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Effect of Multisensory Stimulation on Analgesia in Term Neonates: A Randomized Controlled Trial

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ABSTRACT

Many attempts have been made to obtain safe and effective analgesia in newborns. Oral glucose-water has been found to have analgesic properties in neonates. We investigated whether other sensory stimulation added to oral glucose provided more effective analgesia than oral glucose alone. In a randomized prospective double-blind trial, we studied 120 term newborns during heel prick. The babies were divided randomly into six groups of 20, and each group was treated with a different procedure during heel prick: *A*) control; *B*) 1 mL 33% oral glucose given 2 min before the heel prick; *C*) sucking; *D*) 1 mL 33% oral glucose plus sucking; *E*) multisensory stimulation including 1 mL 33% oral glucose (sensorial saturation); *F*) multisensory stimulation without oral glucose. Sensorial saturation consisted in massage, voice, eye contact, and perfume smelling during heel prick. Each heel prick was filmed and assigned a point score according to the Douleur Aiguë du Nouveau-né (DAN) neonatal acute pain scale. Camera recording began 30 s before the heel prick, so it was impossible for the scorers to distinguish procedure A (control) from B (glucose given 2 min before), C (sucking water) from D (sucking glucose), and E (multisensory stimulation and glucose) from F (multisensory stimulation and water) from the video. Procedure E (multisensory stimulation and glucose) was found to be the most effective procedure, and the analgesia was even more effective than that produced by procedure D (sucking glucose). We conclude that sensorial saturation is an effective analgesic technique that potentiates the analgesic effect of oral sugar. It can be used for minor painful procedures on newborns. **(*Pediatr Res* 51: 460–463, 2002)**

Newborns feel pain (1, 2). Repeated painful stimuli lower their pain threshold (3, 4) by overstimulation of NMDA receptors, which may lead to excitotoxic brain damage (5). Until a few years ago, it was claimed that the word pain was inappropriate for newborns, as pain is a subjective experience that newborns, because of their age, cannot have (6). Until the 1980s, analgesics were rarely administered to newborns even in the case of surgery (7). Now we know that anesthesia reduces brain damage due to hypoxemia, hypertension, tachycardia, variations in heart rate, and increased intracranial pressure (8, 9), all of which are particularly dangerous because of immature cerebral vasoregulation in the premature (10).

The number of painful stimuli needs to be kept to a minimum, and every effort should be made to render them less painful. Guidelines for neonatal analgesia have been suggested (11–15), especially for the most routine type of pain, blood sampling, which is usually performed by heel prick. To avoid the drawbacks of general and local analgesics (16–21), types of nonpharmacologic analgesia have been proposed, including nonnutritional sucking and instillation of glucose or other sweet liquids on the newborn's tongue (22). The analgesic effect of glucose is thought to stimulate an increase in plasma concentrations of β-endorphin (23–27) by a preabsorptive mechanism (28).

Very recently, we observed that sensory stimuli combined with oral glucose during heel prick greatly reduced manifestations of pain in preterm babies (29). This combination was even more effective in premature babies than oral glucose. We called it sensorial saturation (SS) because it works through competition between nonpainful and painful stimuli, not to indicate that nonpainful stimuli cause saturation of sensorial pathways. In the present study, we investigate whether SS promotes analgesia in term babies and whether it is more effective than that obtained with sugar alone. We also studied the various components of SS (sucking, oral glucose, other sensory stimuli) to determine which components were the most effective.

METHODS

Subjects. This prospective randomized double-blind clinical study was designed to study the reaction of normal term neonates to pain in the Siena hospital. The study was approved

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by the local ethics committee, and the parents gave their written informed consent. Five parents refused. Inclusion criteria were the following: Apgar score at least 9 at 5 min; gestational age 38–41 wk; more than 48 h after delivery; more than 2 h after last meal; availability of the physiotherapist and a researcher to film the heel prick. The blood sampling studied was that carried out at 96 h of age for phenylketonuria and hypothyroid screening. This particular sampling was chosen because it is compulsory for all babies, has a standard procedure, is always carried out 3 h after a meal, and is long enough after delivery to permit stabilization after cesarean section. None of the babies had ever been given analgesic or sedative drugs.

