

Effective Analgesia Using Physical Interventions for Infant Immunizations

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KEY WORDS

immunizations, vaccines, pain management, infant, analgesia

ABBREVIATIONS

5 S's—swaddling, side/stomach position, shushing, swinging, and sucking

ANOVA—analysis of variance

IRB—internal review board

This trial has been registered at www.clinicaltrials.gov (identifier NCT01368861).

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WHAT'S KNOWN ON THIS SUBJECT: Pain during routine infant immunization causes parental anxiety. Oral sucrose solutions are effective pain-reduction strategies. Few studies have measured a combined strategy of a physical intervention along with sucrose to decrease the infant's pain response.



WHAT THIS STUDY ADDS: We demonstrate that a physical, nonpharmacological intervention called the 5 S's (swaddling, side/stomach position, shushing, swinging, and sucking) provides significant pain reduction with or without sucrose during routine 2- and 4-month vaccinations.

abstract

FREE

BACKGROUND: To measure the analgesic effectiveness of the 5 S's (swaddling, side/stomach position, shushing, swinging, and sucking) alone and combined with sucrose, during routine immunizations at 2 and 4 months.

METHODS: We conducted a prospective, randomized, placebo-controlled trial with 2- and 4-month-old infants during well-child visits. Patients were assigned into 4 groups (2 × 2) receiving either 2 mL of water or 2 mL of 24% oral sucrose and then either standard-of-care comfort measures by parents or intervention with the 5 S's immediately postvaccination. The Modified Riley Pain Score was used to score the infants' pain at 15-second intervals for 2 minutes, then every 30 seconds up to 5 minutes postvaccination. Repeated-measures analysis of variance examined between group differences and within-subject variability of treatment effect on overall pain scores and length of crying.

RESULTS: Two hundred thirty infants were enrolled. Results revealed significantly different mean pain scores between study groups with the exception of the 5S's and 5S's with sucrose groups. These 2 groups had lower similar mean scores over time, followed by sucrose alone, then control. The same trend was found with the proportion of children crying as with the mean pain score outcome measure.

CONCLUSIONS: Physical intervention of the 5 S's (swaddling, side/stomach position, shushing, swinging, and sucking) provided decreased pain scores on a validated pain scale and decreased crying time among 2- and 4-month-old infants during routine vaccinations. The use of 5S's did not differ from 5S's and sucrose. *Pediatrics* 2012;129:815–822

Immunization administration is one of the most common office procedures performed on a healthy infant in a pediatric practice.¹ Although parents understand the importance of immunizations, the pain and discomfort associated with this procedure is the primary reason parents elect not to perform timely vaccinations.² Parents are not the only ones concerned about causing unwanted pain. Physicians and nurses are 6 times less likely to give all the recommended vaccines at a visit if the number of injections is ≥ 3 ³ and physicians have “strong concerns over administering 4 or more vaccines at a single visit.”⁴

It is clear that clinicians would like to reduce the pain and parental anxiety, during and soon after vaccination; however, there is little evidence that the use of analgesics such as acetaminophen or ibuprofen are effective.^{5,6} One study surveyed 140 pediatricians and found that $>80\%$ used acetaminophen, which has added sucrose for palatability as an oral analgesic, pre- or postvaccination, as a pain-reducing mechanism.⁷ However, a more recent study conducted by Pymula found that acetaminophen use at the time of vaccination significantly reduces antibody levels to several of the vaccine antigens.⁸ In light of this finding, it is prudent to reevaluate the use of oral antipyretic analgesics with sucrose during routine vaccination and provide alternative pain-reduction mechanisms. Nonpharmacologic pain relief may be the best option for infants undergoing painful procedures.

