RESEARCH REPORTS

CARDIOLOGY
997 Diastolic Filling Parameters in Hypertensive Urgency

ANTICOAGULATION
1002 Low-Dose Warfarin After Orthopedic Surgery
1008 Influence of Ethnicity on Warfarin Dosage

PHARMACOGENETICS
1013 PLA Polymorphism and Aspirin Resistance

COMPLEMENTARY AND ALTERNATIVE MEDICINE
1019 Herb, Vitamin, and Mineral Use in the Elderly

DIABETES
1024 Point-of-Care HbA1c vs Standardized Laboratory

NEONATOLOGY
1029 Efficacy of Sucrose During Eye Examinations for Retinopathy of Prematurity

NEPHROLOGY
1034 Effect of Indapamide on Calcium

TOXICOLOGY AND POISON CONTROL
1039 Tramadol Exposures
1045 Atomoxetine Ingestions in Children

ARTICLES

AMBULATORY CARE
1049 Anticoagulation Monitoring: Part I

NEW DRUG DEVELOPMENTS
1056 Nelarabine: A Nucleoside Analog with Efficacy in T-Cell and Other Leukemias

ARTICLES (continued)

DRUG INTERACTIONS
1064 Predicting Inhibitory Drug-Drug Interactions and Evaluating Drug Interaction Reports

CARDIOLOGY
1073 NSAIDs' Impact on the Cardioprotective Effects of Aspirin

COMPLEMENTARY AND ALTERNATIVE MEDICINE
1080 Glucosamine Long-Term Treatment and Progression of Knee Osteoarthritis

DRUG INFORMATION ROUNDS
1088 Nebulized Morphine for Relief of Dyspnea
1093 The Effect of Creatine Intake on Renal Function

RECENT ADVANCES

THERAPEUTIC MONITORING
1097 Transporters and Their Impact on Drug Disposition

CASE REPORTS
1109 Tacrolimus-Metronidazole Interaction
1114 Hypersensitivity Reactions to Oxaliplatin in Two Asian Patients
1119 Extensive Prolongation of aPTT with Argatroban
1124 Miller Fisher Variant of Guillain-Barré Syndrome with Tacrolimus
1128 Phenazopyridine-Induced Sulfhemoglobinemia
1131 Fluphenazine-Induced Neuroleptic Malignant Syndrome

LETTERS AND COMMENTS

1136 Use of Gabapentin for Rest Pain in Chronic Critical Limb Ischemia
1137 Levofloxacin-Induced Fatal Toxic Epidermal Necrolysis
1137 Pure Red Cell Aplasia Associated with Dapsone Therapy
1138 Celecoxib-Induced Deep-Vein Thrombosis
1138 Acceleration of Left-Ventricular Diastolic Dysfunction and Pulmonary Hypertension After TNF-a Blocker
1139 Correction: Impact of Stress Ulcer Prophylaxis Algorithm Study

See Detailed Table of Contents Inside

1140 New Publications
1145 PharmaCE Test Questions
1149 Personnel Placement
1149 Educational Events
1151 News and Comments
TABLE OF CONTENTS is available through E-mail from our Web site (www.theannals.com).

SUBSCRIBERS should notify The Annals (www.hwb.com/ser/index.html) of the effective date of any address change and include both old and new addresses. Missing issues will be replaced free of charge for claims by subscribers received within six months after the issue date.

SUBSCRIPTION ORDER FORM is printed on page 993.

REPRINTS are available in bulk quantities. Contact the Publisher for prices.

AUTHOR GUIDELINES are available in the January and July/August issues of The Annals. They may also be accessed directly from The Annals Web site at www.theannals.com or by request from the Editorial Office. Manuscripts receive several critical reviews to maintain high publication standards. All articles and letters are peer reviewed.

