CLIPPINGS

Bubble CPAP *versus* standard oxygen therapies for severe pneumonia (*Lancet. 2015;386:1057-65*)

In developing countries, mortality in children with very severe pneumonia is high, even with the provision of appropriate antibiotics, standard oxygen therapy and other supportive care. The authors assessed whether oxygen therapy delivered by bubble continuous positive airway pressure (CPAP) improved outcomes compared with standard low-flow and high-flow oxygen therapies. In this open-label randomized controlled trial from Bangladesh, authors randomly assigned children younger than 5 years with severe pneumonia and hypoxemia to receive oxygen therapy by either bubble CPAP (5 L/min starting at a CPAP level of 5 cm H_2O), standard low-flow nasal cannula (2 L/min), or high-flow nasal cannula (2 L/kg/min up to the maximum of 12 L/min). The primary outcome was treatment failure (*i.e.*, clinical failure, intubation and mechanical ventilation, death, or termination of hospital stay against medical advice) after more than 1 h of treatment. The authors conducted two interim analyses and stopped the trial after the second interim on directions of their data safety and monitoring board. Before trial could be stopped, 225 eligible children were recruited; 79 (35%) to receive oxygen therapy by bubble CPAP, 67 (30%) to low-flow oxygen therapy, and 79 (35%) to high-flow oxygen therapy. Treatment failed for 31 (14%) children, of whom 5 (6%) had received bubble CPAP, 16 (24%) had received low-flow oxygen therapy, and 10 (13%) had received high-flow oxygen therapy. Significantly fewer children in the bubble CPAP group (and high flow oxygen group) had treatment failure than in the low-flow oxygen therapy group. Twenty-three (10%) children died; 3 (4%) in the bubble CPAP group, 10 (15%) in the low-flow oxygen therapy group and 10 (13%) in the high-flow oxygen therapy group. Children who received oxygen by bubble CPAP had significantly lower rates of death than the children who received oxygen by low-flow oxygen therapy (P=0·022). The authors suggest that use of bubble CPAP oxygen therapy could have a large effect in hospitals in developing countries where the only respiratory support for severe childhood pneumonia and hypoxemia is low-flow oxygen therapy. The trial was stopped early because of higher mortality in the low-flow oxygen group than in the bubble CPAP group, and the authors acknowledge that the early cessation of the trial reduces the certainty of the findings.

New polio vaccination schedule –Does it work? (*Lancet. 2015 Sep 17. doi: 10.1016/S0140-6736(15)00237-8*)

Polio eradication needs a new routine immunization schedule – three or four doses of bivalent type 1 and type 3 oral poliovirus vaccine (bOPV) and one dose of inactivated poliovirus vaccine (IPV), but no immunogenicity data are available for this schedule. The authors aimed to assess immunogenicity of this vaccine schedule. They conducted this open-label, randomized controlled trial in four centers in India. Healthy newborn babies were randomly allocated to one of five groups: trivalent OPV (tOPV); tOPV plus IPV; bOPV; bOPV plus IPV; or bOPV plus two doses of IPV (2IPV). OPV was administered at birth, 6 weeks, 10 weeks, and 14 weeks; IPV was administered intramuscularly at 14 weeks. The primary study objective was to investigate immunogenicity of the new vaccine schedule, assessed by seroconversion against poliovirus types 1, 2, and 3 between birth and 18 weeks. Neutralization assays tested cord blood and sera collected at 14 weeks, 18 weeks, 19 weeks, and 22 weeks by investigators masked to group allocation. Of 900 newborn babies enrolled, 782 (87%) completed the protocol requirements. Between birth and age 18 weeks, seroconversion against poliovirus type 1 in the tOPV group occurred in 98-99% in all groups. Seroconversion against poliovirus type 2 occurred in 157 (96·3%) of 163 in the tOPV group, 153 (100%) of 153 in the tOPV plus IPV group, 29 (18.7%) of 155 in the bOPV group, 107 (68·6%) of 156 in the bOPV plus IPV group, and in 121 (78·1%) of 155 in the bOPV plus 2IPV group. Seroconversion against poliovirus type 3 was achieved in 147 (90·2%) of 163 in the tOPV group, 152 (99·3%) of 153 in the bOPV plus IPV group, 151 (97·4%) of 155 in the bOPV group, 155 (99·4%) of 156 in the bOPV plus IPV group, and 153 (98·7%) of 155 in the bOPV plus 2IPV group. Superiority was achieved for vaccine regimens including IPV against poliovirus type 3 compared with those not including IPV (tOPV plus IPV *vs* tOPV alone; and bOPV plus IPV *vs* bOPV alone).

Do early life infections increase the risk of celiac disease? (*Am J Gastroenterol. 2015;110:1475-84*)

Studies on early life infections and risk of later celiac disease are inconsistent but have mostly been limited to retrospective designs, inpatient data, or insufficient statistical power. Using prospective population-based data, the authors aimed to test whether early life infections are associated with increased risk of later celiac disease. This study, based on the Norwegian Mother and Child Cohort Study, includes prospective, repeated assessments of parent-reported infectious disease data up to 18 months of age for 72,921 children born between 2000 and 2009. Celiac disease was identified through parental questionnaires and the Norwegian Patient Registry. During a median follow-up period of 8.5 years (range, 4.5–14.5), 581 children (0.8%) were diagnosed with celiac disease. Children with e”10 infections (e”fourth quartile) up to age 18 months had a significantly higher risk of later celiac disease, as compared with children with £4 infections (£first quartile; aOR=1.32; 95% CI 1.06,1.65; per increase in infectious episodes, aOR=1.03; 95% CI 1.02,1.05). The aORs per increase in specific types of infections were as follows: upper respiratory tract infections: 1.03; lower respiratory tract infections: 1.12; and gastroenteritis: 1.05. This study suggests that early life infections may have a role in development of celiac disease. However, non-causal explanations for this association due to surveillance bias and reverse causation cannot be excluded.

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