Recent reviews of the literature support the use of concentrated sucrose alone as effective analgesia for the immunization of infants.^{9–12} Although topical anesthetics work,¹³ they are generally not used in a busy practice because of expense and a prolonged waiting period after application. Additional interventions to reduce pain during procedures in neonates include nonnutritive

suck, breastfeeding, skin-to-skin, and swaddling.^{14–19} Two studies report moderate success at alleviating infant pain when combining 2 nonpharmacologic techniques together: (1) swaddle and pacifier²⁰ or (2) swaddle and sucrose.²¹ Psychological interventions, in which a parent or nurse distracts the infant with a toy or a parent is coached by a health care provider, have also shown some promise.²² Taddio et al have advocated for health care providers to consider combining multiple strategies to help mitigate pain and to enlist parental support when possible.⁹ Breastfeeding combines several analgesic effects (a comforting person [mother], skin-to-skin contact, diversion of attention, and the sweetness of lactose) as effective for procedural pain.^{23–25} Unfortunately, if the mother is no longer breastfeeding or if she would rather not breastfeed while the baby receives immunizations, than alternative analgesic techniques are necessary.

In his book *The Happiest Baby on the Block*,²⁶ Dr Harvey Karp describes the 5 S's: swaddling, side/stomach position, shushing, swinging, and sucking and explains how these interventions together trigger an infant's calming reflex. The primary objective of our study was to identify if the 5 S's could be used as a physical intervention to provide analgesia to infants receiving immunizations.

METHODS

Randomized Controlled Trial

This was a prospective, randomized, partially blinded, controlled study designed to test the effectiveness of a physical intervention by using the 5 S's for analgesic pain control, alone and in conjunction with sucrose analgesia, after routine immunizations at 2 and 4 months of age. This study was approved by the Internal Review Board (IRB) at Eastern Virginia Medical School and was registered with clinicaltrials.gov (NCT01368861).

Statistical Analysis

Power Analysis

The primary outcome variable of pain score was evaluated by using a total sample of 230 distributed evenly across 4 groups. A 1-way analysis of variance (ANOVA) has 99% power to detect at the .05 level a difference in means of pain scores characterized by a variance of means of .19, assuming that the common SD is 0.43.

Secondary analyses were conducted by using a .05 level χ^2 test, yielding 99% power to detect differences in crying among participants characterized by a variance of proportions of 0.024 and an average proportion of 0.20.

Statistical Methodology

Demographics variables such as age, gender, and race were evaluated for significant differences between intervention groups by using χ^2 analysis. For remaining demographic variables such as gestational age and weight at birth, 1-way ANOVA tests were used to determine if there were significant differences between intervention groups.

To evaluate mean pain across intervention groups over time, a 1-way ANOVA was used followed by least significant difference post hoc comparisons. To evaluate pain scores at each time interval across intervention groups, repeated measure general linear modeling was performed.

To determine significant differences in proportions of children crying at each time interval, χ^2 analyses were performed.

For all statistical tests, a P value $<.05$ was considered significant.

Study Sample and Group Randomization

All patients were enrolled from the General Academic Pediatric outpatient practice located at the Children's Hospital of the King's Daughters in Norfolk, VA.

This practice serves a predominantly urban, Medicaid-enrolled, African American population and has ~30 000 annual visits per year. Inclusion criteria included infants with a gestational age between 32 and 42 weeks at delivery and postnatal age of <20 weeks. Exclusion criteria included acetaminophen or ibuprofen administration within 4 hours before immunization, current neurologic disorder, known genetic anomaly, moderate to severe illness with or without fever at the time of vaccination, anaphylactic reaction to previous dose of vaccine, or if infant was previously enrolled in the study at 2 months.

Study Procedure

Infants meeting inclusion criteria were identified daily by reviewing the list of patients scheduled for a 2- or 4-month well-child visit at the outpatient site. The parent or legal guardian was approached before vaccination by the research assistant for participation in the study. If the parent or guardian accepted participation in the vaccine study, the consenting process was performed, and patients were brought to a designated examination room. Infants of parents or guardians who consented were randomly assigned to 1 of 4 study groups by using presealed cards. The cards were then selected by the nurses and only reviewed by the nurses to instruct them as to the group assignment. Ten cards were assigned to each group for a total of 40 cards, which were recycled with each group of 40 infants enrolled into the study. The 4 groups of the study included the following:

1. 2 mL of water 2 minutes before immunization and comfort by parent or guardian after immunization (Control Group),
2. 2 mL of 24% oral sucrose 2 minutes before immunization and comfort by parent or guardian after immunization (Sucrose Group),

3. 2 mL of water 2 minutes before immunization and physical intervention using the 5 S's by researcher after immunization (Physical Group), and
4. 2 mL of 24% oral sucrose 2 minutes before immunization and physical intervention using the 5 S's by researcher after immunization (Physical and Sucrose Group).

