ACETYLCYSTEINE AND CARBOCYSTEINE FOR ACUTE UPPER AND LOWER RESPIRATORY TRACT INFECTIONS IN PAEDIATRIC PATIENTS WITHOUT CHRONIC BRONCHO- PULMONARY DISEASE

GENERAL DEPARMENT

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BACKGROUND

- The most commonly prescribed mucolytic drugs
- No systematic review
- 2013 The Cochrane Collaboration. Published by John Wiley & Sons
- Randomised controlled trials (RCTs)

SELECTION CRITERIA

PARTICIPANTS

- < 18 years
- Treated in primary, secondary or tertiary care settings
- Respiratory tract infection, acute pneumonia, acute bronchitis, acute bronchiolitis or acute cough (pertussis)
- Duration of symptoms less than four week

SELECTION CRITERIA
PARTICIPANTS- EXCLUDED TRIALS

- Acetaminophen intoxication
- Bronchiectasis, cystic fibrosis or broncho-pulmonary dysplasia
- Underlying immunodeficiency or respiratory tract anatomical defect
- Acute respiratory distress requiring mechanical ventilation

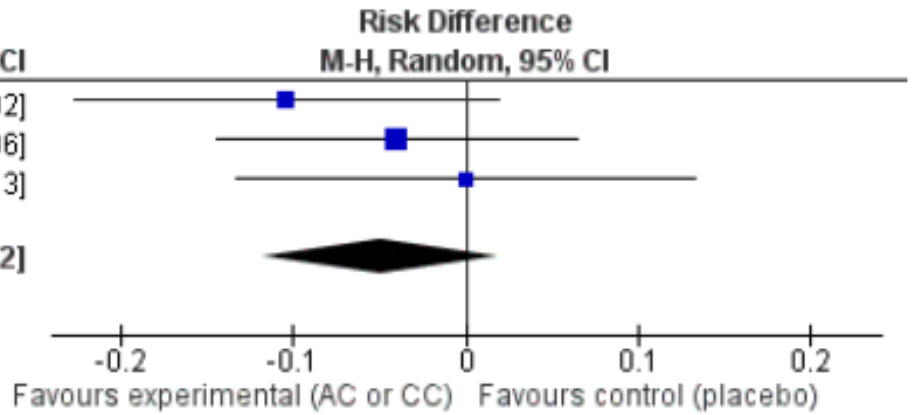
1/ EFFICACY

- Randomised controlled trials (RCTs) comparing versus placebo, either alone or as an add-on therapy
- Six trials (497 participants)

Figure 3. Forest plot of comparison: 1 Febrile state (AC vs placebo), outcome: 1.1 Febrile state after 6 days.

Study or Subgroup	Treatment (AC or CC) Events	Total	Placebo Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Bellomo 1972	0	30	3	29	30.6%	-0.10 [-0.23, 0.02]
Biscatti 1972	0	25	1	25	42.9%	-0.04 [-0.14, 0.06]
Zanini 1974	0	19	0	11	26.6%	0.00 [-0.13, 0.13]
Total (95% CI)		**74**		**65**	**100.0%**	**-0.05 [-0.12, 0.02]**
Total events	0		4			

Heterogeneity: Tau² = 0.00; Chi² = 1.40, df = 2 (P = 0.50); I² = 0%
Test for overall effect: Z = 1.40 (P = 0.16)

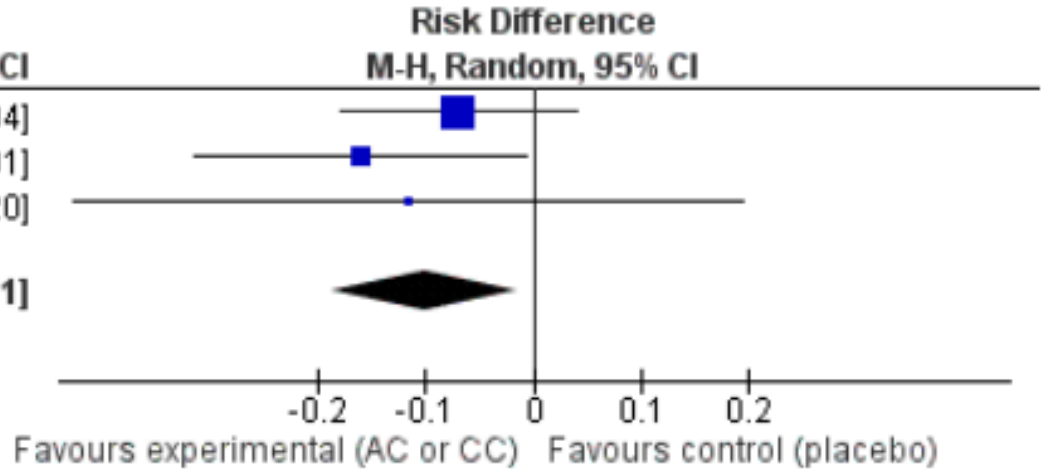


RR: 0,21

Figure 4. Forest plot of comparison: 4 Cough (AC vs placebo), outcome: 4.1 Cough after 6 to 7 days.

