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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** |
| Flores-Gonzalez, 2015 | Type of study:  RCT  Setting and country:  - Inpatients  - Spain  Funding and conflicts of interest:  Funding: This work was supported by grants from  the Spanish Ministry of Health, Social Politics and  Equality for the promotion of independent clinical  research of 2010 (EC10-180). The funder had no role  in study design, data collection and analysis, decision  to publish, or preparation of the manuscript.  Competing Interests: The authors have declared  that no competing interests exist. | Inclusion criteria:  Eligible patients included infants aged under 24 months admitted to Hospital with a clinical diagnosis of acute bronchiolitis classified as moderate in severity. The diagnosis was based on a first episode of respiratory distress with wheezing and/or crackles, preceded by an infection of the upper airways.  Exclusion criteria:  Infants were excluded  if they had any of the following risk factors: premature birth as defined by the World Health  Organization (< 37 weeks), in infants with an adjusted age of less than 6 weeks at the time of  enrollment, chronic respiratory disease, hemodynamically significant heart disease, immunodeficiency,  and neuromuscular disease. Infants with previous episodes of wheezing or a physician’s  diagnosis of asthma were also excluded. Finally, we also excluded patients receiving  other non-study treatments during hospitalization.  N total at baseline:  - 208 were randomized  - 185 in analyses  Intervention:  104 randomized, 94 in analyses  Control:  104 randomized, 91 in analyses  Important prognostic factors2:  *age Mean months (SD):*  I: 2.10±2.37  C: 2.12±2.08  *Sex % M:*  I: 46 (48.9)  C: 46 (50.5)  *Wood-Downes Scale modified by Ferres (WDF) severity score, N (%)*  I: 5.36±0.98  C: 5.24±1.17  Groups comparable at baseline?  yes | Patients received nebulized epinephphine (3 ml of a 1:1000 solution), in  3% hypertonic saline (7 mL).  The nebulized solution was administered by means of a mask  using an ultrasonic hospital nebulizer (Shinmed model Sw918) with a frequency of 1.7 MHz and a mist particle size of 1 to 5 μm.  The solutions were administered initially every  4 hours.  Infants received the same standard support (elevation  of the head of bed, supplemental oxygen when oxygen saturation dropped below 94%,  acetaminophen if fever, and a nasal lavage with sterile saline before and after the administration  of the nebulized solution). | Patients received nebulized 3% hypertonic  saline (7 mL) plus 3 mL placebo (sterile water).  The nebulized solution was administered by means of a mask  using an ultrasonic hospital nebulizer (Shinmed model Sw918) with a frequency of 1.7 MHz and a mist particle size of 1 to 5 μm.  The solutions were administered initially every  4 hours.  Infants received the same standard support (elevation  of the head of bed, supplemental oxygen when oxygen saturation dropped below 94%,  acetaminophen if fever, and a nasal lavage with sterile saline before and after the administration  of the nebulized solution). | Follow-up:  Patients were monitored only until hospital discharge.  Lost in follow-up:  I: 10/104 lost  - 6 were admitted to intensive care  - 2 were withdrawn by the pediatrician  - 1 was withdrawn by parent  - 1 failed to fulfil inclusion criteria  C: 13/104 lost  - 6 were admitted to intensive care  - 2 were withdrawn by pediatrician  - 3 were withdrawn by parent  - 2 failed to fulfil inclusion criteria  **NB: Only those who completed the study were included in the analyses.**  **I: 94**  **C: 91** | LOS days, mean (SD)  I: 3.94±1.37  C: 4.82±2.3  P = 0.011  Required more than 4 days of hospitalization, n (%)  I: 13 (13.8)  C: 28 (30.8)  P = 0.006  RR: 0.45, IC95%: 0.25–0.81  Comparison of survival curves  showed significant differences in the LOS from day 4 onwards (P = 0.001)  WDF severity score at day 3, mean (95% CI)  I: 3.93 (3.68–4.17)  C: 4.31 (4.01–4.59)  p = 0.029  WDF severity score at day 5  I: 3.37 (3.02–4.72)  C: 4.03 (3.67–4.40)  p = 0.036 | The primary efficacy outcome was length of hospital stay (LOS), defined as the number of days from admission to the time at which the patient fulfilled the study discharge criteria: aWDF score of 3 or less, an oxygen saturation of 97% or more without supplemental oxygen, adequate oral tolerance, and no further need for nebulized therapy.  Authors report no adverse  events (i.e. tachycardia, sweating, pallor, trembling, or hypertension), during hospitalization.  NB: However, patients with such severe adverse events that PICU admission was necessary (6 in each group), were excluded from analyses.  Group n confusing: figure group data are swapped.  Article conclusion:  Nebulized epinephrine in 3% saline significantly shortens the length of hospital stay of infants with acute moderate bronchiolitis in our setting, where it normally exceeds 4 days, and reduces the risk of a prolonged stay, without any increase in the occurrence of adverse events, when compared with placebo in 3% saline. |