The nursing staff administering the immunizations selected an opaque presealed card and a prefilled syringe according to the card instructions. The prefilled syringes, labeled as "water" or "sugar" in zip-lock bags, were kept in the examination room. The emptied syringe would then be placed into an obscured sharps container after the contents were given to the infant. The trained observer, who would be grading the infant response, would then enter the immunization room after the infant had received the syringe contents and the syringe had been placed in the sharps container.

Every infant enrolled in the study was given a 2-mL solution of either water or 24% oral sucrose 2 full minutes before the administration of immunizations. The oral sucrose solution consisted of a 24% disaccharide solution (TootSweet 24%; Hawaii Medical, Seattle, WA), which has 240 mg of sugar per milliliter. The investigators and observer were blinded to which 2-mL solution each infant received at the beginning of the study. Investigator and parent were simply told by the nurses whether the infant was in the physical intervention group or parent comfort group.

The vaccinations used during the study were those that are routinely used at the practice site to meet the American Academy of Pediatrics requirements. Vaccines were administered in a standardized prescribed fashion of rapid injection and no aspiration technique by the same 2 senior nurses. After the 2-mL solution administration, each infant was given routine well vaccinations

with oral (1.5 mL) Rotarix first, followed by 3 intramuscular injections (0.5 mL) in alternating thighs of hepatitis B vaccine, Pentacel (combined diphtheria-tetanus-acellular pertussis/Inactivated polio vaccine-Haemophilus influenzae type b) and Prevnar given last because of its documented increased discomfort noted in previous studies.²⁷ All injectable vaccinations were predrawn into a 1-mL syringe under sterile technique and administered intramuscularly to the anterior thigh at a 90° angle to the skin with a 23-gauge 1.59-cm needle by senior nursing staff. The third and last injection was placed lateral to the first with >3 cm between shots given in the same leg. All injections were given with the infant lying on the examination table. When the last injection was finished, the parent or caregiver in the non-physical intervention group was allowed to soothe and hold the baby by using any techniques they wished (swaddle, shushing, sucking on a pacifier, breastfeeding, etc.). Comfort strategies by the parents or caregivers were not collected, and therefore no statistical analysis could be done.

Physical Intervention

For the physical groups, additional criteria were outlined for study inclusion. Three pediatric resident physicians viewed the 5S's video and practiced rapidly swaddling the infant. The infants would have the blanket placed underneath them during the immunizations to facilitate swaddling. Each resident was required to have each infant swaddled within 15 seconds postvaccination, begin side/stomach position with shushing and swinging/swaying with the pacifier provided after 30 seconds. As suggested by Dr Karp, the pacifier was the last of the 5 S's implemented during the physical intervention group because the infant should slowly be calming, and the nonnutritive suck theoretically helps soothe the infant even more.²⁵ Large, square 47 × 47

inch cotton muslin Aden and Anais blankets were used during the investigation to ensure secure swaddling of all infants. All 5 S's were incorporated to the best ability of the pediatric resident. A minimum completion of 4 of 5 physical interventions needed to be successfully completed by the resident for inclusion in the study (to see a video of the 5S's preformed, go to http://www.youtube.com/watch?v=WkR_e1L6zxl).

Data Collection

The subject age, gender, ethnicity, current weight, and gestational age were recorded. One resident preformed the function of being the timer, and a stop watch was started immediately after the injection of the third and final vaccination in the series to commence the assessment of pain. Table 1 shows the modified Riley Infant Pain Scoring Method used to measure the infant's pain score postvaccination.²⁸ Infant's scores were based on 3 behaviors: quality of cry (eg, from whimpering to high-pitched scream), facial grimace, and body movement by using 15-second intervals for a minimum of 2 minutes and then every 30 seconds to a maximum 5 minutes' postvaccination. After the infant was calm, scoring was continued for an additional 1 minute post-cry. There was a minimum score of 0 to a maximum score of 3 for each behavior. The lowest possible total pain score was 0, and the highest total pain score was 9. A single research assistant was present to score all infant assessments of pain and crying. A slight modification of facial scoring method was used for the term "clenched teeth"; the observer substituted "clenched jaw/mouth."

