

Formula Thickeners for Gastroesophageal Reflux in Infants up to 6 Months: A Meta-analysis

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Introduction

Gastro-esophageal reflux is a physiologic self-resolving phenomenon in infants that does not require treatment most of the time but could become pathological when it causes complications and bothersome symptoms. Among the non-pharmacologic measures used to treat reflux in infants, many people turn towards using pre-thickened formula that are advertised as "anti-reflux". Research on these formula thickeners are conflicting in their effect on the reduction of symptoms of regurgitation among infants.

Objectives

To synthesize available evidence from published studies on the effectiveness of formula thickeners in the management of symptoms of GER in infants up to six months

Methodology

A meta-analysis was done using randomized controlled trials published up to 2020 which compared the effectiveness of pre-thickened formula in decreasing the symptoms of GER. A database search using The Cochrane Library, PubMed®, Medline, Embase, and Google Scholar, was done by the investigators. Pooled estimates of Risk Ratio for quit rates was computed using DerSimonian and Laird random-effects model.

Results

BASELINE

	Experimental Control							Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Chao et al., 2007 Baseline	3.69	0.74	32	3.71	0.69	31	25.2%	-0.03 [-0.52, 0.47]	+
Hegar et al., 2008 Baseline	5.7	1.9	20	5.9	1.7	20	24.4%	-0.11 [-0.73, 0.51]	-
Moukarzel et al., 2007 Reg/Baseline	7.1	3.9	28	6.5	3.7	32	25.1%	0.16 [-0.35, 0.66]	
Vanderhoof et al., 2003 Baseline	13	1	55	11	1	48	25.3%	1.99 [1.51, 2.46]	
Total (95% CI)			135			131	100.0%	0.51 [-0.52, 1.53]	-
Heterogeneity: $Tau^2 = 1.02$; $Chi^2 = 46.3$ Test for overall effect: $Z = 0.97$ (P = 0.3		-4 -2 0 2 4							
1651 101 Overall ellect. 2 = 0.57 (F = 0.33)									Experimental Control

WEEK 1

	Experimental Control				,	Sta. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Hegar et al., 2008 W1	4	1.7	20	5.4	1.8	20	44.5%	-0.78 [-1.43, -0.14]	
Vanderhoof et al., 2003 W1	6	1	50	6	1	47	55.5%	0.00 [-0.40, 0.40]	+
Total (95% CI)			70			67	100.0%	-0.35 [-1.11, 0.41]	•
Heterogeneity: Tau ² = 0.23; C Test for overall effect: Z = 0.9		-4 -2 0 2 4 Experimental Control							

WEEK 4

	Experimental			Control				Sta. Mean Difference	Sta. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Chao et al., 2007 W4	2.84	0.81	32	2.39	0.86	31	34.1%	0.53 [0.03, 1.04]	-	
Hegar et al., 2008 W4	2.1	2.1	20	3.3	2.3	20	32.4%	-0.53 [-1.17, 0.10]		
Moukarzel et al., 2007 Reg/W4	2.3	2	28	5.2	3.1	32	33.5%	-1.08 [-1.63, -0.54]		
Total (95% CI)			80			83	100.0%	-0.35 [-1.35, 0.64]	-	
Heterogeneity: Tau ² = 0.68; Chi ² :		-4 -2 0 2 4	-							
Test for overall effect: Z = 0.70 (P	= 0.48)	Experimental Control								

Conclusion

The results of this meta-analysis revealed inconclusive evidence that formula thickeners decrease the frequency of regurgitation among infants up to six months old. However, the current study had several limitations and factors affecting the data analysis. Recommendations to future studies exploring the same topic include: a) doing subgroup analysis comparing the effect of different types of formula thickeners and different duration of intervention on the frequency of regurgitation, b) using other outcomes such as esophageal pH and manometry findings, and c) exploring other nonpharmacologic co-intervention such as parental reassurance, positional therapy, and adjustment of timing and frequency of feedings.

KEYWORDS:

Gastroesophageal reflux, infants, formula thickeners, pre-thickened formula, regurgitation