Author(s): VS/AT
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Question: Should sucrose solution vs placebo/no treatment be used for reducing vaccine injection pain in children up to 2 years?[1,2]
Settings: hospital, clinics
Bibliography: Allen 1996 (1-12), Barr 1995, Chattopadhyay 2011, Dilli 2009 (3), Harrison 2014 (1,2), Hatfield 2008, Hatfield 2008 a, Harrington 2012 (3,4), Lewindon 1998, Liaw 2011 (2), Moradi 2012 (1,2), Mowery 2008, Poulsen 2009, Priambodo 2008, Ramenghi 2002 (1,2), Sahebihagh 2011 (4), Soriano Faura 2003, Yilmaz 2014 (1,2)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sucrose solution	Placebo/no treatment	Relative (95% CI)	Absolute		
Distress Acute[3,4,5] (measured with: validated tools (Neonatal Infant Pain Scale 0-7, Neonatal Facial Coding System 0-48, Modified Behavioural Pain Scale 0-10, Visual Analog Scale 0-10, University of Wisconsin Children's Hospital Pain Scale 0-20, Faces Legs Activity Cry Consolability 0-10, Cry duration) by researchers, parents and clinicians; Better indicated by lower values)												
12	randomised trials[6]	no serious risk of bias	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	421	460	-	SMD 0.37 lower (0.67 to 0.06 lower)[3,4,5]	⊕⊕⊕⊕ HIGH	CRITICAL
Distress Acute + Recovery[4,5,8,9,10] (measured with: validated tools (Neonatal Infant Pain Scale 0-7, Modified Riley Pain Score 0-9, Faces Legs Activity Cry Consolability 0-10, Cry duration) by researchers, parents and clinician; Better indicated by lower values)												
14	randomised trials[11]	no serious risk of bias	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	1134	937	-	SMD 0.76 lower (1.19 to 0.34 lower)[4,5,8,9,10]	⊕⊕⊕⊕ HIGH	CRITICAL
Distress Recovery[3,4,5] (measured with: validated tools (Neonatal Infant Pain Scale 0-7, Neonatal Facial Coding System 0-48, Modified Behavioural Pain Scale 0-10, University of Winsconsin Children's Hospital Pain Scale 0-20) by researchers, parents and clinicians; Better indicated by lower values)												
7	randomised trials[6]	no serious risk of bias	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	308	359	-	SMD 0.5 lower (0.96 to 0.03 lower)[3,4,5]	⊕⊕⊕⊕ HIGH	CRITICAL
Distress Acute (yes/no)[10] (assessed with: validated tools (Neonatal Infant Pain Scale 0-7, Children's Hospital of Eastern Ontario Pain Scale 4-13, Cry, yes/no) by researcher)												

2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[12]	none	127/371 (34.2%)	159/186 (85.5%)	RR 0.37 (0.2 to 0.69)[10]	539 fewer per 1000 (from 265 fewer to 684 fewer)	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		
Distress Acute + Recovery (yes/no) (assessed with: validated tools (Neonatal Infant Pain Scale 0-7, crying) by researcher)												
3	randomised trials[11]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[13]	none	26/87 (29.9%)	45/88 (51.1%)	RR 0.71 (0.27 to 1.87)	148 fewer per 1000 (from 373 fewer to 445 more)	⊕⊕⊕O MODERATE	CRITICAL
								0%		-		
Safety (assessed with: observation of infant for cough or gagging)												
3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[14]	none	4/119 (3.4%)	1/117 (0.85%)	RR 2.83 (0.45 to 17.61)[15]	16 more per 1000 (from 5 fewer to 142 more)	⊕⊕⊕O MODERATE	IMPORTANT
								0%		-		
Procedure Duration (measured with: validated tool (stopwatch, number of seconds) by researcher; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[13]	none	25	24	-	SMD 0.15 lower (0.71 lower to 0.41 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Use of Intervention[16] (assessed with: acceptability/acceptance by infant)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[12]	none	-	-	not pooled[16]	not pooled[16]	⊕⊕⊕O MODERATE	IMPORTANT
								0%		not pooled		
Parent Preference[17] (assessed with: questionnaire about future use)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[14]	none	-	-	-	-	⊕⊕⊕⊕ HIGH	IMPORTANT
								0%		-		

Parent Fear, Vaccine Compliance, Preference, Satisfaction (assessed with: no data were identified for these important outcomes)												
0	No evidence available					none	-	-	-	-		IMPORTANT
								0%		-		

[1] In included studies, the concentration of sucrose solution ranged from 12% to 75%; the dose was not specified in one study, however, it was described as a saturated solution. The volume used was 2 mL in all but 3 studies where it was 0.75 mL (Barr 1995) and 0.6 mL/kg (Hatfield 2008, 2008a).

[2] In the studies by Allen (7-12), Dilli 2009 (3), Liaw 2011 (2), and Sahebihagh 2011 (4), there was a no treatment control group; the remaining studies included placebo water.

[3] In study by Poulsen (2009), data are not provided; however, researchers report no statistically significant differences between groups. That study compared 12% sucrose to placebo water.

[4] In the study by Moradi (2012), the sample size in the control group was divided by 2.

[5] In the study by Allen 1996, the sample size in the sucrose group was divided by 2

[6] Study by Poulsen (2009) could not be included in the meta-analysis as pain scores not provided for intervention (sucrose) and control (water) group

[7] Heterogeneity can be explained by variability in dose, administration technique and personnel involved, cointerventions, and age of participants

[8] In the study by Harrington (2012), oral rotavirus vaccine was administered prior to vaccine injections; since this vaccine contains sweet-tasting substances, there may have been contamination

[9] In the study by Ramenghi 2002, the sample size in the control group was divided by 2.

[10] In the study by Yilmaz (2014), the sample size in the control group was divided by 2.

[11] In study by Chattopadhya (2011), the concentration of sucrose solution is not specified; however, it is reported to be a saturated solution

[12] Sample size was below the recommended optimum information size (OIS) of 400 for an effect size of 0.2

[13] Confidence interval crosses line of nonsignificance and sample size was below the recommended optimum information size (OIS) of 400 for an effect size of 0.2

[14] Sample size was below the recommended optimum information size (OIS) of 400 for an effect size of 0.2

[15] Duration < 10 seconds and not clinically important

[16] In 1 study (Hatfield 2008), 4/100 (4%) of infants refused to accept sucrose. Separately, in study of tactile stimulation vs control whereby all infants were given sucrose (Taddio 2014 a), 28/121 (23%) were unsettled or crying during sucrose administration.

[17] In study by Harrison 2014 (1,2), only 2 parents reported they would not use the intervention (sucrose or water) out of 29