Protocol. A total of 120 babies were studied. Heel prick was carried out in a quiet room barred to other persons. Parents could be present, but they had to be silent and abstain from interfering during the preparatory phase and for 30 s after the heel prick. The sampling was performed by experienced nurses; they held the baby's heel in their hands before the prick to warm it; after the preparatory period, they disinfected the heel and lanced it with a sterile blood lancet, waited 2 s, and began sampling. In all cases, the analgesic procedure was carried out by the same experienced physiotherapist (A.N.).

The babies were randomly assigned to one of six groups on the basis of a random number table. Calculation of sample size with mean and SD of 2.5 showed that to achieve 80% power and 0.02 type I error (α) in detecting a 2-point difference in Douleur Aiguë du Nouveau-né (DAN) scale between groups, at least 17 subjects were required in each group.

Each group underwent a different procedure for the heel prick:

A Control group. No analgesic procedure.

B Glucose before heel prick. The tip of a 1-mL syringe without needle was placed in the baby's mouth, and 1 mL of 33% glucose solution was instilled with gentle movements of the syringe to stimulate sucking for 30 s; heel prick was performed 120 s later.

C Water during heel prick (sucking). The tip of a 1-mL syringe without needle was placed in the baby's mouth, and 1 mL of distilled water was instilled with gentle movements of the syringe to stimulate sucking for 30 s before, during, and after heel prick.

D Glucose and sucking. As for C, but the syringe contained 33% glucose solution.

E Sensorial saturation. As for D, but with a series of sensory stimuli before, during, and after the heel prick (see below).

F Sensorial saturation without sugar. As for E, but the syringe contained distilled water.

We used 33% glucose/water solution because of its availability in our ward.

The physiotherapist did not know whether the syringe contained water or glucose solution. The baby's reaction was filmed with a SONY video camera from 30 s before to 30 s after the heel prick. The films were seen by observers who did not know the method used each time. It was impossible for them to distinguish the following pairs of groups in the films: A (control) from B (glucose given 2 min before), C (sucking water) from D (sucking glucose), and E (multisensory stimulation and glucose) from F (multisensory stimulation and water).

The observers attributed a state of alertness according to the observational rating system of Prechtl and Beintema (30), which distinguishes five types of behavioral state: *1*) eyes closed, regular breathing, no movements; *2*) eyes closed, irregular breathing, no movements; *3*) eyes open, no gross movements; *4*) eyes open, continual gross movements, no crying; *5*) eyes open or closed, fussing, or crying. They then assigned a score on the DAN scale (Table 1) (31, 32). This scale scores pain from 0 to 10, where 0 is no pain and 10 is maximal pain. It evaluates three items: facial expression, limb movements, and vocal expression.

SS. This procedure consisted of the following: *1*) laying the infant on its side with legs and arms flexed but free to move; *2*) looking the infant in the face, close up, to attract its attention and, simultaneously, *3*) massaging the infant's face and back; *4*) speaking to the infant gently, but firmly; *5*) letting the infant smell the fragrance of baby perfume (Colonia Analcolica-Humana) on the physiotherapist's hands; *6*) instilling 33% glucose on the infant's tongue with the timing and method described in C.

Statistical analysis was performed with GBStat v 6.5 PC software, using multiple t test comparisons with Bonferroni adjustment to α (cry data) and the Kruskal-Wallis ANOVA test for comparison of median DAN scores between groups.

RESULTS

From February to June 2001, we studied 120 newborns, all of white Caucasian race. (Table 2 shows the characteristics of the six groups of infants enrolled in the study.

