

Heliox Use in Ventilation of Preterms

The recent randomized controlled trial by Xue, *et al.* [1] aims at reducing the length of ventilation as primary aim. The authors have also looked into lung inflammatory markers like Interleukin-6, which was positively correlated with the length of ventilation but was not proved significant.

Heliox gas flows in laminar fashion creating less resistance because of its property of low density and lower Reynolds number which thereby helps in gas exchange and reduced work of breathing, particularly in disease states where there is evidence of airway obstruction [2,3]. It is still unclear how heliox helps in improving outcome in respiratory distress syndrome; the possible explanation other than reducing lung inflammation is improving oxygenation and carbon dioxide elimination and thereby improving the blood pH and reducing pulmonary hypertension.

The participants in this study were mid-late premature infants (mean gestation 34 weeks); many ongoing/completed trials aim to assess interventions for reducing morbidity, particularly chronic lung disease, in preterm cohorts born earlier than 34 weeks. Reduction in length of ventilation in this study cohort may not be too great as these babies generally require short term ventilation. Moreover, heliox is likely to be a costly intervention; the reported cost is 750• for 12 hours of treatment [4].

The authors have concluded that nasal intermittent positive pressure ventilation might have increased the efficacy of delivering heliox, as an earlier study [4] failed to show reduction in length of ventilation when CPAP was used. The population in the earlier trial was more premature (30 weeks) and the reduction in the length of ventilation was not the primary objective. Practically, heliox reduces the increasing oxygen requirement by effective delivery of gas thereby decreasing the threshold for surfactant/ventilation and is unlikely to affect the length of ventilation. We suggest that the utility of heliox should be tested in more immature infants with the objective to reduce chronic lung disease and other morbidity.

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Heliox Use in Ventilation of Newborns: Authors' Reply

Even though the distinct mechanisms of helium-induced organ protection have not been completely unraveled, several signaling pathways have been identified [1]. It has been shown that heliox could decrease neutrophil infiltration, intra-alveolar edema, perivascular hemorrhage and hyaline membrane formation of acute respiratory distress syndrome in rats [2]. Nawab, *et al.* [3] reported that heliox attenuated lung inflammation and structural alterations of piglets in acute lung injury. In our study, serum IL-6 at baseline was found to be positively and significantly correlated with the length of ventilation (LoV) [4], which supported the speculation that helium might have anti-inflammatory effect in humans *in vivo*. Thus, we speculated that there might be other mechanisms of action of heliox, besides its physical effects in respiratory diseases.

Heliox has been demonstrated to decrease the threshold for surfactant and ventilation by reducing the increasing oxygen requirement in Colnaghi's study [5], which has important practical application. It is very important that the utility of heliox in reducing chronic lung disease should be expanded in more immature infants. However, one purpose of our study was to assess the effectiveness of heliox on lung inflammation cytokines. We tried to explain the reason why heliox could improve the outcome of RDS from another perspective.

Infants born before 32 weeks contribute to high occurrence of complications of prematurity such as

retinopathy of prematurity, intraventricular hemorrhage and periventricular leukomalacia. Nevertheless, premature infants born between 32-36 weeks form a large proportion in NICU, and some need assisted ventilation. Longtime ventilation will increase the risk of lung injury. Length of ventilation should be the primary outcome as it plays an important role leading to ventilator-associated lung injury. Further research on the mechanisms of heliox in respiratory diseases are still needed.

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Immunization Recommendations Should not be Ambiguous

This refers to the Guidelines regarding immunization schedule for children upto the age of 18 years recommended by IAP [1]. There are some contradictory or confusing statements which need clarification:

Rotavirus vaccine: There is no change in the existing schedule of RV1 vaccine that includes the first dose at 10 weeks of age instead of 6 weeks in order to achieve better immune response, and the second dose at 14 weeks to fit with existing National immunization schedule [2]. It is further stated RV1 (Rotarix) should preferably be employed in 10 and 14 week schedule, instead of 6 and 10 weeks, which suggests that for RV5 (Rota Teq) 1st dose is to be administered at 6 weeks.

Hepatitis B vaccine: Under footnotes it is stated that ideally, the final (3rd or 4th) dose in the Hepatitis B vaccine series should be administered no earlier than age 24 weeks, and at least 16 weeks after the first dose, whichever is later. On the contrary, it also states "Hepatitis B vaccine may also be given in any of the following schedules: birth, 1 and 6 mo; birth, 6 and 14 weeks; 6, 10 and 14 weeks; birth, 6, 10 and 14 weeks."

HPV vaccine: It is stated that "two doses of HPV vaccine are advised for adolescent/pre-adolescent girls aged 9-14 years; for girls 15 years and older, current 3 dose schedule will continue." In the figure 1, range of recommended ages for all children in yellow shade is for 11 and 12 years,

which would suggest that it is not recommended for 9 and 10 year old girls, and also that two doses are required till the age of 12 years, and not till age of 14 years.

Changing the needle: Under General instructions in the footnotes, authors state that changing needles between drawing vaccine into the syringe and injecting it into the child is not necessary. Currently used syringes and needles are meant for single use. When the needle pierces skin or rubber stopper, it loses its sharpness. To reduce pain, after refilling the syringe, it would be advisable that the needle be changed. There is no need to change the needle if vaccine or other liquid has been withdrawn from an ampule, and injected. In case liquid from one container is withdrawn and pushed in another containing vaccine and withdrawn, then needle should be changed.

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