturing, was shorter in the neonates of group 2 (2 sec) than in those of group 1 (9 sec), a difference shown to be statistically signifi-

Table 1: Demographic and biomedical data of subjects in two groups of neonate

Variable	n (%)		P value
	Group I	Group II	
Sex			
Male	58 (55)	55 (48.5)	
Female	48 (45)	59 (51.5)	NS*
Total	106 (100)	114(100)	
Mean age in days (range)	4 (2-15)	4.2 (2-15)	NS
Mean weight in g (range)	3250 (2350-4560)	3257 (2340-4450)	NS
Mean bilirubin mg/dl, (SD)	11 (6-22.5)	10.5 (6.5-23)	NS

*NS: Not significant

Table 2: Median of crying time period and pain score in two groups

Variable	Group I (n=106)	Group II (n=114)	P value
Median of time crying period/sec (range)	9 (0-70)	2 (0-75)	<0.01
Median of pain score/NIPS (range)	3(0-10)	2(0-9)	<0.001

cant (P<0.01). NIPS score of more than 3 was found in 29% and 12% of neonates in groups 1 and 2 respectively, a difference found to be highly significant (P<0.01). A distinct erythema was observed on the skin of 3 neonates in group 1 exposed to EMLA cream. This, however, was not found in any of the newborns in group 2.

Discussion

It was shown that oral prescription of glucose could reduce pain caused by venipuncturing in neonates.[8] EMLA cream has recently been shown to exert a similar effect.[14,22,23] Quantitative studies, however, have compared the pain reducing properties of these treatments in neonates. Our study, which is probably the first randomized clinical trial, aimed to compare the pain reducing efficacy of orally prescribed glucose and EMLA cream in Iranian neonates. The results obtained showed that orally administered glucose could be more effective than EMLA cream. NIPS and time of crying within two minutes used as criteria for comparing these methods showed that the values were lower in newborns receiving oral glucose than the neonates treated with EMLA cream. This is consistent with the results of two separate studies showing that neonates receiving oral glucose had lower scores of pain and crying times compared to those treated with EMLA cream.[8, 26] In these studies, no harmful effect was reported in regard to oral prescription of 30% solution of glucose. In another study performed on 201 neonates in Sweden, it was also shown that pain scores and crying times were lower in newborns receiving glucose [25]. Such a significant difference was reported in another study although criteria used for pain evaluation was Neonatal /infant pain scale (NIPS) score.[24] Carbajel believed that short period of crying and low score of pain in glucose group was due to longer time of sucking. However, other studies suggested that it could result from releasing endorphins and mechanism of preabsorption of sweet-tasting.[12,13] In a study conducted by Malekan Rade et al. in Iran, it was shown that the effect of lidocaine ointment and orally prescribed glucose were significantly more effective than breastfeeding and placebo. In this study, lidocaine was more effective than oral glucose in reducing crying time in neonates.[27] There was no side effect in relation to consumption of oral glucose in our study. This was also reported in a study carried out by Maria et al. who used 30% solution of glucose.[25] Similar studies also showed that full-term babies could easily take up oral glucose without any side effect.[8,24] Three neonates in our study showed a moderate erythema in the prescription site of EMLA cream. This was also shown by other studies.[14,21] Another advantage of using oral glucose over EMLA cream was that blood sampling could

be done immediately after prescription. This is useful in acute conditions, in which time saving is crucial. On the other hand, EMLA cream could have its limitation with respect to repeat venepunture,[14] a practice which increased the chances of met-hemoglobinemia.[23] Therefore, various studies recommend oral prescription of glucose, because it is less harmful, more effective and time saving compared to EMLA cream.[8,14,22,23] Further studies are needed to evaluate concurrent administration of EMLA cream and oral glucose in relation to pain reducing effect.

Our study showed that compared with EMLA cream, oral administration of glucose could be more effective, tolerable and convenient in reducing pain from venepunture in neonatal period. This may be explained by the fact that oral glucose could stimulate the release of endorphin in CNS, thereby leading to a more efficient control of pain as compared to EMLA cream which is a local pain alleviator.

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