Figure 1 shows mean DAN scores obtained with the five analgesic procedures and controls. We observed no statistically

Table 1. *DAN*: behavioral acute pain-rating scale for neonates*

Measure	Score
Facial expressions	
Calm	0
Snivels and alternates gentle eye opening and closing	1
Determine intensity of one or more of eye squeeze, brow bulge, nasolabial furrow	
Mild, intermittent with return to calm	2
Moderate	3
Very pronounced, continuous	4
Limb movements	
Calm or gentle movements	0
Determine intensity of one or more of the following signs: pedals, toes spread, legs tensed and pulled up, agitation of arms, withdrawal reaction	
Mild, intermittent with return to calm	1
Moderate	2
Very pronounced, continuous	3
Vocal expression	
No complaints	0
Moans briefly; for intubated child, looks anxious or uneasy	1
Intermittent crying; for intubated child, gesticulations of intermittent crying	2
Long-lasting crying, continuous howl; for intubated child, gesticulations of continuous crying	3

* See Ref. 31.

Table 2.

	A Control	B Glucose before heel prick	C Sucking water during heel prick	D Sucking glucose during heel prick	E SS	F SS
Mean birth weight (range) grams	3320 (3900–2950)	3160 (3790–2820)	3150 (3570–2840)	3570 (3900–3120)	3610 (3840–3470)	3430 (3900–2690)
Boys/girls	11/9	12/8	9/11	10/10	9/11	11/9
Median arousal state score (1–5)	3	3	3	3	3	4
Range	1–4	1–4	1–4	1–4	1–4	2–5

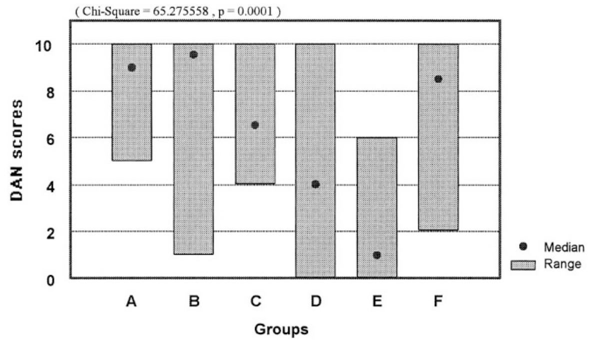

Figure 1. Comparison of median DAN scores of the five analgesic treatments and controls. (*A*) controls, (*B*) oral 33% glucose, (*C*) sucking, (*D*) glucose and sucking, (*E*) SS with glucose, (*F*) sensorial stimulation without oral glucose.

significant reduction of score in procedures B (glucose) and F (SS without sugar) with respect to A (controls). Procedure C (sucking) disclosed a reduction of DAN score ($p = 0.001$), but the maximum of analgesia with respect to controls was obtained with procedures D (glucose plus sucking) ($p < 0.0001$) and E (SS) ($p < 0.0001$). Procedure E was even more effective than procedure D ($p = 0.004$).

Figure 2 shows the mean duration of crying in the first 30 s after lancing. We observed a decrease from a mean value of 25 s with procedure A (control) to 7 s with procedure D and 2.8 s with procedure E (SS).

DISCUSSION

The methods used in previous studies of nonpharmacologic analgesia in neonates have led to a considerable reduction but not elimination of signs of pain perception (21, 33–39). The best results have been obtained with simultaneous administration of oral sugar and pacifier (40), which also has been used during venous blood sampling (31). Nevertheless, most of these studies were performed with a waiting time of 2 min between instillation of sweet solution and heel prick, sometimes too long a time for a busy ward. Moreover, analgesia limited to administration of analgesic substances leaves out human presence, which is most important in moments of pain (41, 42). SS includes human presence and requires only a few seconds.