RESULTS

Patients were recruited over a 6-month period from May 1 through October 31, of 2010. As indicated in Fig 1, 286

TABLE 1 Modified Riley Pain Score

| Behavior | Scoring | | | |
|---------------|-----------------|-------------------------|--------------------------------|--|
| | 0 | 1 | 2 | 3 |
| Facial | Neutral/smiling | Frowning/grimacing | Clenched teeth | Full cry expression |
| Body movement | Calm, relaxed | Restless/fidgeting | Moderate agitation or mobility | Thrashing, flailing, incessant agitation or strong, voluntary immobility |
| Verbal/vocal | No cry | Whimpering, complaining | Pain crying | Screaming, high-pitched cry |

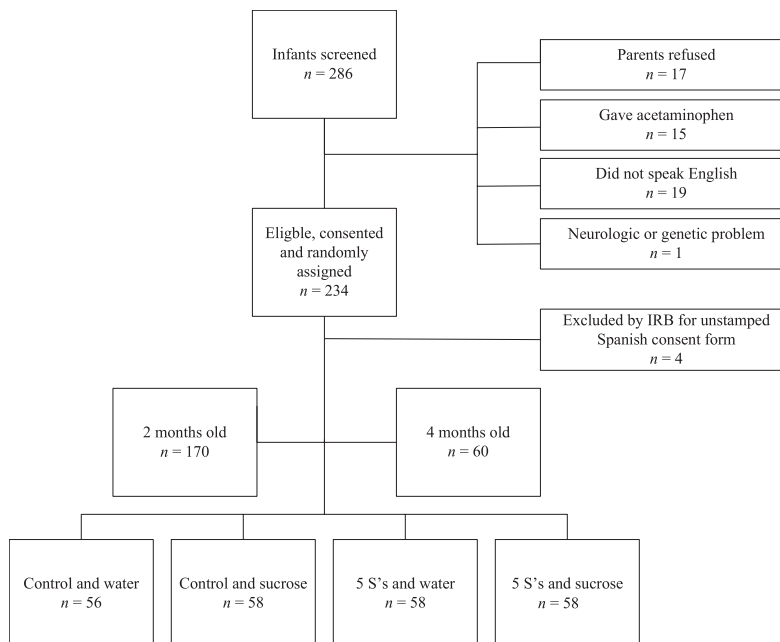


FIGURE 1 Randomization table.

two- and four-month-old patients who were scheduled to receive vaccines were screened for participation in the study. Ninety-four percent (270) met inclusion criteria, and of those, 87% (234) agreed to participate. Four subjects were excluded after enrollment by our IRB after data collection because a directly translated Spanish consent form did not have an official stamp from the IRB and was deemed unacceptable. Of these patients, 56 were randomly assigned to the control group, 58 to the sucrose group, 58 to the physical group, and 58 to the physical and sucrose group. Demographic data for each of the groups is listed in Table 2. Overall, 73%

were 2-month-olds, 54% were boys, 81% were African American, and 13% were Caucasian. Demographic variables did not vary significantly between study groups.

Four of the first 5S's were completed in 100% of the patients, and our residents found that "sucking" was the most difficult of the 5 S's to complete for 3 reasons: extreme discomfort, the infant had already become calm, or the infant was unaccustomed to using a pacifier.

Repeated-measure ANOVAs in Fig 2 show that for all groups, pain significantly decreased over time; post hoc testing also showed a significant difference in

TABLE 2 Characteristics of Participating Population

| Demographics | Control | Sucrose | 5 S's | 5 S's and Sucrose | P Value |
|------------------------------------|---------|---------|-------|-------------------|--------------------|
| Mean gestational age at birth (wk) | 38.3 | 38.2 | 38.3 | 38.6 | .569 ^a |
| Mean wt at immunization (kg) | 5.6 | 5.9 | 5.6 | 5.8 | .314 ^a |
| % 2 mo in age | 84.5% | 63.8% | 76.3% | 69.5% | .0686 ^b |
| % boys | 53.4% | 55.2% | 54.2% | 55.9% | .994 ^b |
| % African America | 75.9% | 89.7% | 71.2% | 86.4% | .14 ^b |

^a One-way analysis of variance.