The Annals of Pharmacotherapy is included in major abstracting and indexing services, including MEDLINE, PubMed, Current Contents, Index Medicus, Science Citation Index, EMBASE, and SSCI Data Bases. Microfilm and microfiche editions are available from ProQuest Information and Learning, 300 N. Zeeb Rd., Ann Arbor, MI 48106, or ProQuest Co. The Quornum Barnwell Rd., Cambridge CB4 8SW, UK.

REPUBLICATION of material submitted to The Annals that has appeared or will appear in another publication (e.g., journal, book, newspaper, newsletter), even if the wording is altered, is unacceptable without permission and could violate copyright law. The whole content of The Annals is under copyright; permission to reproduce any part must be obtained in writing from the Publisher.

Printed in the USA on acid-free paper.

ADVERTISING is accepted subject to editorial approval.

Advertising Representative: Young Associates, George R Young, President, 109 S. Main St., Ste. 16, Cranbury, NJ 08512; 609/371-5085; FAX 609/371-5086

Copyright 2005 HARVEY WHITNEY BOOKS COMPANY

THE ANNALS OF PHARMACOTHERAPY (ISSN 1060-0280; Coden AHPHER) is published by HARVEY WHITNEY BOOKS COMPANY

Correspondence: P.O. Box 42696, Cincinnati, OH 45242-0696 USA; Telephone 803/793-3555, FAX 513/793-3600; www.theannals.com

Street Address: 8044 Montgomery Rd., Ste. 415, Cincinnati, OH 45236-2919

Subscription price: $175.00 per year (individuals); Periodical postage paid at Cincinnati, OH, and additional mailing offices. Printed in the USA on acid-free paper. POSTMASTER: Send address changes to The Annals of Pharmacotherapy, Subscription Department, Harvey Whitney Books Company, P.O. Box 42696, Cincinnati, OH 45242-0696 USA, www.theannals.com.
Efficacy of Sucrose to Reduce Pain in Premature Infants During Eye Examinations for Retinopathy of Prematurity

Peter Gal, Grace E Kissling, William O Young, Kimberly K Dunaway, Virginia A Marsh, Susan M Jones, Dawn H Shockley, Nicole L Weaver, Rita Q Carlos, and J Laurence Ransom

BACKGROUND: Eye examinations for retinopathy of prematurity (ROP) are painful to the neonate. The use of topical anesthetic for eye examinations to evaluate ROP is routine in our neonatal intensive care unit (NICU), but does not completely suppress painful responses. Sweet solutions have been shown to reduce procedural pain in newborns.

OBJECTIVE: To examine whether the addition of sucrose 24% to topical anesthetic improves procedural pain control during the ROP eye examination.

METHODS: Neonates born at ≤30 weeks' gestation were included in this placebo-controlled, double-blind, crossover study. Patients were randomly assigned to receive treatment with either proparacaine HCl ophthalmic solution 0.5% plus 2 mL of sucrose 24% or proparacaine HCl ophthalmic solution 0.5% plus 2 mL of sterile water (placebo) prior to an eye examination. In a subsequent eye examination, each patient received the alternate treatment. Oral sucrose and sterile water were prepared in the pharmacy in identical syringes, and physicians, nurses, and pharmacists in the NICU were blinded to the treatment given. Pain was measured using the Premature Infant Pain Profile (PIPP) scoring system, which measures both physical and physiologic measures of pain, and the scores were simultaneously assessed by 2 study nurses. PIPP scores were recorded 1 and 5 minutes before and after the eye examination and during initial placement of the eye speculum. The same ophthalmologist performed all eye examinations. Several different definitions of a pain response were investigated.

RESULTS: Twenty-three infants were studied, with 12 receiving sucrose and 11 receiving placebo as the first treatment. For 3 of the 5 definitions of pain response, patients experienced significantly less pain at speculum insertion with sucrose than with placebo. After the ROP examination, pain responses were similar with either sucrose or placebo.

CONCLUSIONS: Oral sucrose may reduce the immediate pain response in premature infants undergoing eye examination for ROP.

KEY WORDS: pain, retinopathy of prematurity, sucrose.

