LEUKOTRIENE INHIBITORS FOR BRONCHIOLITIS IN INFANTS AND YOUNG CHILDREN
Leukotriene inhibitors for bronchiolitis in infants and young children (Review)

Bronchiolitis is a common acute inflammatory illness of the bronchioles.

10% of children in high-income countries contract bronchiolitis in the first year of life, 2% - 3% : hospitalisation.
The cause: respiratory syncytial virus (RSV), parainfluenza, influenza, adenovirus and rhinovirus.

The absence of clear scientific evidence for a specific treatment approach.

Bronchodilators, antibiotics and steroids are widely used but not routinely recommended.

→ new treatment approaches are necessary.
Leukotriene inhibitors (LI) can decrease the concentration of leukotrienes and reduce the symptoms of wheezing and coughing.
Montelukast has been approved by the US Food and Drug Administration (FDA) for use in children < 2 years.
To assess the efficacy and safety of leukotriene inhibitors for bronchiolitis in infants and young children.
METHODS

Criteria for considering studies for this review:

- **Types of studies:** RCTs comparing leukotriene inhibitors with control (placebo or other interventions).

- **Types of participants:** infants and children < 24 months, with physician-diagnosed bronchiolitis
TYPES OF OUTCOME MEASURES:

Primary outcomes
1. Length of hospital stay.
2. All-cause mortality.

Secondary outcomes
1. Clinical severity score.
2. Percentage of symptom-free days.
3. Percentage of children requiring ventilation.
4. Oxygen saturation.
5. Recurrent wheezing.
6. Respiratory rate.
7. Clinical adverse effects.
Figure 1. Study flow diagram.

170 records identified through database searching

2 additional records identified through other sources

172 records for title and abstract screening

123 records excluded

49 records for full-text screening for eligibility

37 records (33 studies) excluded with reasons

12 records involving 6 studies met the inclusion criteria

1 study was excluded because the investigators could not provide original data

5 studies included in this review
RESULTS OF THE SEARCH

- 5 RCTs: Denmark, Mexico, Singapore, South Africa, USA, South Korea and Japan, Belgium, Egypt and Israel.
- 1296 participants hospitalised.
- Intervention: 4 mg montelukast → discharge/ for several weeks.
- Follow up: 3 - 12 months.
RESULTS

1. Length of hospital stay: mean difference (MD) - 0.95 days, 95% confidence interval (CI) -3.08 - 1.19, P = 0.38.
RESULTS

2. All - cause mortality:

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Leukotriene inhibitors n/N</th>
<th>Placebo n/N</th>
<th>Risk Ratio IV/Random, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio IV/Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisgaard 2008</td>
<td>2/634</td>
<td>0/318</td>
<td></td>
<td>100.0%</td>
<td>2.51 [0.12, 52.16]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>634</strong></td>
<td><strong>318</strong></td>
<td></td>
<td>100.0%</td>
<td>2.51 [0.12, 52.16]</td>
</tr>
</tbody>
</table>

Total events: 2 (Leukotriene inhibitors), 0 (Placebo)
Heterogeneity: not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable
4. Clinical severity day score (day2):

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Leukotriene inhibitors</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amirav 2008</td>
<td>23 (3.52 (1.77))</td>
<td>30 (3.42 (1.22))</td>
<td>-0.10 [-0.74, 0.94]</td>
<td>51.9 %</td>
<td></td>
</tr>
<tr>
<td>Zedan 2010</td>
<td>46 (3.34 (1.38))</td>
<td>37 (5.42 (3.47))</td>
<td>-2.08 [-3.27, -0.89]</td>
<td>48.1 %</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>69 (3.38 (1.38))</td>
<td>67 (5.42 (3.47))</td>
<td>-0.95 [-3.08, 1.19]</td>
<td>100.0 %</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 2.10; \text{Chi}^2 = 8.60, df = 1 (P = 0.003); I^2 = 88%$
Test for overall effect: $Z = 0.87 (P = 0.38)$
Test for subgroup differences: Not applicable
5. Clinical severity day score (day3):

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Leukotriene inhibitors</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amirav 2008</td>
<td>20</td>
<td>29</td>
<td>6.15 (2.43)</td>
<td>4.86 (2.23)</td>
<td>47.9 %</td>
</tr>
<tr>
<td>Zedan 2010</td>
<td>46</td>
<td>37</td>
<td>3.64 (2.58)</td>
<td>4.5 (2.19)</td>
<td>52.1 %</td>
</tr>
</tbody>
</table>

Total (95% CI) 66 66 100.0 % 0.17 [-1.93, 2.28]

Heterogeneity: Tau² = 1.94; Chi² = 6.24, df = 1 (P = 0.01); I² = 84%
Test for overall effect: Z = 0.16 (P = 0.87)
Test for subgroup differences: Not applicable
RESULTS

6. Percentage of children requiring ventilation
7. Oxygen saturation
8. Respiratory rate
   → No relevant data were available
9. Recurrent wheezing:
   One study reported/1 years: did not reduce the incidence of recurrent wheezing.
10. **Clinical adverse effects:**

- One study of 952 children reported 2 deaths in the leukotriene inhibitors group: neither was determined to be drug-related.
- Adverse events: diarrhoea, wheezing shortly after administration and rash.
CONCLUSIONS

- The current evidence does not allow definitive conclusions to be made about the effects of LI on length of hospital stay and clinical severity score.
- The quality of the evidence was low.
- Further large studies are required.
THANK YOU!