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Publication Date
2016
Perinatal Risk Factors for Lung Morbidity in Children Born Premature
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Background: In the last two decades, the rate of preterm births has generally increased in developed countries. In the US, the rate has increased from 9.5% in 1981 to 12.7% in 2005(1). Premature delivery interferes with normal growth of the lung in the saccular phase of development, and therefore alters normal organ function (2,3,4). This disruption has been linked to increased rates of respiratory distress in the neonatal period as well as increased hospital readmission in the first years of life. Differences in lung development are further illustrated by the higher susceptibility to respiratory infections, most commonly RSV, in preterm infants compared to term infants. Many of these neonates also go on to require prolonged oxygen supplementation, qualifying them as having bronchopulmonary dysplasia (oxygen requirement at 36 weeks post-conceptional age (5,6). Along with decreased quality of life, chronic obstructive lung disease in children is a leading cause of health care costs and hospitalizations (3,7,8,9).

The underlying mechanisms of how specific adverse events in the prenatal and postnatal period affect respiratory morbidity in children are not fully understood. Studies looking at known risk factors such as gestational age, birth weight and BPD have shown variable long-term outcomes regarding respiratory sequela (10,11,12,13,14). The discrepancy in lung function decline, disease development and health care utilization suggests that there are other main contributors outside the ones previous listed. There is a lack of information regarding preventative treatment measures done after the neonatal period and its long term affect in lung function.

Aim: To identify any specific risk factors that have a strong positive or negative correlation with acute health care use, such as ED visits and hospital admissions.

Methods: A list of 574 patients treated at Rady Children’s hospital who meet the 2013 Synagis criteria (<32 weeks gestational age and/or diagnosis of bronchopulmonary dysplasia/chronic lung disease) was compiled in EPIC. From this list, patients ages 0-3 years between 12/1/2012 and 12/1/2015 without substantial cardiac history or neurological/developmental delay were identified. Thus far, 101 patients meeting criteria listed above were evaluated for certain known risk factors for lung disease, such as birth history, NICU history, family history, oxygen use, pulmonary follow up and medications. Records from these patients were also analyzed for presence and frequency of hospital admissions/ED visits from 12/1/2012 to 12/1/2015. All data was recorded in excel in order to analyze cumulative data across patients.

Results: When looking at 101 patients who qualified for Synagis, under the 2013 criteria, 69 obtained Synagis while 32 did not. 57% of the patients who received Synagis did not have any hospital admission or ED visits recorded between 12/1/2012 and 12/1/2015, as opposed to 6% of the patients who did not receive Synagis. Patients who received Synagis were, therefore, 0.46 times at risk to present to the ED or be admitted compared to those who did not receive Synagis (RR 0.46); in other words, there was a 54% percent relative risk reduction (RRR) with patients who received Synagis compared to those who did not. Number to Treat (NTT) is 1.99,
meaning that the average amount of patients needed to be treated to prevent one bad outcome is near 2.

Another parameter predicted to reduce the risk of admission/ED presentation was the presence or absence of pulmonary follow up. Out of the 101 patients analyzed, 63 had pulmonary follow up and 38 did not. 49% of those without pulmonary follow up did not have any hospital admissions or ED visits between 12/1/2012 and 12/1/2015, as opposed to only 26% of patients who did not have pulmonary follow up. Relative risk (RR) of admission/ED visit for those who received pulmonary follow up versus those who did not is 0.696. Patients who received pulmonary follow up, therefore had a 30.4% relative risk reduction (RRR) compared to those who were not followed in pulmonary clinic after NICU discharge. Number needed to treat (NTT) is 4.347 meaning that the average amount of patients needed to be treated to prevent one bad outcome is near 4.

Of the 101 patients analyzed, 38 were discharged home from the NICU on supplemental oxygen and 63 were not. 63% of the 38 patients discharged on supplemental oxygen were admitted or presented to the ED at least once. 57% of the patients who were not discharged on supplemental oxygen had at least one admission/ED presentation, making the relative risk (RR) of admission/ED visit of patients discharged home on oxygen compared to those who were not 1.107. Patients, therefore, discharged home from the NICU on supplemental oxygen were at 10.7% increased risk (Percent Relative Effect) for admission/ED presentation.

Another parameter analyzed for its effect on admission/ED visits was family history of asthma. In the set study population 32 had a positive family history of asthma while 69 did not. 75% of patients with a positive family history had at least one admission/ED visit compared to 52% of patients who did not have a family history. The relative risk (RR) for admission/ED visit of patients with a positive family history versus none is 1.437, meaning there is a 43.7% increase risk between these two patient populations.

**Conclusion**

According to data collected among these 101 patients, early school-aged children, who meet 2013 Synagis criteria, are at lower risk of hospital admissions or ED visits if they receive pulmonary clinic follow up after NICU discharge and Synagis each season. Conversely, they are at higher risk of hospital admission or ED visit if they were discharged from the NICU on supplemental oxygen or have a family history of asthma. It can be argued that increased risk of hospital admission or ED visit in patients discharged home on supplemental oxygen is more reflective of other confounding factors within this specific patient population rather than an adverse effect of the home oxygen. Further statistical analysis and studies will need to be done in order to decipher the reasoning for this increased risk.

**Resources**