Published Online, 26 Apr 2005, www.theannals.com, DOI:10.1345/aph.1E477

Newborns in intensive care are exposed to many painful stimuli, and sucrose has proven to be effective in reducing procedural pain from a variety of causes. The neonatal eye examination required to evaluate for the presence of retinopathy of prematurity (ROP) is one painful procedure for which sucrose has been poorly studied. Painful response occurs in virtually all neonates during manipulation of the eye. In our unit, topical anesthetics reduce, but do not eradicate, pain associated with the neonatal eye examination. Consequently, we designed a placebo-controlled, double-blind, crossover study to determine whether sucrose pretreatment can prevent pain associated with neonatal eye examinations.

Methods

The study in the preceding paper examined the efficacy of topical anesthetic for eye examination pain. This study is a sequel and used an identical design except for routine addition of topical anesthetic and oral study drugs. Patients were admitted to the study if they were ≤30 weeks gestation, required at least 2 eye examinations to monitor for ROP, were sufficiently clinically stable to tolerate the eye examination based on the neonatologist’s clinical assessment, and did not require analgesia (fentanyl) or sedation (lorazepam) for at least 12 hours prior to the procedure. The study was approved by the hospital’s institutional review board. The nature of the procedure was explained to the parents, and consent was obtained. ROP eye examinations are routinely performed in our neonatal intensive care unit (NICU) for high-risk patients, and all study days coincided with previously scheduled eye examinations. Patients were enrolled by the study nurses. Examinations were performed by a single consultant pediatric ophthalmologist who has been the primary ophthalmology consultant for our NICU for >10 years. He was assisted by the NICU nurse responsible for the infant’s care on that day and 2 pain study nurses who
had gone through special training with the Premature Infant Pain Profile (PIPP) scoring system to promote interobserver consistency.

Mydriatic eye drops (phentolamine chloride [HCl] 1%, cyclopentolamine HCl 0.2%) were administered approximately 60–90 minutes before the procedure. The infant was swaddled several minutes before the procedure and held by a nurse during the eye examination. The ophthalmologist inserted a spring-loaded wire Sauer prematurity eyelid speculum to hold the eyelids open. The retina of each eye was examined with an indirect ophthalmoscope through dilated pupils using a thimble-type Scheppen scleral depressor to rotate the eye and indent the sclera to allow thorough examination of the retina.

The study observation interval began 5 minutes prior to the procedure and ended 5 minutes after completion of examination of the second eye. For each procedure, 2 pain study nurses performed pain assessments using the PIPP scale and reached consensus scores that were recorded in a study form at 5 different times throughout the observation period. All individuals involved in the direct care or assessment of the patient were blinded to the sucrose or sterile water administered during the study.

A standard procedure was followed for each eye examination. The ophthalmologist examined patients in the order prescribed by the nurses, allowing the nurses to record baseline PIPP scores on each infant 5 minutes and 1 minute prior to the procedure. The patient's nurse administered 2 mL of sucrose 24% (Sweet-case, Children's Medical Ventures, Murrayville, PA) or 2 mL of sterile water, placing drops on the infant's tongue for 1–2 minutes before the procedure. The ophthalmologist administered local anesthetic eye drops (proparacaine HCl) ophthalmic solution 0.5%, Bausch & Lomb, Tampa, FL), 2 drops in each eye, prior to examination of the first eye, then about 30 seconds later inserted an eyelid speculum to facilitate keeping the eye open and performed an examination lasting about 5 minutes to complete both eyes. The study nurses recorded PIPP scores during initial insertion of the wire eyelid speculum and 1 and 5 minutes after completion of the entire examination of both eyes.