^b χ^2 test.

mean pain scores for each group over time. In terms of mean pain scores, all groups were significantly less than control, and the 5S's only group was significantly less than the sucrose group as well. In addition to the repeated-measure ANOVA, a 1-way ANOVA was performed to explore differences in mean modified Riley Pain Scores that were averaged over the first 120 seconds. Table 3 reveals that the mean Riley Pain Score averaged over the first 120 seconds was 4.46 for the control group, 3.95 for the sucrose group, 3.24 for the physical group, and 3.61 for the physical and sucrose group. Overall, the mean pain score for the 5S's group was 1.2 points less than the control group. Post hoc analysis revealed significantly different mean pain scores between study groups ($P < .001$) with the exception of the physical and physical with sucrose groups ($P = .11$). These

2 groups had similar mean scores throughout, which were the lowest over time, followed by sucrose alone and then control. There was a trend toward greater efficacy of all interventions in the 2-month age range over the 4-month age range, although this was not statistically significant ($P = .077$). In the sucrose, physical, and physical and sucrose groups, the 2-month-old patients had lower mean pain scores than the 4-month-olds, as shown in Table 3.

Similarly, the χ^2 analysis in Fig 3 reveals a significantly different percent of children crying at 45, 60, 75, 90, and 105 seconds between the control, sucrose, and the 2 physical groups at $P < .01$. The same trend was found with the proportion of children crying as with the median pain score outcome measure. The lowest proportion of children crying at each of the times was found in the physical and physical with sucrose groups.

DISCUSSION

This study demonstrates that the physical intervention of the 5 S's resulted in decreased pain scores and decreased crying time among 2- and 4-month-old infants during their routine vaccinations. The 5 S's appear to be a viable nonpharmacologic option for clinics to implement when providing analgesia during vaccinations. In this study, the researchers alone implemented the physical intervention; however, interested caregivers were instructed in performing the 5 S's for future immunizations.

The use of sucrose has been well established to reduce pain in infants during vaccination or procedures, and it has been suggested that it should be the standard of care.¹¹ However, it is unknown whether concomitant use of other analgesics with sucrose may produce a combined effect. We hypothesized that sucrose and our physical intervention together would have a synergistic effect in decreasing pain. However, the pain scores and crying time in the group of physical intervention alone were essentially identical and sometimes even lower than the physical intervention with sucrose group. More important, both groups using the physical intervention showed decreased pain scores when compared with the sucrose only group. In addition, when looking at the percent of infants crying at the set time points, there were significantly fewer infants crying who received the physical intervention when compared with the sucrose-only or control groups. Thus, the physical intervention of the 5 S's had more of an analgesic effect than sucrose, yet there did not appear to be an overall synergistic effect with sucrose. Future studies should be done to see if these findings of the 5 S's can be replicated, as well as effectively taught to parents in a clinical setting.

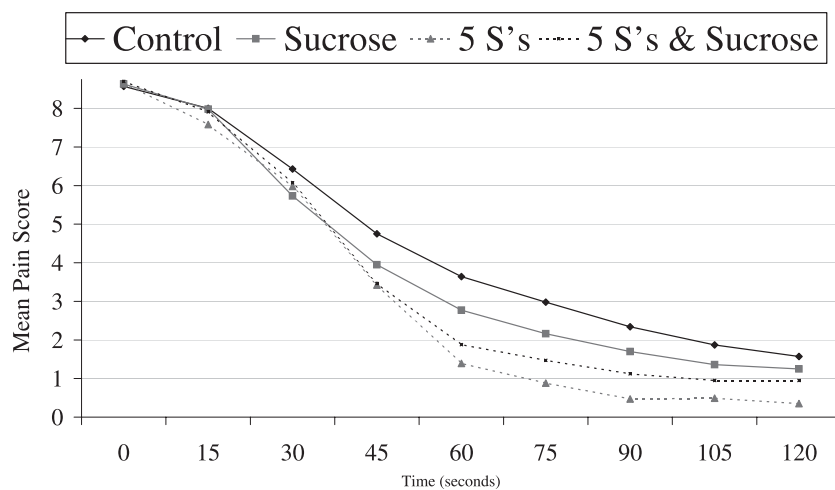


FIGURE 2 Mean modified Riley Pain Score over time by intervention.