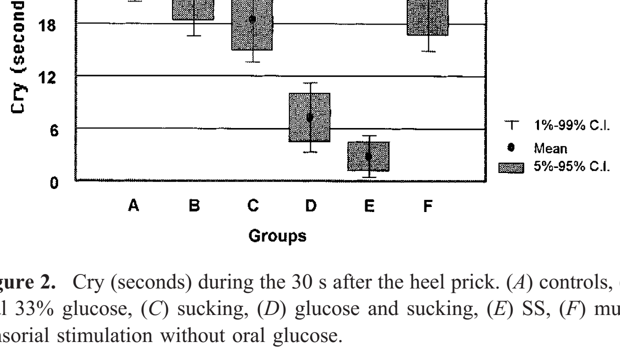

Figure 2. Cry (seconds) during the 30 s after the heel prick. (*A*) controls, (*B*) oral 33% glucose, (*C*) sucking, (*D*) glucose and sucking, (*E*) SS, (*F*) multisensorial stimulation without oral glucose.

Our results confirm the analgesic effect of orally administered glucose: analgesia was statistically greater in the group of babies who sucked 33% glucose (group D) than that of babies who sucked water (group C).

When glucose was given 2 min before heel prick (B), pain score was not significantly different from control (A). Signs of pain, nevertheless, decreased when sugar was offered immediately before and during heel prick to stimulate sucking (D). This is in line with Johnston *et al.* (43) who advised giving sugar 2 min before and during heel prick in preterm babies for maximal analgesic effect and with those authors proposing pacifiers plus glucose during heel prick (31). Sugar, therefore, does not seem to create analgesia by a pharmacologic effect alone but seems rather to have an effect on the central control of painful stimuli (44) according to the gate control theory (45): the brain is not a passive receiver of nociceptive input but can influence the information received, deciding whether it is important enough to record. Stimulation of sensory channels prevents nociceptive nerve impulses from getting through (46, 47).

So we increased with SS the number of channels engaged during heel prick by adding auditory, tactile, visual, olfactory, and vestibular stimuli to the gustatory one. Alone (F), these stimuli did not produce an analgesic effect, or rather they increased awareness and irritated the baby (Table 2). When combined with glucose (E), however, they increased the analgesic effect. To function, they evidently require a favorable background situation such as that of a baby already intent on sucking a sweet liquid.

The preeminence of the gustatory stimulus may be explained by the fact that the chemoreceptor system is the first to become active in all species of animals and is already functional in the fetus (48–50).

Different sensory stimuli have been used to activate gate-control mechanisms to block nociceptive transmission: massage (51) or water mattresses (52), tactile (53) and acoustic (54) stimuli or both (55), sucking (39), oral sucrose or glucose (28, 35, 36, 38, 40, 56–58), and other sweet liquids (22, 34). Nevertheless, the technique used in the present study is the first to obtain an evident and significant decrease in the response to

pain in term neonates by stimulating various sensory channels simultaneously and in a codified manner. Simultaneous stimulation of various channels had already been used or in a noncodified manner, namely, general consolation by parents (33) or unsuccessfully combining sucrose with rocking (59).

With SS, we found an almost complete absence of pain reaction during heel prick; the babies rarely cried, and if they did, only for a few seconds (Fig. 2). Other researchers (33–37) succeeded in reducing crying of premature babies with oral sucrose, but the infants nevertheless cried for many seconds and in some cases for more than 1 min, much more than with our technique, which reduced the mean crying time in the 30 s after heel prick to 2.8 s.

Haouari *et al*. (37) were on the right track when they wrote, "We don't know whether simply cuddling an infant after heel prick is as effective in reducing crying as 50% sucrose." In actual fact, concentrated sugar solution is much more effective than cuddling, but the latter or at least its sensory component, *i.e.* massage, voice, rocking, eye fixing, adds further analgesia to the analgesic effect of glucose and provides a human factor in the form of company to a baby facing pain. SS is a technique that can be used for all newborns undergoing blood samples or other minor painful procedures.

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