Treatment allocation was made in groups of 6 based on the results from a dice roll. The hospital pharmacist was the only one familiar with the individual treatment assignments. One investigator who was never present during eye examination studies (PG) reviewed interims study results after 12 patients had been treated to ensure that patients were not unnecessarily given sterile water if sucrose proved beneficial. The study was stopped after 23 patients had been treated because a new ophthalmologist was scheduled to rotate onto the service and we did not want to confound the study by altered examination technique. Study nurses evaluated pain using the PIPP scale, which measures both physical and physiologic pain indicators and has been validated in prior publications. The PIPP score is determined by assigning 0–3 points for various factors including gestational age at the time of observation, behavioral state (eg, quiet or active), increase in maximum heart rate, decrease in O2 saturation, and facial features involving brow bulge, eye squint, and nasolabial furrow. Possible scores range from 1 to 21. Four study nurses underwent special training to ensure reliable PIPP scores. For each ROP examination, 2 of the study nurses observed the infant as described above and recorded their consensus scores 5 minutes and 1 minute before the examination, at wire eyelid speculum insertion, and 1 minute and 5 minutes after the examination.

Each patient received sucrose 24% and the placebo on different days in random order using a double-blind crossover design. The study was designed assuming that, without intervention, 80% of infants would have a pain response associated with the eye examination, and administration of sucrose would reduce this to 40%. We estimated that 24 patients would be needed to detect this effect with a p value <0.05 and a power of 80%. Statistical analyses of PIPP scores were performed several different ways because definitions of pain in premature infants may vary and are somewhat arbitrary. Consequently, analyses were performed to consider (1) actual PIPP scores, (2) number of PIPP scores increasing by ≥4 points from baseline (average of 1 and 5 min preexamination), (3) number of PIPP scores ≥10, (4) number of PIPP score differences ≥4 points between treatment and placebo conditions, and (5) areas under the PIPP score curves from 5 minutes before the examination to eyelid speculum insertion and from lid speculum insertion to 5 minutes after the examination. AUCs were calculated using the trapezoidal rule. Statistical analyses compared sucrose 24% and sterile water treatments.

For statistical comparisons of the number of patients with PIPP scores ≥10, increases in PIPP scores ≥4 points from baseline, and differences of ≥4 points between treatment and placebo, the binomial test was used. For comparisons of actual PIPP scores and AUCs, paired t-tests were used. Paired t-tests were also used to compare postnatal ages between the sucrose ≥4% and sterile water treatments. The influences of postconceptional age at time of examination and of the order of treatment on PIPP score were examined with a mixed model repeated measures analysis of covariance. The number needed to treat to expect one patient to benefit from sucrose 24% was estimated as the reciprocal of the absolute risk reduction for patients to experience pain with sucrose than with placebo.

Results

Twenty-three patients were enrolled in the study from January 2003 through June 2004. All patients completed the study without deviation from the protocol. Twelve infants received sucrose first, and 11 received sterile water first. The length of time between each patient's 2 eye examinations ranged from 8 to 35 days (median 21). Gestational ages ranged from 24 to 329 weeks, and postnatal ages at time of treatment ranged from 28 to 93 days. Postnatal ages at time of examination were not significantly different between the sucrose and placebo conditions (p = 0.38; Table 1).

| Table 1. Demographic Information and PIPP Scores for 22 Neonates |
|----------------------------------|-----------------|-----------------|-----------------|
| Parameter                        | Treatment Group | Placebo         | Paired Difference |
|                                 | Sucrese         | Placebo         |                  |
| Gestational age (wk)             | 26.4 ± 1.5      | 26.4 ± 1.5      | NA               | NA               |
| Day of life                      | 47.3 ± 15.2     | 48.8 ± 16.2     | -1.5 ± 21.6      | 0.38             |
| PIPP score                       | 2.6 ± 1.1       | 2.5 ± 1.4       | -0.1 ± 2.2       | 0.39             |
| 5 min pre-examination            | 3.1 ± 1.5       | 3.0 ± 1.7       | -0.2 ± 2.6       | 0.37             |
| 1 min pre-examination            | 8.3 ± 4.5       | 10.5 ± 4.0      | -2.2 ± 3.9       | 0.01             |
| eye speculum insertion           | 7.7 ± 3.6       | 8.3 ± 3.5       | -0.6 ± 4.1       | 0.24             |
| 1 min post-examination           | 3.3 ± 1.4       | 4.1 ± 2.3       | -0.9 ± 2.7       | 0.07             |
| 5 min post-examination           | 17.3 ± 6.2      | 17.7 ± 7.1      | -0.4 ± 10.6      | 0.38             |
| AUC (cumulative pain)            |                 |                 |                  |                  |
| preexamination                   | 29.8 ± 12.5     | 34.2 ± 14.0     | -4.4 ± 15.8      | 0.10             |
| postexamination                  |                 |                 |                  |                  |
| O2 desaturation ≥10% on PIPP score | 0              | 0               | NA               |                  |
| preexamination                   | 3 (17.4%)       | 7 (30.4%)       | 0.34             |
| eye speculum insertion           | 1 (4.3%)        | 2 (8.7%)        |                  | 1.00             |

