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| **Study reference** | **Study characteristics** | **Patient characteristics 2** | **Intervention (I)** | **Comparison / control (C) 3** | **Follow-up** | **Outcome measures and effect size 4** | **Comments** |
| Skjerven, 2013 | Type of study:  RCT  Setting and country:  - Inpatients  - Norway  Funding and conflicts of interest:  Supported by Medicines for Children, a publicly funded body  administered by Haukeland University Hospital.  Disclosure forms provided by the authors are available with  the full text of this article at NEJM.org. | Inclusion criteria:  The inclusion criteria were clinical signs of bronchiolitis as defined by Court, Med J 1973;49:771-6, an  age of less than 12 months, and an overall clinical score of at least 4 on a scale of 0 to 10. The clinical score was the sum of points allotted, from 0 (indicating normal findings) to 2 (indicating severe illness), for each of the following: general condition, skin color, findings on auscultation,  respiratory rate, and retractions.  Exclusion criteria:  The exclusion criteria were the presence of any serious cardiac, immunologic, neurologic, or oncologic disease or any serious pulmonary disease other than bronchiolitis; more than one previous episode of obstructive airway disease; symptoms of disease of the lower airway (e.g., coughing) for more than 4 weeks; and receipt of any glucocorticoid therapy in the preceding 4 weeks.  N total at baseline: 404 Infants underwent randomization  Intervention:  - adrenaline on demand: 102  - adrenaline fixed schedule: 101  Control:  - NS on demand: 98  - NS fixed schedule: 103  Important prognostic factors2:  *age days, Mean (SD):*  Intervention:  - adrenaline on demand: 134.9±91.6  - adrenaline fixed schedule: 116.9±87.8  Control:  - NS on demand: 117.8±68.1  - NS fixed schedule: 136.0±97.0  *Sex % M:*  Intervention:  - adrenaline on demand: 63 (61.8)  - adrenaline fixed schedule: 60 (59.4)  Control:  - NS on demand: 54 (55.1)  - NS fixed schedule: 63 (61.2)  Groups comparable at baseline?  yes | 10 ml of racemic adrenaline dissolved in  0.9% saline to form a solution of 20 mg per milliliter.  on demand or on a fixed schedule  The dose administered was based on the infant’s weight: 0.10 ml for infants weighing less  than 5 kg, 0.15 ml for those weighing 5 to 6.9 kg, 0.20 ml for those weighing 7 to 9.9 kg, and 0.25 ml for those weighing 10 kg or more. The medications were diluted in 2 ml of saline before  nebulization and were administered with a Respironics  Facemask.  No other inhaled medications, with the exception of 0.9% inhaled saline could be administered during the period when the infant was participating in the trial. Supportive  therapy and any other treatments were provided  in accordance with routine care. | 0.9% saline alone.  The medications were diluted in 2 ml of saline before  nebulization and were administered with a Respironics  Facemask.  on demand or on a fixed schedule  No other inhaled medications, with the exception of 0.9% inhaled saline could be administered during the period when the infant was participating in the trial. Supportive  therapy and any other treatments were provided  in accordance with routine care. | Follow-up:  No Follow-up, only monitored children until discharge.  Inclomplete data:  Intervention:  - adrenaline on demand  17 Discontinued study  11 Had treatment  failure  4 Were withdrawn by  parent  2 Were inappropriately  Withdrawn  - adrenaline fixed schedule  19 Discontinued study  12 Had treatment  failure  2 Had side effects  4 Were withdrawn by  parent  1 Was inappropriately  Withdrawn  167 Completed inhaled RA  Control:  - NS on demand  20 Discontinued study  15 Had treatment  failure  1 Had side effects  3 Were withdrawn by  parent  1 Was inappropriately  Withdrawn  - NS fixed schedule  27 Discontinued study  21 Had treatment  failure  5 Were withdrawn by  parent  1 Was inappropriately  Withdrawn  154 Completed inhaled saline  The study medication was discontinued  in 83 children (20.5%) for the reasons listed above.  321 Completed study | LOS in hours  The mean (±SD) length of stay for all infants was 80±67 hours  I: Inhaled Racemic Adrenaline (N=203), Mean (range)  63.6 (46.2 to 81.0)  C: Inhaled Saline (N=201), Mean (range)  68.1(49.8 to 86.4)  Mean difference (95% CI): 4.5 (-6.5; 15.5)  P=0.42  change in the clinical  score 30 minutes after the first inhalation  I: Inhaled Racemic Adrenaline (N=203), Mean (range)  -1.26 (-1.44; -1.08)  C: Inhaled Saline (N=201), Mean (range)  -1.08 (-1.23;-0.92)  Mean difference (95% CI): Not reported.  Ventilatory support  I : Inhaled Racemic Adrenaline (N=203), n/N (%)  15/203 (7.4)  C: Inhaled Saline (N=201), n/N (%)  15/201 (7.5)  Rate Ratio (95% CI): 0.99 (0.50 to 1.97) | The primary outcome, length of hospital stay, was defined as the time from the first study inhalation until discharge from the hospital.  No serious adverse events were reported. Three  children (including one who was receiving inhaled  saline) discontinued treatment because of moderate tachycardia, which may have been due to the study medication.  Article conclusion: There was no significant difference in length of hospital stay between children treated with inhaled racemic adrenaline and those treated with inhaled saline (P = 0.43). There were also no significant between-group differences in the use of nasogastric-tube feeding, supplemental oxygen, or ventilatory support; clinical scores before and after the first inhalation of the study medication; or the number of children in whom the study medication was discontinued. |