EDITORIAL

Pre-extubation Dexamethasone: Does It Merely Muffle Stridor or Provide Real Benefit for Mechanically Ventilated Children?

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Mechanical ventilation is a commonly used life-supporting technology for critically ill children admitted to the pediatric intensive care unit (PICU). Around 17–64% of PICU admitted patients need mechanical ventilation in the developed world.[1–3] while it varies from 20 to 50% in Asian PICUs.[4,5] Common indications include acute respiratory failure (72%), altered mental status (14%), and acute chronic pulmonary conditions (10%).

Although mechanical ventilation has various applications, there are also multiple risks. Prolonged mechanical ventilation increases the risk of airway trauma, infections including ventilator-associated pneumonia (VAP), complications of immobility, ventilation-induced diaphragmatic dysfunction, oxygen toxicity, ventilator-induced lung injury (VILI), cardiovascular instability, prolonged exposure to sedatives and narcotics, and increased hospital stay and expenses.[6,7] Liberating from mechanical ventilation is crucial to the management of children on mechanical ventilation support. A few of them may need reintubation for various reasons. Research shows extubation failure rates, when done according to clinical judgement vary from 16 to 22%.[8,9] Populations with failed extubation will have higher mortality rates, morbidity rates, longer mechanical respiratory support, intensive care unit (ICU) stays and costs.

Common causes of extubation failure are postextubation stridor (PES) (due to laryngeal edema, laryngospasm, vocal cord dysfunction), poor airway reflexes to protect the airway, excessive airway secretions, poor cardiovascular reserve and neuromuscular weakness causing respiratory fatigue.

Postextubation stridor reported in frequency up to 2–73% in critically ill pediatric patients and PES is a contributing factor in 17–22% of extubation failures.[10,11]

In this issue of IJCCM, Anjali RV et al. studied the role of intravenous dexamethasone in the prevention of postextubation airway obstruction in mechanically ventilated children in pediatric intensive care units through double blind randomized controlled trial. Steroids were being used in postextubation airway edema for ages.[12]

In 1952, work by Chesney JG, showed the effectiveness of cortisone in relieving the symptoms of croups who is a refractory to supportive measures such as humidified oxygen and who were at risk for tracheostomy. It has been included as standard of care in the management of croups since then. The same mechanism was extrapolated to treat postextubation subglottic edema by using intravenous dexamethasone as a rescue measure in the operation theatre by Margerg V et al. in 1961. The dose of dexamethasone used by Margerg V was 4 mg in infants and 8 mg in older children, and the response to relieve stridor and retractions was between 20 and 40 minutes.[13]

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Subsequently, there were publications on the study of prophylactic steroids to prevent postextubation airway edema. Few randomized controlled trial (RCT) were conducted to determine the efficacy of dexamethasone in preventing postextubation airway obstruction. Many of these showed decrease in airway obstruction symptoms, but not the reintubation rate. Narayanan P et al. A metanalysis of dexamethasone for preventing postextubation upper airway obstruction in children, included RCTs involving various regimens of Dexamethasone, viz high early (≥0.5 mg/kg/dose given >12 hours pre-extubation), low early (<0.5 mg/kg/dose given >12 hours pre-extubation), high late (≥0.5 mg/kg/dose given <12 hours pre-extubation) and low late (<0.5 mg/kg/dose given <12 hours pre-extubation). Out of all these high dose dexamethasone (0.5 mg/k/dose) and started early (>12 hour before extubation), found to be the most effective strategy in preventing postextubation airway obstruction, but reintubation rates, mortality, length of invasive mechanical ventilation, and length of PICU stay were not statistically significant. Limitations of these RCT are variation in inclusion population, lack of objective criteria in reporting upper airway obstruction, many are non-blinded RCTs.

Anjali RV et al. in their RCT, used injection dexamethasone 0.5 mg/kg/dose, and started 12 hours pre-extubation. The conclusions drawn are similar to those drawn in the previous RCT which used the same regimen, decreased the incidence of clinically significant stridor, but did not alter the reintubation rate. The authors also compared sequential organ failure assessment (SOFA) scores, length of PICU stay, and mortality, which are similar in the intervention and control groups.