NA = not applicable; PIPP = Premature Infant Pain Profile. *Mean ± SD. **Percentages refer to the percent of patients who had a ≥10% reduction in O2 saturation from prestudy baseline.
Efficacy of Sucrose During Eye Examinations in Neonates

PIPP scores 1 minute and 5 minutes prior to the eye examination were similar in the sucrose and placebo conditions. However, PIPP scores during placement of the wire eyelid speculum were significantly higher with placebo compared with sucrose treatment \( (p = 0.01; \text{Table 1}) \). At 1 minute and 5 minutes after completion of the eye examination, PIPP scores, while generally higher with placebo, were not significantly higher compared with sucrose.

Table 2 contains a summary of the results for all 5 potential definitions of pain response. Defining pain as an increase in PIPP score of ≥4 points from baseline (the average of scores at 5 and 1 min before examination), 18 (78%) of the 23 infants had a painful reaction with eyelid speculum insertion when placebo was administered, while 13 (57%) had a painful reaction with eyelid speculum insertion when sucrose was administered. One minute after the examination, 6 infants had painful reactions with placebo but not with sucrose and 2 had painful reactions with sucrose but not placebo. Five minutes after the examination, none of the patients had painful reactions with sucrose and 4 had painful reactions with placebo. Using this definition of painful reaction, there were no statistically significant differences between the placebo and sucrose pretreatment. Alternatively, defining a painful reaction as PIPP score ≥10, no patients had a painful reaction 1 or 5 minutes before the examination.

During the examination, painful reactions occurred in 14 (61%) placebo- and 9 (39%) sucrose-treated patients. Eight infants had painful reactions with the placebo but not sucrose, while 3 had painful reactions with sucrose but not placebo at eyelid speculum insertion (binomial test, \( p = 0.04 \)). One minute after the examination, painful reactions were observed in 4 patients with placebo but not sucrose and in 4 with sucrose but not placebo (binomial test, \( p = 0.64 \)). Five minutes after the examination, painful reactions occurred in one patient with placebo but not sucrose and in none of the infants with sucrose but not placebo (binomial test, \( p = 0.50 \)).

Defining a painful reaction as a difference of ≥4 points in PIPP scores between the sucrose and placebo conditions, at placement of the eyelid speculum, 10 patients had a painful reaction with placebo and 2 had a painful reaction with sucrose (binomial test, \( p = 0.02 \)). One minute after the procedure, 3 infants had a painful reaction to placebo, while 3 had a painful reaction with sucrose (binomial test, \( p = 0.66 \)). Five minutes after the procedure, 3 patients had painful reactions with placebo and none had painful reactions with sucrose (binomial test, \( p = 0.13 \)).

The AUC for PIPP score was used as a global marker of pain for the 5 minutes from beginning the eye examination. Before insertion of the speculum, the AUC for PIPP scores did not differ between the placebo and sucrose conditions \( (p = 0.38) \). After insertion of the speculum, the AUC for PIPP scores also did not differ significantly between the groups \( (p = 0.10; \text{Table 1}) \).

