Variability in Clinical Practice Guidelines for Sweetening Agents in Newborn Infants Undergoing Painful Procedures

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Objective: Sweetening agents have been recommended in position statements and consensus documents for procedural pain management in neonates; however, it is not clear if this has resulted in widespread adoption in clinical practice. The objective of this study was to investigate unit-specific protocols for the use of sweetening agents.

Methods: Structured telephone survey with qualified personnel in special care (level II) nurseries and neonatal intensive care (level III) units across Canada. The frequency and pattern of recommended use of sweetening agents was documented.

Results: Eighty-six of 92 units (93.5%) participated. Sixty-four percent recommended sucrose and 2.3% recommended glucose for procedural pain management; 87.7% had a guideline. Sweetening agents were most commonly recommended for venipuncture/venous cannulation (91.2% for both), lumbar puncture (87.7%), and heel lance (82.5%). Dosing guidelines ranged from 0.05 mL of 24% sucrose solution to 3 mL of 25% sucrose solution. Sweeteners were not recommended for infants with necrotizing enterocolitis (77.2%) or those who were nil per os (75%).

Conclusions: Sweetening agents were recommended for procedural pain management in two-thirds of special care nurseries and neonatal intensive care units across Canada with extensive variability in specific dosing guidelines. Audits of pain management practices should therefore account for unit-specific practice guidelines.

Key Words: sucrose, practice guidelines, pain management, infant/newborn

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Newborn infants in special care (level II) nurseries and intensive care (level III) units are exposed to many painful medical procedures as part of clinical care.[1] Not only do these procedures cause acute pain, but when performed repeatedly, lead to long-term changes in the central nervous system that causes alterations in the processing of subsequent painful stimuli.[2,3] As a result, pain prevention and management strategies have been identified as a priority for this patient population.[4]

Dozens of clinical trials have demonstrated analgesic effects from sweet-tasting substances such as sucrose when administered to newborn infants during painful medical procedures.[5] Although not fully understood, the underlying mechanism of action is hypothesized to involve activation of the endogenous opioid system by sweet taste.[6] Sucrose has been the most widely studied of the sweetening agents currently in use for the relief of pain, followed by glucose. Between 2000 and 2006, several consensus documents and position statements by pain researchers and national organizations [American Academy of Pediatrics (AAP) and Canadian Paediatric Society (CPS)] were published recommending routine use of sucrose for the management of procedural pain in neonates.[4,7–10]

It is not known if these recommendations have been adopted by special care nurseries and neonatal intensive care units. In the only previous national survey of neonatal unit protocols for analgesia conducted in Australia in 2004,[11] 23% of units reported using sucrose or other sweet-tasting solutions. That study was conducted before publication of a large systematic review and AAP and CPS position statements.[5,9] The objective of the present study was to determine current practice guidelines for the use of sweetening agents in newborn infants undergoing painful medical procedures in Canadian special care nurseries and neonatal intensive care units.

MATERIALS AND METHODS

We conducted a Canada-wide survey of special care nurseries and neonatal intensive care units regarding their clinical practice guidelines for sweetening agents. Potential units were identified from the provincial ministries of health for each province. Using a structured telephone interview, a trained interviewer questioned the charge nurse, nurse educator, or qualified designate in each unit about the use of sweet-tasting solutions and unit characteristics (such as number of inpatient beds, type of newborn care services provided, number of attending physicians). Potential respondents were identified by senior investigators (via local and national research and clinical networks) or by the units themselves (during first telephone contact by the

interviewer). All respondents verified their qualification to answer questions before their participation. The survey was designed according to standard survey construction guidelines and included mainly closed-ended questions.[12] It was pretested for clarity and completeness on respondents from 3 local institutions. The time needed to administer the survey was approximately 10 minutes. For units that used sweeteners, respondents mailed or faxed their protocols to the investigators to verify responses. The study was approved by the ethics boards of the University of Toronto and The Hospital for Sick Children. The study was explained and verbal consent was obtained from respondents before participation.

SAMPLE SIZE AND STATISTICAL ANALYSIS

We estimated a sample size of 100 units, with 23% having unit-specific protocols for sweeteners (as per the prior survey).[11] This resulted in a precision of approximately 10%.[13] Logistic regression was performed to identify factors predictive of sweetening agent utilization, including: type of unit; number of inpatient beds; number of physicians; presence of a pain committee; presence of nurse practitioners; and a pain champion. Categorical data were reported as frequency (percent) and continuous data were reported as mean (SD) or mode (range). Data were analyzed using the statistical software package SPSS (v.15.0, Chicago, IL). A P value of ≤ 0.05 was considered significant.

RESULTS

The study was conducted between June 12, 2007 and September 19, 2007. Out of 98 potential units identified by the provincial ministries of health, 92 qualified; in excluded units, neonatal special care and intensive care services were not being provided. In 4 cases, respondents could not be reached after multiple attempts, and in 2 cases, respondents declined participation. Therefore, interviews were conducted with respondents from 86 (93.5%) units.