Study or Subgroup	AC or CC Events	Total	Placebo Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Bellomo 1972	0	30	2	29	62.0%	-0.07 [-0.18, 0.04]
Biscatti 1972	0	25	4	25	30.4%	-0.16 [-0.31, -0.01]
Zanini 1974	3	19	3	11	7.6%	-0.11 [-0.42, 0.20]
Total (95% CI)		**74**		**65**	**100.0%**	**-0.10 [-0.19, -0.01]**
Total events	3		9			

Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 2 (P = 0.62); I² = 0%
Test for overall effect: Z = 2.30 (P = 0.02)

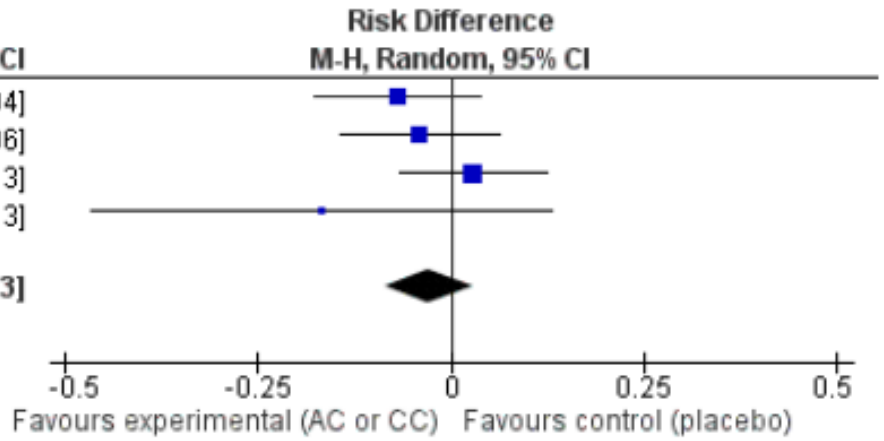


RR: 0,37

Figure 5. Forest plot of comparison: 3 Dyspnoea (AC or CC versus placebo), outcome: 3.1 Dyspnoea after 6 to 7 days.

Study or Subgroup	Treatment (AC or CC) Events	Total	Placebo Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Bellomo 1972	0	30	2	29	28.6%	-0.07 [-0.18, 0.04]
Biscatti 1972	0	25	1	25	31.1%	-0.04 [-0.14, 0.06]
Malka 1990	4	49	3	57	36.4%	0.03 [-0.07, 0.13]
Zanini 1974	2	19	3	11	3.8%	-0.17 [-0.46, 0.13]
Total (95% CI)		**123**		**122**	**100.0%**	**-0.03 [-0.09, 0.03]**
Total events	6		9			

Heterogeneity: Tau² = 0.00; Chi² = 2.81, df = 3 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)

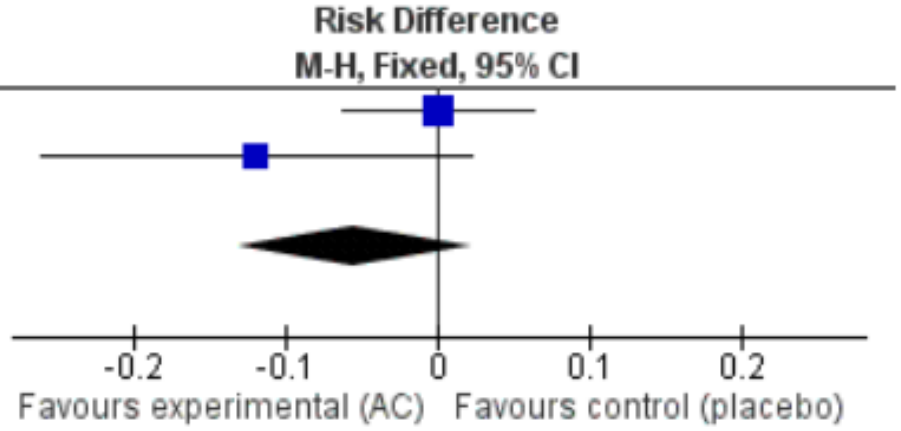


RR: o,66

Figure 6. Forest plot of comparison: 3 Thoracic semeiologic alterations (AC vs placebo), outcome: 3.1 Thoracic semeiologic alterations (after 3 days).

Study or Subgroup	AC Events	Total	Placebo Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Bellomo 1972	0	30	0	29	54.1%	0.00 [-0.06, 0.06]
Biscatti 1972	0	25	3	25	45.9%	-0.12 [-0.26, 0.02]
Total (95% CI)		**55**		**54**	**100.0%**	**-0.06 [-0.13, 0.02]**
Total events	0		3			

Heterogeneity: Chi² = 3.67, df = 1 (P = 0.06); I² = 73%
Test for overall effect: Z = 1.41 (P = 0.16)



CONCLUSION

- Some benefits on frequency, intensity and duration of symptoms
- Differences were sometimes small, not statistically significant and/or of little clinical relevance.
- Not statistically significant except for cough

2/ SAFETY

- Comparing versus active treatment or no treatment and case reports
- Thirty-four studies (2064 children)

* 10 studies included participants under 2 years (262 patients)

- Evaluated: clinical, biological, radiographic or pulmonary function test parameters

CONCLUSION

- Good clinical safety
- very few data in infants younger than 2 years
- Gastrointestinal side effects (nausea, vomiting, diarrhea) (2-13%)
- Bronchorrhoea : 59 cases in the French pharmacovigilance system


Thank
You