As a separate issue, the effect of postconceptional age on PIPP score was examined. Postconceptional age, defined as gestational age plus day of life at treatment expressed in weeks, was inversely related to PIPP score as assessed with bivariate correlations. In a mixed-model, repeated-measures analysis of covariance, a (postconceptional age × treatment) interaction indicated that the inverse relationship was similar with sucrose and placebo. A similar repeated-measures analysis of covariance showed no order effect of the treatments.

Table 3 gives the numbers of patients who experienced less pain with sucrose 24% than with placebo using each of the 5 definitions of pain response. Depending on the definition of pain response, the number needed to treat to expect one patient to benefit from the sucrose ranges between 1.4 and 23. No adverse events, except pain response due to the eye examination, were associated with either placebo or sucrose.

---

**Table 2. Summary of Results Based on Different Definitions for Pain Response**

<table>
<thead>
<tr>
<th>Definition of Pain Response</th>
<th>1-sided ( p ) Values for Differences Between Placebo and Sucrose*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Examination</td>
</tr>
<tr>
<td>Actual PIPP score</td>
<td>0.39, 0.37</td>
</tr>
<tr>
<td>Increase PIPP score by ≥4 points above baseline</td>
<td>NA, NA</td>
</tr>
<tr>
<td>PIPP score ≥10</td>
<td>NA, NA</td>
</tr>
<tr>
<td>PIPP scores for placebo and sucrose differ by ≥4 points</td>
<td>0.69, 0.34</td>
</tr>
<tr>
<td>PIPP AUC</td>
<td>0.38</td>
</tr>
</tbody>
</table>

*Significant difference identified as \( p < 0.05 \). The \( p \) values in the Before Examination column apply, respectively, to the scores for 5 and 1 minute before examination. The \( p \) values in the After Examination column apply, respectively, to the scores for 1 and 5 minutes after examination, except for the AUC, which was calculated for all periods of time before and after examination.

**Table 3. Number Needed to Treat to Expect One Patient to Benefit from Sucrose**

<table>
<thead>
<tr>
<th>Definition of Pain Response</th>
<th>Pts. with Less Pain with Sucrose vs Placebo at Wire, n (%)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual PIPP score</td>
<td>16 (70)</td>
<td>1.4</td>
</tr>
<tr>
<td>Increase PIPP score by ≥4 points above baseline</td>
<td>1 (4)</td>
<td>23.0</td>
</tr>
<tr>
<td>PIPP score ≥10</td>
<td>3 (13)</td>
<td>7.7</td>
</tr>
<tr>
<td>PIPP scores for placebo and sucrose differ by ≥4 points</td>
<td>10 (39)</td>
<td>2.3</td>
</tr>
<tr>
<td>PIPP AUC after lid speculum insertion</td>
<td>13 (67)</td>
<td>1.7</td>
</tr>
</tbody>
</table>

NNT = number needed to treat; PIPP = Premature Infant Pain Profile.
Discussion

The neonatal eye examination is well documented to cause pain. The response to pain in neonates is actually exaggerated with important physiologic consequences in contrast to the relative insensitivity to pain previously believed. The eye examination in our population caused pain in 78% of the neonates pretreated with topical anesthetic and placebo and, in the previous study without topical anesthetic, occurred in 100% of neonates. The concurrent O₂ desaturation episodes in 30% of placebo-treated patients highlights the importance of these painful events.

As a result of a recent study in our NICU, the use of topical anesthetic prior to the eye examination has become routine in our unit. The issue was whether oral sucrose would provide additional benefit to patients during eye examination for ROP, since it is well documented to reduce pain in neonates during several other procedures. Our study used a blinded crossover approach in which patients functioned as their own control, thus increasing the statistical power to detect differences if they exist. As with prior studies, the reaction to pain in this study was not affected by gestational age. This study also used the PIPP scale because this test considers both physiologic and physical markers; has good intrater reliability, internal consistency, and construct validity; and was developed for premature infants. Also, the PIPP scale was used in our previous study examining eye pain prevention in neonates after pretreatment with a topical anesthetic, as well as in several other pain studies. The use of sucrose 24% reduced pain during the insertion of the eyelid speculum regardless of the definition for pain that was used. The analgesic effect of sucrose was not sustained after lid insertion and does not benefit all patients, but the acute pain prevention benefits are sufficient to justify routine use.

