ORAL GLUCOSE SOLUTION BEFORE VENEPUNCTURE FOR NEONATAL PAIN RELIEF

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BACKGROUND

- Newborns feel pain
- Pain caused brain damage → hypoxia, tachycardia, increased ICP
- Pain experienced → long term effect
- Effective treatment of pain is needed
- Analgesic effect of glucose → beta endorphin

OBJECTIVES

- To assess analgesic effect of glucose during venepuncture
- Hypothesis:

  *Oral glucose more effective than placebo

  *Oral glucose < 2ml less effective

  *Effect increased if combined with other technique

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

TYPES OF STUDIES

- All RCT, crossover studies comparing outcome oral glucose vs other interventions
- Contamination & co-intervention → excluded

TYPES OF PARTICIPANTS

- Healthy infants: preterm & term, 1-30 days, APGAR score at least 7 at 5 min.

TYPES OF INTERVENTION

- Oral glucose before venepuncture vs no treatment, placebo, sucrose, fructose, sucking, multisensorial stimulation

TYPE OF OUTCOME MEASURED

- Evaluation of pain

SEARCH STRATEGY FOR IDENTIFICATION OF THE STUDIES

- Medline search
- Cochrane controlled trial registry search

METHODS OF REVIEWS IN PREPARATION

- Abstract and title were screened
- Inclusion criteria applied
- Methods of randomization → summarized
- Quality of study → specified criteria for elimination bias (selection bias, performance bias, attrition bias and detection bias) → scored
- Pain score: DAN score & PIPP score

Douleur Aiguë Nouveau-né (DAN) pain score

1) Eyes closed, regular breathing, no movements
2) Eyes closed, irregular breathing, no movements
3) Eyes open, no gross movements
4) Eyes open, continual gross movements, no crying
5) Eyes open or closed, fussing, or crying

Pain score from 1 to 10, where 1 is no pain and 10 is maximum pain

Premature Infant Pain Profile (PIPP) pain score

Has been designed to assess pain in preterm and term infants

- Calculated from 7 different items, each graded from 0 to 3
- 2 items: neonatal characteristics (gestational age and behavioral state before the painful event)
- 2 items: physiologic measurements (heart rate and oxygen saturation)
- 3 items: facial movements (brow bulge, eye squeeze and naso-labial furrow)
- 5 items: change from baseline during a successive observation period of 30 second

A total PIPP score of 6 or less generally indicates minimal or no pain

STUDIES DESCRIPTION

- 7 RCT: 5 true rct, 2 crossover studies
- All in developed countries: Italy, Germany, Sweden, France
- Sample size: 386, participants: 402 infants
- 2 Studies excluded
- 4 Std → term infant; 1 std →preterm
- 5 Std→ DAN score, 2std → PIPP score
- Characteristics of the studies in table 1

Table 1. Characteristics of include studies

STUDIES	METHODS	PARTICIPANTS	INTERVENTION	OUTCOME
Valerio Belliani, 2002	RCT, blind; allocation concealment :B selection bias B, Performed bias A Attrition bias :A Detection bias: A	120 infants 30-40weeks	Each group 20 infants: 1). Control ,no analgesic 2)1ml glucose30% 3)1mlsterilwater&sucking 4)1ml glucose & sucking 5)Sensorial saturation &glucose 1ml glucose30% 6)Sensorial saturation	Pain score (DAN score) Duration of crying
Karl Bauer, 2004	RCT, double blind Allocation concealment: A Selection bias :A Performance: A Attrition :A Detection: A	58 infants, ≥30 weeks >12h-8days	1)2ml oral glucose30% (n=18) 2)0.4mlglucose30%(n=20) 3)2ml sterile water(n=20)	Pain score (PIPP score) Duration of crying
R Carbajal, 1999	RCT, prospective Allocation concealment: A Selection :A Performance: B Attrition :A Detection: A(	150 infants ,full term ≥ 24 hours	Each group:25 infants 1) No treatment 2) Placebo 2ml sterile water 3) 2ml 30% glucose 4) 2ml 30%sucrose 5) Pacifier 6) 2ml30% glucose &pacifier	Pain score (DAN score)
Mustapa Akcam,2004	RCT, placebo control, crossover study Allocation of concealment; A Selection bias A Performance :A Attrition: A	34healthy infants, 37-42 weeks >48hours to <28days,	Each infant was assessed three time 1)0.5ml of 30% fructose 2)0.5ml of 30%glucose 3)0.5ml of sterile water	Pain score (DAN score)
Ricardo Carbajal, 2002	RCT, prospective, two crossover study. Allocation of concealment: A Selection bias : A Performance :B Attrition :A	40 stabile infants, ≤32 weeks, ≥48 hours.	1) 25 infants:0.3ml 30% oral glucose Vs 0.3ml sterile water 2) 15 infants:0.3ml 30% oral glucose Vs 0.3ml glucose+ sucking or pacifier	Pain score (DAN score)

Table 2.Characteristic of exclude studies

STUDY	Reason for exclusion
Ricardo Carjabal, 2003	Co-intervention effect of glucose by sucking pacifier It was not possible to extract data relating only to the effect of glucose because it co- intervention with effect of pacifier.
Maria Gradin ,2002	Contamination effect of glucose by addition placebo (sterile water) The effect of placebo also was studied comparing to effect glucose . It was not possible to extract data of pure glucose and pure placebo.

