

Randomised controlled trial of sucrose by mouth for the relief of infant crying after immunisation

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Abstract

Objectives—To evaluate the effect of sucrose solution given by mouth on infant crying times and measures of distress in the immunisation clinic.

Design—Randomised, double blind, placebo controlled trial of sucrose solution 75% wt/vol *v* sterile water as a control.

Setting—The immunisation clinic of the Women's and Children's Hospital, Adelaide.

Patients—A total of 107 healthy infants attending for 2, 4, or 6 month immunisations with polio by mouth (Sabin), intramuscular diphtheria, tetanus, and pertussis (DTP), and intramuscular *Haemophilus influenzae* type b were randomised to receive 2 ml 75% sucrose solution or sterile water by mouth before the two injections.

Methods—The duration of infant crying was recorded during and immediately after two intramuscular immunisations and infant distress was assessed by a visual analogue scale (Oucher scores) independently by a nurse and a parent.

Results—The administration of 2 ml 75% sucrose solution by mouth reduced the infant crying time and Oucher distress scores after immunisation with DTP/H influenzae type b.

Conclusions—Infant immunisation by intramuscular injection is a distressing procedure for infants and parents. Sucrose solution at a high concentration reduces infant distress and is safe and clinically useful in this setting.

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Keywords: infant analgesia; sucrose; immunisation

Infants undergoing medical procedures experience pain and its unpleasant consequences, and this pain is often underestimated and undertreated.¹ The issue of appropriate analgesia for younger paediatric patients is gaining interest as methods are developed to evaluate pain in this population.² In the developed world the most common painful procedure performed on infants is immunisation, a process involving repeated injections in the first year of life. The infants are usually healthy outpatients, performance is swift, immediate distress shortlived, and their "analgesic" needs are overlooked. Sucrose may provide a simple, safe, and effective reduction in the distress experienced by these infants as the taste of sucrose by mouth has been shown to stimulate endogenous cerebral opioid pathways in labo-

ratory settings.^{3,4} The effects are rapid and persist for three to five minutes,⁵ ideal for the immunisation procedure.

"Sugarball anaesthesia" for newborn infants undergoing circumcision was used as early as the 1940s⁶ and the use of glycerine on pacifiers is familiar to ultrasonographers. In 1991 Blass and Hoffmeyer showed that term infants receiving 12% sucrose solutions before heelprick blood collection cried 50% less than infants who received sterile water.⁷ Subsequently, Haouari *et al* showed a significant trend in the reduction in crying time in full term neonates undergoing heelprick blood collection with increasing concentrations of 2 ml sucrose solutions from 12.5 to 50% wt/vol.⁸ The dose dependent phenomenon may explain the failure of another study, using lower sucrose concentrations, to show a clinically worthwhile effect.⁹ The study of Haouari *et al* was criticised because the infants were denied any additional soothing or tactile comforting during the post heelprick phase.¹⁰ A modest analgesic effect was shown by Barr *et al* using three 0.25 ml doses of a 50% sucrose solution by mouth in infants receiving immunisation with diphtheria, tetanus, and pertussis (DTP) alone, but this study also disallowed parental cuddling.¹¹

We explored the clinical efficacy of sucrose as an analgesic in the immunisation clinic as a supplement to the natural practice of infant soothing applied by the parents and a single nurse practitioner.

Patients and methods

PATIENTS

The immunisation clinic at the Women's and Children's Hospital is a "drop in" service provided by a single nurse practitioner. Routine paediatric immunisation advice and administration are offered. The infants attending the clinic are representative of the general population of Adelaide, South Australia.

INCLUSION CRITERIA

The parents of all healthy infants attending the Women's and Children's Hospital immunisation clinic for the routine 2, 4, and 6 month polio by mouth (Sabin) and DTP and *Haemophilus influenzae* type b intramuscular immunisations according to the Australian National Health and Medical Research Council recommendations¹² were invited to participate in the study.

EXCLUSION CRITERIA

The following infants were excluded from the study: infants with an intercurrent illness; infants born at less than 34 completed weeks'

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Table 1 Details of infants enrolled into study

Solution	No of infants	Mean (SD) age (weeks)	Sex (male:female)	Pacifier use	Paracetamol given
Control	53	16.7 (8.2)	24:29	7	3
75% Sucrose	54	17.4 (8.0)	32:22	3	5

gestation; infants where there was a parental desire for an arm injection site; infants unable to tolerate fluids by mouth; infants with a diagnosis of cerebral palsy where the response to painful stimuli may have been altered; infants where there was a modification of standard protocol (for example, combined diphtheria and tetanus or *H influenzae* type b alone); and infants where informed parental consent was not obtained.