TABLE 3 Average Modified Riley Pain Score Over 120 Seconds by Age

| Age | Control | | Sucrose | | 5S's | | 5 S's and Sucrose | | Total | | One-Way ANOVA P Value |
|-------|---------|------|-------------------|------|---------------------|------|-------------------|------|-------|------|-----------------------|
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Mean | SD | |
| 2 mo | 4.40 | 1.32 | 3.76 ¹ | 1.19 | 3.21 ^{a,b} | 0.66 | 3.55 ¹ | 1.17 | 3.75 | 1.20 | <.001 |
| 4 mo | 4.83 | 1.01 | 4.25 | 1.37 | 3.36 | 1.53 | 3.76 | 1.38 | 3.98 | 1.42 | .077 |
| Total | 4.46 | 1.28 | 3.95 ¹ | 1.27 | 3.24 ^{a,b} | 0.94 | 3.61 ¹ | 1.23 | 3.81 | 1.26 | <.001 |

^a Least significant difference post hoc revealed significantly less than control.

^b Least significant difference post hoc revealed significantly less than sucrose.

We had several inherent and methodologic limitations in our study. We had a disproportionate number of 2-month-olds compared with 4-month-olds because of our exclusion criteria for 4-month-olds being ineligible if enrolled at their 2-month appointment. In addition, when the researchers performed the 5 S's, it was noted that the technique was much easier to perform on the smaller 2-month-olds compared with the bigger and heavier 4-month-olds. These 2 factors make our results difficult to interpret for the older infant. For example, when looking at our results for percent crying and age, it appears that the 2-month-old group is driving the significance for percent crying by intervention at times 45 seconds, 75 seconds, 90 seconds, and 105 seconds. However, it is impossible to tell if the significance is being driven by the

difference in age between 2 and 4 month olds or because there was a limited number of 4-month-olds for comparison.

Although the pain scoring was all done by a single researcher, there were 3 researchers who performed the physical intervention of the 5 S's, and each may have had a slightly different technique in swaddling. However, all the residents who performed the 5S's practiced and viewed the online video mentioned earlier in the text until they could complete the process in <15 seconds. Other limitations were noted in the modified Riley Pain Score itself, because the behavior of body movement may have been restricted by a tight swaddling and therefore would have made it difficult to accurately assess body movement in the intervention group.

Our study population was predominantly African American (79.5%) based on the population that the clinic serves and may not be generalizable to other populations of patients.

Our control group was made up of the caregivers, and in an attempt to comfort their children, they instinctively did some of the 5 S's. According to Harvey Karp's book *Happiest Baby on the Block*, you need at least 3 of the 5 S's to elicit the calming reflex, and usually the mother would do 2 of the S's, including shushing in their ear and having them suck on a pacifier. However there were some instances when a mother in the control group would do 3 or more of the S's, thus possibly eliciting the calming reflex. This may account for the few outliers we had in the control group.

Another concern reflects methodologic issues with waiting 2 minutes after the sucrose administration. Some authors have theorized that the length of analgesic time for sucrose is different between the pre- and postneonatal period,²⁹ extrapolating that sequential doses of sucrose would modulate this effect in older infants.^{30,31} Conversely, the introduction of the oral Rotarix and Rotateq into the series of immunizations