METHODOLOGICAL QUALITY

- 7 Std met inclusion criteria
- Methods of randomization
  - *6 used random number table
  - *1 no mention of sample size calculation
  - *1 used pharmacy performed randomization
  - *1 no description of concealment allocation
- 5 Std used placebo controls

- Performance bias: 4 std → high score
  3 std → medium score
- Attrition bias: all std → high score
- Detection bias: 2 std (contamination and co-intervention) → excluded

RESULTS

Studies	Participants N(n1&n2)	Outcome	Statistic methods	Result	Effect size
1) 1ml glucose 30% VS no treatment					
Bellieni CV, 2002	120(20&20)	Pain score/ DAN score	Median	9.5(1-10) Vs 9(5-10)	median diff: 0.5
2) 1ml glucose 30% Vs 1ml sterile water and sucking					
Bellieni CV, 2002	120(20&20)	Pain score/ DAN score	Median	9.5(1-10) Vs 6.3(4-10)	Mediandif.3.2 P=0.001
3) 1ml glucose 30% Vs 1ml glucose and sucking					
Bellieni CV, 2002	120(20&20)	Pain score/ DAN score	Median	9.5(1-10) Vs 4(1-10)	Median dif.5.5 p<0.0001
4)1ml glucose 30% Vs multisensorial stimulation					
Bellieni CV, 2002	120(20&20)	Pain score/ DAN score	Median	9.5(1-10)Vs 8.5(1-10)	Median dif.1 P>0.5
5)1ml glucose 30% Vs multisensorial stimulation and 1ml glucose 30%					
Bellieni CV, 2002	120(20&20)	Pain score/ Dan score	Median	9.5(1-10) Vs 1(0-6)	Median dif.8.5 P<0.0001

Studies	Participants N(n1&n2)	Outcome	Statistic methods	Result	Effect size
6) 2 ml glucose 30% Vs no treatment					
Carbajal R,1999	150(25&25)	Pain score/ DANscore	Median	5(3-7) vs 7(5-10)	Median dif.2
7) 2ml glucose 30% Vs 2ml placebo (sterile water)					
Bauer K,2004	58 (18&20)	Pain score/ PIPP score	Median	5.5(4-9) vs 11(7-12)	Median dif.5.5 P=0.01
Carbajal R,1999	150(25&25)	Pain score/ DAN score	Median	5(3-7) Vs 7(6-10)	Median dif. 2 P=0.005
8) 2ml glucose 30% Vs pacifier (sucking)					
Carbajal R,1999	150(25&25)	Pain score/ DAN score	Median	5(3-7) vs 2(1-4)	Median dif.5.5 P=0.01
9) 2ml glucose 30% Vs 2ml Sucrose 30%					
Carbajal R,1999	150(25&25)	Pain score/ DAN score	Median	5(3-7) Vs 5(2-8)	Median dif.0 P>0.5
10) 2ml glucose 30% Vs 0.4 glucose 30%					
Bauer K,2004	58(20&20)	Pain score/ PIPP score	Median	5,5(4-9) vs 7(4-11)	Median dif.1.5 P=0,01

Studies	Participants N(n1&n2)	Outcome	Statistic methods	Result	Effect size
11) 0.5ml glucose 30% Vs 0.5 fructose 30%					
Akcam M,2004	34(34&34)	Pain score/ DAN score	Median	4.0(2-4) vs 4.0(2-5)	Median dif.0
12) 0.5 ml glucose 30% Vs 0.5 ml sterile water					
Akcam M,2004	34(34&34)	Pain score/ DAN score	Median	3.6±1.5 Vs 5.6±1.4	Median dif.2 P<0.001
13) 0.3 ml glucose 30% Vs 0.3 ml sterile water					
Carbajal R.2002	40(24&24)	Pain score/ DAN score	Median	4.5(1-6) Vs 7.0(2.59.75)	Median dif.2.5
14) 0.3 ml glucose 30% Vs 0.3 ml sterile water and pacifier					
Carbajal R,2002	40(15&15)	Pain score / DAN score	Median	4.6(3-6.2) Vs 3.8(2-5.5)	Median dif.0.8 P=0.4

DISCUSSION

- Quality of the std → some bias. 3 std → performed bias, 2 std → detection bias
- 5 Std → placebo controlled
- 2 Std using 2ml glucose 30% → pain score: <6 comparable to 2ml sucrose 30%
- Effect of low dose glucose (<2ml) → variation in pain score
- Belliani: 1ml glucose 30% →pain score >9

  Pain score decreased → if combined with sucking or multisensorial stimulation → sensorial stimulation blocked nociceptive transmission
- Akcam: using 0.5ml and Carbajal using 0.3ml → still effective (pain score<6)
- Analgesic effect → activation of endogenous opioid

REVIEWER'S CONCLUSION

- IMPLICATION FOR PRACTICE

  * Pain must be treated because: ethical reasons, pain caused brain damage
  * Pharmacological treatment → rarely
  * Low dose glucose 30% → variation in effectiveness
  * 2 ml glucose 30% most effective as effective as sucrose 30%
  * In present time, glucose can be as analgesic in minor painful procedure

- IMPLICATION FOR RESEARCH

* Need to carry out studies: larger sample size, variation in dose and gestational age in developing countries

* Non pharmacologic treatment

THANK YOU