

# “Sucrose analgesia”: absorptive mechanism or taste perception?

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## Abstract

**It remains unclear whether “sucrose analgesia” is related to a pre- or postabsorptive mechanism. In a double blind cross over study sucrose reduced the pain response of preterm infants exposed to heel prick blood samples only when it was administered into the mouth. It was ineffective when administered intragastrically.**

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The intraoral administration of sugars can have analgesic actions after minor invasive procedures in neonates.<sup>1</sup> However, it is not clear whether these effects are related to the pre- or postabsorptive mechanism, and by what route this effect is mediated.

A study was undertaken to evaluate the pre- and postabsorptive analgesic effects of sucrose in premature infants using a randomised, double blind, placebo controlled trial.

## Methods

Thirty preterm infants (gestational age 32 to 36 weeks; postnatal age > 24 hours) were recruited to the study. All were fed through a nasogastric tube and at least two heel prick blood samples were taken for bilirubin determination, within a period of no longer than 48 hours.

Each baby was randomly allocated to receive solution A (sterile water placebo) or solution B (25% w/v sucrose) before the first heel prick.

The same baby was given the same solution, before the second heel prick, but by the alternative route (nasogastric tube or intraoral). Two minutes after the administration of the test solution the heel prick was performed by lancing the heel with an Autolet device. Blood samples were taken by the same operator, standardising the procedure.

The baby's response to the heel prick was measured by behavioural response and crying time. Behavioural response (score) was based on five features—four facial expressions (brow bulge, eye squeeze, nasolabial furrow and open mouth)—and the presence of cry. Each feature was recorded at 1, 3, and 5 minutes after lancing as either 0 (absent) or 1 (present).<sup>2</sup> Maximum score was 15, minimum 0.

Crying in the five minutes after sampling was recorded onto an audiotape and later analysed as the percentage observation time spent crying.<sup>2</sup>

The baby's behavioural state<sup>3</sup> was recorded before the intervention.

Differences between unpaired data (group A vs group B, same route of administration) were assessed using the Mann-Whitney U test; differences between paired data (same solution group, different route of administration) were assessed using the Wilcoxon matched pairs signed rank test.

The study was approved by the hospital ethics committee and informed parental consent was obtained.

## Results

Details of the group of 15 infants receiving the placebo (group A) and of the 15 infants receiving the sucrose (group B) are shown in table 1. The percentage of time spent crying and the behaviour score after lancing in the two different groups of babies, receiving the test solution into the mouth or into the stomach, are shown in table 2.

A significant reduction in crying time ( $p=0.006$ ) and in behaviour score ( $p=0.002$ ) was present in the sucrose group (group B) compared with controls (group A) when babies received the solution intraorally. There was no significant difference for either behaviour score or crying time between solutions A and B when the nasogastric route was used. For infants given solution A (placebo), there were no significant differences in any of the two measured variables for either method of administration. For infants given solution B (25% sucrose), there was a significant reduction in behaviour score ( $p=0.001$ ) and crying time ( $p=0.008$ ) when they received the solution intraorally compared with when it was administered through the nasogastric tube.

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Table 1 Details of 30 infants receiving either placebo or sucrose

	Gestational age (median) (weeks)	Birthweight (median) (g)	Median postnatal age (days) (range)	Median arousal state before intervention (1-5) (range)	Median time spent squeezing heel(s) (range)
Group A (water group)	34	2410	4 (2-6)		
Intraoral				2 (1-4)	76 (35-120)
Tube				1 (1-4)	73 (43-131)
Group B (sucrose group)	35	2380	3 (2-5)		
Intraoral				2 (1-4)	90 (45-150)
Tube				2 (1-4)	82 (40-175)

Table 2 Percentage of time spent crying and behaviour score after lancing

	Percentage cry				Behaviour score			
	Water group intraoral	Water group tube	Sucrose group intraoral	Sucrose group tube	Water group intraoral	Water group tube	Sucrose group intraoral	Sucrose group tube
Median	22*	27	6	18.3	9	10	5*	9
Interquartile range	10.6-40	11.6-47	0.6-15	11.6-41.6	6-12	6-14	3-6	8-10
Range	1-72	0-93	0-31	0-72	4-15	1-20	1-10	6-17

### Discussion

This study was designed principally to determine whether the route by which sucrose is delivered determines its "analgesic" effect. The crying time and behaviour score were both significantly reduced when the neonates were given the sugar via the intraoral route rather than the nasogastric route (group B). Sucrose was no better than placebo when administered directly into the stomach as the babies receiving nasogastric administration of either solution A or B did not show any significant differences.

The possibility that rapid absorption of sugars through the buccal mucosa may be involved in is contradicted by the lack of effects of sucrose after intragastric administration and the absence of scientific evidence that the absorption of sugars takes place through the buccal mucosa even for those sugar based drugs used intraorally to treat acute hypoglycaemia.<sup>4</sup>

Alternatively, the recruitment of "taste sense" could be the method by which intraoral administration of sucrose initiates analgesia and, possibly, activates the endogenous opioid system.<sup>1</sup>

The quality and the intensity of the sweet signal stimulating the taste sense is difficult to investigate. Human beings seem unable to dis-

criminate between the taste of different sugars, a condition called "monogeusia".<sup>5</sup> The different sugars probably act along a common sensory pathway binding to a single class of cellular membrane receptors.<sup>5</sup> The incapacity to distinguish between sucrose, fructose, and glucose could also explain why these three sugars promoted the same intensity of analgesia in rut pups, as observed by Blass.<sup>6</sup> We obtained similar results in human neonates when comparing the effects due to sucrose and glucose.<sup>2</sup>

In conclusion, this study shows that the engagement of the taste sense is essential to promote the "sucrose analgesia" in neonates exposed to minor painful procedures.

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