METHODS

Permission to perform the study was obtained from the ethics committee of the Women's and Children's Hospital, Adelaide. Informed consent was obtained from the parents. Infants were randomised consecutively to receive solutions of 2 ml 75% sucrose solution (wt/vol) or sterile water according to the closed envelope technique. Solutions were drawn from coded bottles and administered by syringe. The nurse and parents were blinded to the nature of the solutions throughout the study. The dose of sucrose was higher than that used in other studies and was based on a pilot study in 18 infants using a 50% sucrose solution where no clinically appreciable infant relief could be shown.

The single nurse practitioner conducted the consultation in her standard manner including advice, data collection, preparation and administration of immunisation solutions, and the supervision of soothing techniques. She administered all the test solutions given by mouth. Infant injections were given in the thigh. Polio immunisation was given by mouth first, followed by the test solution which was given over a period of up to 15 seconds. *H influenzae* type b immunisation was then administered in the left leg and immediately after (within five seconds) DTP was administered in the right leg. The nurse used her usual soothing techniques (encouraging parents to cuddle the infant over one shoulder while she employed a distracting, low pitched rattling noise). The use of an infant pacifier or pretreatment with paracetamol was specifically noted. All infants were in the awake state at the time of the procedure.

Crying from onset after the first injection until all crying activity had ceased, up to a maximum of three minutes, was recorded on audio tape and later analysed blindly by a separate investigator for the duration of crying.

Crying time was defined in three ways: (a) the first cry (seconds), defined as the duration of continuous audible crying from onset until a crying free interval of more than five seconds; (b) the total sum (seconds) of audible crying within the first three minutes from onset; and (c) the duration (seconds) from the start of crying until the finish of the last cry (maximum three minutes). Analyses were repeated in a blinded fashion to confirm the reproducibility of measurement, which was high (> 95%). Crying time data were analysed by a two tailed Student's *t* test.

At the end of the consultation the nurse and care giver recorded their subjective assessment of distress suffered by the infant on an Oucher chart, a visual analogue score from 0 to 100.¹³ A score of 0 indicated no distress, whereas a score of 100 was the worst distress possible for the infant. The nurse and parent remained blinded to each other's response. Oucher scores are not normally distributed and were analysed by the Mann-Whitney U test (Systat).

Results

One hundred and ten infants were enrolled in this study. Three were withdrawn after randomisation. Technical difficulties with the cry recording occurred in two of these infants and, in the third, the parent did not complete an Oucher chart. Of the remaining 107 infants there were 56 boys and 51 girls, mean (SD) age 17.1 (8) weeks, with an age range of 7–38 weeks. Two infants were born prematurely at 34 weeks' gestation; the others were born at term. A pacifier was used with 10 infants and paracetamol was administered to eight by the parent before immunisation. One child had haemophilia and another was in a hip spica for congenital hip dislocation. The administration of test solutions was well tolerated by all infants. There was no significant difference between the groups in age, sex, pacifier use, and paracetamol administration.

Table 1 gives details of how the infants were distributed between the groups. Table 2 gives the crying times and Oucher scores recorded in the sucrose treatment group compared with controls. Infants receiving 75% sucrose solution had a significant reduction in all measures of crying and a less significant reduction in Oucher scores compared with the controls. The mean duration of the first cry was reduced from 42 to 29 seconds ($p < 0.0003$), the mean total sum of crying time in the first three minutes was reduced from 59 to 36 seconds ($p < 0.000008$), and the mean duration of crying from start to finish was reduced from 69 to 43 seconds ($p < 0.00002$). The mean Oucher scores awarded by the nurse were reduced from

Table 2 Crying times and Oucher scores (0–100 scale) of infants receiving sucrose or control solution; values are mean (SD)

Solution	First cry (s)	Sum total crying (s)	Start to finish crying (s)	Oucher score (nurse)	Oucher score (parent)
Control (n=53)	42 (21)	59 (30)	69 (34)	43 (19)	54 (24)
75% Sucrose (n=54)	29 (18)	36 (21)	43 (24)	35 (18)	47 (23)
	($p < 0.0003$)	($p < 0.000008$)	($p < 0.00002$)	($p < 0.02$)	($p < 0.1$)
Difference in means (SE)	13 (3.8)	23 (5.0)	26 (5.7)	8 (3.8)	7 (4.5)

43/100 to 35/100 ($p < 0.02$) and by the parents from 54/100 to 47/100 ($p < 0.1$, not significant).