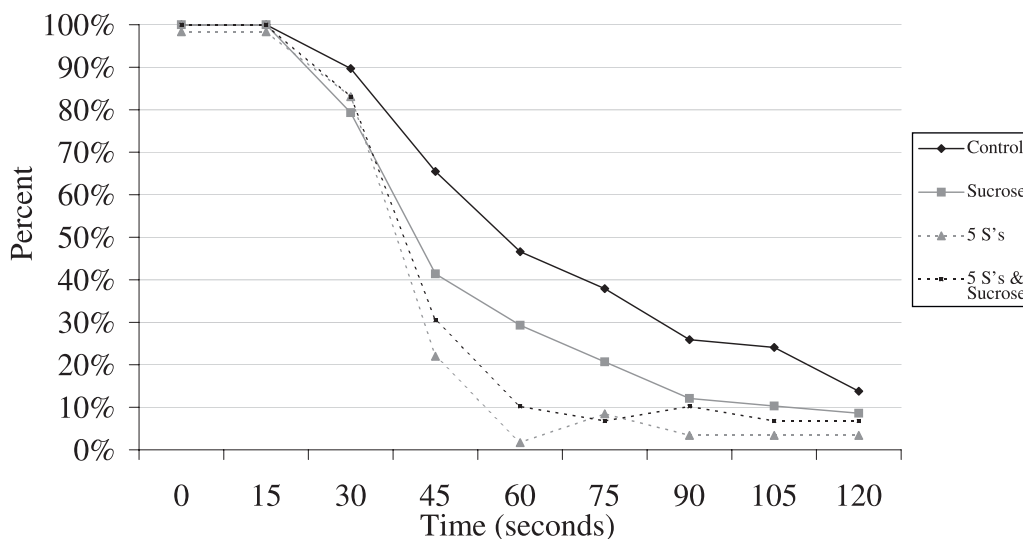


FIGURE 3 Percent of participants crying over time by intervention.

given at 2 and 4 months also introduces the chance for the infant to be exposed to an incipient dose of dextran or sucrose in the vaccine. The concentration of the incipient, however, is significantly less than what is found in 24% sucrose (the ratio being 240 mg/mL to 6 mg/mL), and the vaccines were given immediately after the oral vaccine dose. Therefore, it is unlikely that the oral vaccine had any measurable analgesic effect given that there have been studies showing no added analgesic effect from formula after 24% sucrose^{32,33}

and that 12% sucrose was considered insufficiently sweet to exert an analgesic effect.^{34,35}

CONCLUSIONS

Overall, our study concluded that the physical intervention of the 5 S's (swaddling, side/stomach position, shushing, swinging, and sucking) provided decreased pain scores on a validated pain scale and decreased crying time among 2- and 4-month-old infants immediately after routine vaccinations.

The use of 5 S's did not differ from the use of 5 S's and sucrose. This simple physical intervention will require additional studies to see whether it is reproducible for other painful procedures and whether parents can be taught to perform the 5 S's reliably.

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A RARE FLOWER: *I like to surprise my wife with flowers now and then. I don't usually buy exotic flowers but she seems reasonably appreciative of the tulips and lilacs I bring home. However, I wonder what she would say if I brought home the flowers of a 32,000-year-old plant? As reported in The New York Times (Science: February 20, 2012), scientists have recreated a plant, the narrow leafed campion, from genetic material stored in the Siberian permafrost. If confirmed by other scientists, the plant would be by far the oldest plant grown from ancient plant tissue. Until now, that honor was held by a date palm grown from a 2,000-year-old seed recovered from an ancient fortress in Israel. This new discovery began when Russian researchers unearthed ancient squirrel burrows buried beneath 125 feet of sediment and permanently chilled at minus 7 degrees Celsius. The burrows contained thousands of seeds. However, while the scientists could not induce any of the found seeds to propagate, cells from the placenta, the organ in the fruit that produces the seeds, were induced to produce the entire plant in the laboratory. The plant looks quite similar to the modern campion except that the flower petals are narrower. Still, scientists are skeptical. While seeds and plant tissue can survive for a long time under optimal conditions, reports of extreme longevity have mostly been disproven. The Russian scientists remain confident, however. Radiocarbon dating of the seeds attached to the placenta that grew the plant suggests they are almost 32,000-years-old. Several other factors may have contributed to the ability of the ancient placenta to propagate. Squirrels construct their storage burrows next to the permafrost; therefore, the seeds may always have been cool and not gone through cycles of heating and cooling. According to the article, the placenta of the campion contains high levels of sucrose and phenols, which can serve as biologic antifreeze agents. Finally, little residual radioactivity has been detected at the site making it less likely that radioactive particles damaged the plant DNA. If the age of the plant is borne out by further examination of the plant DNA, it would mark a remarkable achievement and possibly open the door to the rebirth of other ancient or extinct plants buried in the permafrost.*

Noted by WVR, MD

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