The probable reason behind dexamethasone not significantly effecting reintubation may be due to the dominance of other factors causing extubation failure, like encephalitis, neuromuscular weakness, and lung parenchymal problems.

The proposed mechanism of dexamethasone by which its preventing or decreases stridor is by its anti-inflammatory action. The trigger for inflammation here is by physical trauma to the subglottic region (narrowest portion of the extra-thoracic airway, non-elastic circular cricoid cartilage) during intubation or vigorous neck movements post-intubation, high cuff pressures, repeated intubations, edema as part of systemic inflammation. There are other causes that can cause stridor where dexamethasone may not have much role, like vocal cord paralysis or dysfunction, granulomas, floppy epiglottis and upper airway, laryngospasm, blood and secretion pooling, tracheomalacia, subglottic stenosis and retained dried-up crusts, laryngeal web and hemangioma, retropharyngeal and parapharyngeal abscess. Many of these pre-existing or acquired causes might not be picked up during emergency intubation.

Caveats in uniform, universal recommendations on dexamethasone to prevent postextubation airway edema, are the absence of objective criteria for whom it is going to benefit by preventing reintubation due to PES, need to time it 12 hours prior to extubation, this makes delay in extubation. Potential complications like gastrointestinal hemorrhage, hypertension, tachycardia, immunosuppression, electrolyte dysfunction, myopathy, psychosis, osteopenia and hyperglycemia. In the study published in this issue, the authors actively evaluated for these adverse effects, did not find any of these complications in the intervention group. But adverse event reporting in a hospital depends on the safety culture. It is difficult to establish causal relationship in a complex clinical scenario.

Given the evidence from a well-conducted double-blinded RCT did not prove the advantage of dexamethasone in terms of extubation failure or any other robust outcomes, it's advisable not to use dexamethasone on the basis. It should be used on case by case basis, after assessing risk factors for postextubation airway edema like prolonged ventilation, multiple intubations, traumatic intubation, difficult sedation, and significant positive fluid balance. The concept of cardiopulmonary interaction should be noted while extubating a child with left ventricular dysfunction, post-cardiac surgery, where stridor and associated excessive negative intrathoracic pressure generated by the patient can adversely affect cardiac function and may predispose to extubation failure. Also assess the individual susceptibility to adverse effects of dexamethasone.

Best practice points to be noted to prevent PES and related extubation failure include early identification of respiratory distress, optimal use of NIV and HHHFNC, avoiding traumatic intubations, improving skill level of practitioners, having difficult airway protocols suitable to respective units, having all airway adjuvants, choosing the right size of endotracheal tube (ET) tube, modified the rapid sequence intubation (RSI) protocol in non-crash situations, optimal use of external laryngeal manipulation techniques to best visualisation of glottis. To use adequate sedoanalgesia with monitoring tools as mentioned in pediatric pain, agitation, neuromuscular blockade, and delirium in critically Ill pediatric patients, and early mobilisation (PANDEM) guidelines, cuff pressure measuring and intermittent deflation to prevent subglottic mucosal injuries. Careful monitoring fluid balance, and avoid fluid overload, optimal nutritional support to prevent hypoalbuminemia, and muscle wasting (Diaphragm and other respiratory muscles). In developing country like India where there is a shortage of skilled airway personnel expertise in pediatric population, adequate training programs, including structured simulation and debriefing sessions, are part of the academic curriculum.

Future research directions in this context, include well-designed, multicentric double-blinded RCTs with inclusion of other factors including sedation scales, pain scales, cuff pressures. That diverse population coverage, and better generalizability. With due care on standardized methodology, high-quality data collection, appropriate statistical consideration, and sound quality assurance measures. This can be possible with productive collaboration in a public-private partnership to conduct studies simultaneously in public-sector hospitals, and private hospitals under a common multicentric RCT.

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