Respondents included 33 unit managers, 19 nurse educators, 13 charge nurses, 10 pain committee members, 6 nurse practitioners, and 1 neonatologist. Fifty-two (60.5%) units contained special care nurseries, 3 (3.5%) contained neonatal intensive care units, and the remaining 31 (36%) contained both. The mean (SD) number of inpatient beds was 20 (14).

Overall, 55 (64%) of units had a practice guideline in place for the use of sucrose and 2 (2.3%) for another sweetener (glucose). Fifty (87.7%) units with a written protocol provided it to investigators. Most of the time, the respondent referred to the written protocol when answering survey questions. The respondent also qualified any aspect of the protocol that was unspecific or unclear. Fifty-two (91.2%) units with guidelines recommended sweetening agents for venipuncture/venous cannulation, followed by 50 (87.7%) for lumbar puncture and 47 (82.5%) for heel lancing, respectively (Table 1). In 24 (42.1%) units, a pacifier was always given with the sweetener.

The dose for sucrose ranged from 0.05 mL of 24% solution to 3 mL of 25% solution. In 80% of the units, the sucrose dosage regimen varied according to infant gestational age or weight. For infants < 31 weeks' gestation or < 1500 g, the most commonly recommended dose was 0.5 mL of 24% solution, and for ≥ 31 weeks' gestation or ≥ 1500 g, it was 1 mL of 24% solution. The guidelines restricted the use of sweetening agents to infants of ≥ 27 to 28 weeks' gestation in 11 units, and ≥ 30 to 32 weeks' gestation in 13 units.

TABLE 1. Recommended Use of Sweetening Agents for Different Procedures (N = 57)

Procedures	No. (%)
Venipuncture	52 (91.2)
Venous cannulation	52 (91.2)
Lumbar puncture	50 (87.7)
Heel lance	47 (82.5)
Intramuscular injection	45 (78.9)
Arterial puncture	43 (75.4)
Subcutaneous injection	42 (73.7)
Dressing change	38 (66.7)
Urinary catheterization	36 (63.2)
Suprapubic aspiration	34 (59.6)
Eye examination	33 (57.9)
Chest tube	32 (56.1)
Percutaneous central venous catheter placement	32 (56.1)
Nasogastric tube insertion	13 (22.8)
Tracheal suctioning	8 (14.0)
Endotracheal tube insertion	3 (5.3)

A limit on the maximum number of doses that could be administered during a single procedure was present in 23 (40.4%) units, and ranged from 1 to 4 (mode, 1). In addition, 42 (73.7%) units reported a maximum daily number of doses that ranged from 2 to 24 (mode, 6). The most common contraindications for the use of sweetening agents included proven/suspected necrotizing enterocolitis and nil per os, in 44 (77.2%) and 42 (75%) units, respectively (Table 2). Logistic regression analysis did not identify any factors that significantly predicted the reported utilization of sweetening agents.

DISCUSSION

The present study demonstrated that two-thirds of special care nurseries and neonatal intensive care units across Canada had clinical practice guidelines that support the use of sweetening agents for procedural pain management. This rate is almost 3 times higher than a 2004 survey in Australia,[11] but falls short of currently published consensus guidelines and position statements that recommend use of sweetening agents in all infants undergoing procedures.[9]

TABLE 2. Contraindications for Use of Sweetening Agents (N = 57)

Characteristic	No. (%)
Necrotizing enterocolitis	44 (77.2)
Nil per os (NPO)*	42 (75.0)
Glucose intolerance	21 (36.8)
Concurrent opioid use	21 (36.8)
Specific gestational age group	18 (31.6)
Infant of diabetic mother*	16 (28.6)
Parental refusal	12 (21.1)

*N = 56.

In addition, the present study determined that the dosing regimens for sweeteners were highly variable, and restrictions were often placed on the characteristics of infants that were eligible to receive them. Thus, the presence of a practice guideline did not ensure that all infants were eligible to receive sweetening agents before all painful medical procedures.

We hypothesize that the variability in clinical practice guidelines is due to gaps in knowledge about the pharmacology of sweetening agents, including the mechanism of action, optimal dose, and safety of repeated does.[9] That there is no consensus about what constitutes the "appropriate use of sweetening agents" among units has implications for the interpretation of pain audits that document actual utilization patterns of analgesic agents. Pain management audits are usually discussed in terms of barriers in knowledge, attitudes, and beliefs.[14] It is clear from the results of this study that utilization patterns for sweetening agents need to be interpreted within the context of acceptable practices in individual units rather than externally published consensus statements.

The strengths of the present study are the very high response rate (93.5%) and validation of protocols for analgesic use. In contrast, the previous survey achieved a relatively low response rate (58%), and did not validate responses.[11] We did not measure actual utilization of sweetening agents, and therefore cannot comment on the proportion of infants given sweetening agents relative to guideline recommendations. This is clearly an important area for future study.

In conclusion, this study demonstrated that two-thirds of Canadian special care units and neonatal intensive care units have practice guidelines in place for the use of sweetening agents to manage procedural pain in neonates. There are wide variations in prescribing guidelines, resulting in the potential for many infants to undergo procedures without sweetening agent analgesia. Further study of the pharmacology of sweeteners is needed to answer the current gaps in research knowledge that will in turn, be used to modify and improve practice guidelines.

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