Discussion

The performance of immunisation by injection is essential in the provision of primary care to infants, but is a distressing experience for the infant, parent, and practitioner. This is confirmed by our study. Parents often report withholding follow up immunisation from their infants on account of the distress seen. This will contribute to falling community compliance with recommended schedules. Although immunisation continues to be provided in this manner, the issue of infant analgesia must be addressed. We have shown that the administration of a 75% sucrose solution before two immunisation injections reduces infant crying times by nearly 40% and reduces the level of infant distress perceived by those present. Administration is quick, easy to perform, safe, and well tolerated. Parents were keen to participate in the study, recognising the inadequacy of information in this area of childcare.

There are many factors that may determine the expression of distress by infants in immunisation clinics. Infant factors include the current state of health, underlying personality, state of alertness, and state of satiety. Parental and nurse/practitioner factors include cultural and individual attitudes, competence, personality, and state of relaxation. External factors include methods of soothing and distracting, the use of pacifiers, and the use of analgesia. It is impossible to control for all contributing variables, but in randomisation and the performance of blinded assessments we aimed to assess the clinical utility of sucrose solutions in reducing measures of infant distress.

Unlike other published studies all immunisations were given by the same nurse in a reproducible fashion using her routine methods of soothing for each infant, blinded to the solution they had received. Parents were also encouraged to cuddle and comfort their infants, and this continued until both the nurse and parent perceived that the infant no longer needed soothing. The denial of such practices was not thought to be ethical by the investigators.

A volume of 2 ml (less than half a teaspoonful) is comparable in volume and sugar content to commonly administered proprietary syrups, including antibiotics and antipyretics. There is minimal risk to infant dentition by the infrequent administration of sucrose in this fashion. The utilisation of a pacifier was low. Blass and Hoffmeyer showed that neonates given pacifiers dipped in water during circumcision spent less time crying than a control group without pacifiers, and that the effect was further enhanced with a 24% sucrose solution.⁷ Pacifier use may have an additional benefit in immunisation clinics, but is not acceptable to all parents.

The National Health and Medical Research Council (Australia) guidelines suggest the use of paracetamol before immunisation, primarily as an antipyretic. Unlike sucrose, it provides

little amelioration of "pain" in the immediate postoperative period for neonates circumcised under local anaesthesia¹⁴ and would not be expected to contribute to immunisation analgesia. It is often presented as an artificially sweetened preparation; however, this "analgesic" aspect of paracetamol occurring at least 20 minutes before enrolment in only eight infants should not have affected the study given the short duration of "sucrose taste" analgesia.

The Oucher scale was chosen because it combines a validated pain scoring system with facial representations of increasing distress to reinforce to parents the nature of assessment required.¹³ The scores confirm that DTP/H influenzae type b immunisations are a distressing experience for the infant, parent, and practitioner. There was a significant reduction in nurse Oucher scores with sucrose solution compared with controls (35/100 v 43/100; $p < 0.02$). Parent scores were reduced, but did not reach significance (47/100 v 54/100; $p < 0.1$). These improvements were not as great as seen in crying times and may reflect the avoidance of reporting extremes and a tendency to choose towards the mean. The reduction in perceived distress remains clinically significant, however.

The analysis of audible crying is a crude tool for the assessment of distress in infants, but is an objective measurement. All three measures of crying time showed a 35–40% reduction in infants receiving the sucrose solution. The different measurements were used to obtain a broad picture of the infant's pain response. The reduction in crying is modest compared with the neonatal study of Haouari *et al*⁶ and comparable with the study by Barr *et al*¹¹ in which infants aged 2 and 4 months receiving only DTP immunisation and 0.75 ml (total) of a 50% sucrose solution had a reduction in crying time from 82 to 69% of the first minute after injection. The improvement seen in this study, however, unlike others, is additive to the comfort provided by soothing measures. We should not underestimate the likely analgesic effect of cuddling and auditory stimuli.¹⁰ We should also be wary of regarding sucrose as providing major analgesia or as a substitute for appropriately planned analgesia in today's surgical practice.¹⁵

This study confirms the effectiveness of sucrose for the relief of infant crying and shows that it has great utility in an immunisation clinic. Whether "a spoonful of sugar will help the medicine go down" for older children requiring immunisation is worthy of further study.

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