Conclusions

To expect one patient to benefit from sucrose, 2.3 infants would need to be treated to prevent one additional patient from elevating PIPP scores by 24 during placement of the eyelid speculum. Since sucrose is inexpensive and relatively nontoxic, it is reasonable to use sucrose to reduce pain during ROP examination in neonates who are already receiving enteral feedings.

Peter Gal PhD BCPS FCCP FASHP, Director, Pharmacy Division, Greensboro Area Health Education Center, Greensboro, NC; Clinical Professor, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC; Pharmacotherapy Specialist, Department of Neonatology, Women’s Hospital, Greensboro

Grace E Kiesling PhD, Staff Scientist, Biostatistics Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC

William O Young MD, Consulting Ophthalmologist, Neonatal Intensive Care Unit, Women’s Hospital; Pediatric Ophthalmology Associates PA, Greensboro

Kimberly K Dunaway PharmD, Staff Pharmacist, Pharmacy Department, Women’s Hospital

Virginia A Marsh RN BSN, Staff Nurse, Nursing Department, Neonatal Intensive Care Unit, Women’s Hospital

Susan M Jones RNC BSN, Staff Nurse, Nursing Department, Neonatal Intensive Care Unit, Women’s Hospital

Dawn H Shockley RN BS ADN, Staff Nurse, Nursing Department, Neonatal Intensive Care Unit, Women’s Hospital

Nicole L Weaver RN BSN, Staff Nurse, Nursing Department, Neonatal Intensive Care Unit, Women’s Hospital

Rita Q Carlos MD, Neonatologist, Neonatal Intensive Care Unit, Women’s Hospital

J Laurence Ransom MD, Medical Director, Neonatal Intensive Care Unit, Women’s Hospital; Clinical Professor, Department of Pediatrics, School of Medicine, University of North Carolina at Chapel Hill

Reprints: Dr. Gal, Greensboro AHEC, Ste. 100, 200 E. Northwood St., Greensboro, NC 27401-1020, fax 336/832-7851, peter.gal@ncagreensboro.com

References


EXTRACTO

INTRODUCCIÓN: Los exámenes oculares de la retinopatía del prematuro (ROP) resultan dolorosos para el neonato. La utilización de anestésicos tópicos en el examen ocular de ROP es una práctica habitual en nuestra Unidad Neonatal de Cuidados Intensivos, pero no elimina por completo las respuestas dolorosas. Se ha demostrado que las soluciones azucareadas reducen el dolor del procedimiento en el recién nacido.
Efficacy of Sucrose During Eye Examinations in Neontes

OBJETIVO. Este estudio examina si la administración de sacrosa al 24% junto al anestésico tópico mejora el control del dolor del procedimiento durante el examen ocular de ROP.

MÉTODOS. En este estudio con asignación aleatoria, doble ciego, controlado con placebo, y cruzado, se incluyeron neonatos nacidos con ≤30 semanas de gestación. Previamente al examen ocular, se asignó aleatoriamente al paciente bien solución oftálmica de clorhidrato de proparacaina al 0.5% más 2 mL de sacrosa al 24% o bien solución oftálmica de clorhidrato de proparacaina al 0.5% más 2 mL de agua estéril como placebo. En el examen subsiguiente, cada paciente recibió el tratamiento alternando. La sacrosa oral y el agua estéril se prepararon en la farmacia en jeringas similares, y los médicos, enfermeras, y farmacéuticos en la NICU desconocían el tratamiento administrado en cada caso. La medición del dolor se realizó mediante un sistema de puntuación que incluye la medición física y psicológica del dolor, escala PIPP (Premature Infant Pain Profile), y fue calculado por 2 enfermeras. La puntuación del dolor (PIPP) se realizó 1 y 5 minutos antes y después del examen ocular y durante la colocación inicial del espéculo ocular. Todos los exámenes oculares fueron realizados por el mismo oftalmólogo. Se investigaron diferentes definiciones de una respuesta al dolor.

RESULTADOS. El estudio incluyó 23 pacientes, de los cuales 12 pacientes recibieron inicialmente sacrosa como tratamiento y otros 11 pacientes recibieron el placebo. Para 3 de las 5 definiciones de respuesta al dolor, el dolor fue significativamente inferior durante la colocación del espéculo en aquellos pacientes que recibieron sacrosa en lugar del placebo. Tras el examen de ROP, las respuestas al dolor resultaron similares tanto con sacrosa como con placebo.

CONCLUSIONES. La sacrosa oral puede reducir la respuesta inmediata al dolor en los prematuros que se someten al examen ocular de ROP.

Enrique Muñoz Soler

RÉSUMÉ

OBJECTIF. L'utilisation topique de solutions anesthésiques est pratiquée courante pour contrôler la douleur associée aux examens oculaires lors du diagnostic d'une rétinopathie du nouveau-né. Une alternative possible aux anesthésiques topiques est l'utilisation d'une solution à base de sacrose. L'objectif de cette étude était d'évaluer si l'ajout d'une solution de sacrosa 24% à un anesthésique topique pouvait réduire la douleur associée à une telle procédure.

MÉTHODOLOGIE. Les nouveaux-nés d'un âge gestationnel de 30 semaines, chez qui un minimum de 2 examens oculaires étaient anticipés, ont été inclus dans cette étude à double-insu avec permutation et contrôlée par placebo. Les patients étaient assignés de façon aléatoire à une solution ophtalmique d'hydrochlorure de propacetame 0.5% et de sacrose 24% ainsi qu'à une solution ophtalmique d'hydrochlorure de propacetame 0.5% et d'eau stérile. Chaque patient recevait le traitement avant le premier examen oculaire puis le traitement alternatifs avant l'examen oculaire subséquent. Les solutions oculaires de sacrose 24% et d'eau stérile étaient préparées par le département de pharmacie dans des seringues à tuberculine d'apparence identique. Les médecins, les pharmaciens, et les infirmières de l'unité néonatale n'étaient pas informés de la nature des solutions administrées. La douleur était mesurée par une échelle validée (Premature Infant Pain Profile, PIPP) qui utilise des mesures physiologiques et physiques pour établir un score variant entre 1 et 21. Le score de la douleur était mesuré de façon simultanée par 2 infirmières 1 et 5 minutes avant l'examen oculaire et durant le placement initial du spéculum. Tous les examens oculaires étaient faits par le même ophtalmologiste. Plusieurs interprétations des scores de douleur ont été investiguées (score réel PIPP, augmentation du score PIPP de 4 points, score PIPP supérieur à 10 points, aussi sous la courbe évaluant le score PIPP en fonction du temps, différence de 4 points et plus entre les scores PIPP du groupe placebo et du groupe sacrose).

RESULTATS. Vingt-trois patients ont été recrutés pour cette étude, 12 ayant reçu lors du premier traitement la solution de sucrose 24% et 11 la solution d'eau stérile. Pour 3 des 5 méthodes d'interprétation de la réponse douloureuse, une douleur moins intense a été notée lors de l'insertion du spéculum chez les patients ayant reçu la solution de sucrose par rapport à la solution d'eau stérile. L'intensité de la douleur était toutefois similaire après l'examen oculaire.

CONCLUSIONS. L'utilisation d'une solution de sacrose 24% associée à une solution ophtalmique anesthésique semble réduire la réponse douloureuse immédiate associée à l'examen oculaire lors du diagnostic d'une rétinopathie du nouveau-né.

Sylvie Robert