Original Article

Apnoeic Oxygenation for Paediatric Emergency Intubation – Historic Review and Evidence for Paediatric Practise

Guruprasad Hassan Shankar, Srilakshmi Hassan Shankar

Abstract :

Apnoeic oxygenation, which is the process of providing oxygen supplementation during the period of apnoea when intubation is ongoing, is slowly emerging as a standard of care adopted by anaesthetists, intensivists and emergency physicians during elective or emergency intubations. While evidence in adult population is robust, paediatric work is ongoing and has begun to demonstrate similar benefits. Safety of the technique has been adequately established while more research is needed to clarify the pros and cons of different delivery methods and flow rates. Though the principle of apnoeic oxygenation and technique itself have been known for long, with a rich historical background deeply connected with development of mechanical ventilation itself, challenges remain in the incorporation of the relatively new practise across units. In this paper, we review the historical background, physiology and evidence for practise in the specified context of paediatric emergency intubation. We briefly discuss the practical aspects of the implementation of this useful practise for improving the safety of paediatric emergency intubations in routine care.

Key words :

Apnoeic oxygenation; paediatric emergency intubation

Introduction :

"Primum non nocere". First, do no harm, is a doctrine as old as medicine itself.[1] Actively anticipating and preventing harm is a vital part of any disciplined approach to the practise of medicine. Tracheal intubation is a very often performed intervention in emergency rooms and intensive care units. However, it is associated with a substantial risk of hypoxemia (48% of difficult and 15% of non-difficult intubations in paediatric intensive care unit (PICU)[2]). Hypoxemia during the process of intubation contributes significantly to adverse events including dysrhythmias, hypoxic brain injury, seizures, surgical airway, or cardiac arrest with profound hypoxemia being defined as oxygen saturation of < 70%.[3] While the process of pre-oxygenation prior to endotracheal intubation is standardised, research is ongoing about additional methods to increase the safety of and prevent critical events during intubation. One of these techniques involves providing oxygen supplementation even as the process of intubation is ongoing. This method, called apnoeic oxygenation (AO), is the process by which oxygen moves by mass flow through the upper airways into the alveoli in the absence of any respiratory effort, consisting of administration of oxygen during apnoeic period of intubation to extend the safe apnoea time.[4] Apnoeic oxygenation during intubation may be particularly beneficial in patients who are at risk of rapid desaturation, and in patients for whom airway management may be difficult or prolonged.

[1]Senior Medical Officer for PICU, RKMSP, VIMS
[2]Currently not attached with any institution

Apnoeic oxygenation : historical aspects

The history of apnoeic oxygenation preceded the development of anaesthesia itself. Prior to the safe administration of anaesthetic agents thereby causing apnoea, it was important to establish that it is possible to keep animals and then human beings alive by artificial oxygenation as well as artificial ventilation. This fascinating story begins in 1666, in a published account of the Philosophical Transactions of the Royal Society of London,[5] of an experiment made by M. Hook, of keeping alive animals by blowing into the lungs using bellows. Since it was then believed that "the motion of the lungs is necessary to life, upon the account of promoting the circulating of the blood", Hook performed an experiment of keeping a dog alive for some time by continuously blowing air into its lungs without any respiratory movements. After a long hiatus, in 1908 came a similar description by Volhard.[6] Oxygenation of paralysed dogs was performed using an glass tube in the trachea, but without any respiratory movements. This only worked when 100% oxygen was provided, which was later confirmed by others.[7]

Through the following years, more aspects of this phenomenon were discovered. Draper et al., in 1947 described "diffusion respiration"[8] where in the alveoli can continuously capture oxygen in the absence of ventilatory efforts provided cardiac output remains adequate, oropharyngeal patency is maintained, haemoglobin is in the normal reduced state, denitrogenation and replacement with oxygen occurs, and a continuous oxygen insufflation is performed after the cessation of diaphragmatic movement. However, it was thought that alveolar oxygen attaching to the haemoglobin-oxygen pump provided an inward suction pressure leading to the diffusion of oxygen from the pharynx to the alveoli. On a similar note, the term 'aventilatory mass flow'[9] was coined by Bartlett, Brubach, and Specht (1959). By usage of whole body plethysmography, they demonstrated observable en masse movement of ambient air into the lungs. They postulated that this mass flow is due to the decrease in intrapulmonary pressure caused by the combination of long airway and tissue CO_2 retention. Since CO_2 washout was thought at that time to be equal to oxygen extraction from the alveoli, it provided an explanation for the observed mass flow.

These theories were disproved by Frumin et al. in 1959[10] who suggested to adopt the term apnoeic oxygenation as originally suggested by Nahas.[11] They demonstrated that extraction of oxygen from the alveoli into the blood was not equal to addition of CO_2 into alveoli from the blood. They proposed that a reduction in the barometric pressure gradient between the upper airway and the alveoli due to poor CO_2 diffusion into the alveoli from the blood as well as denitrogenation is the mechanism of apnoeic oxygenation. More physiologic depth and detail was added in the following studies conducted in the following years. Weitzner et al[12] (1959) studied arterial oxygen saturation at different periods of apnoea and showed that it drops to dangerous levels by about 1½ minutes. This paved the way for the concept of safe apnoea time. Millar et al[13] (1961) showed a significant sympathetic surge occurring during apnoeic oxygenation. Heller et al[14] in 1964 became the first team of researchers to perform apnoeic oxygenation in humans. In a group of healthy volunteers, after paralysis with thiopental or succinylcholine, bag and tube ventilation with 100% oxygen for 4 minutes, they induced apnoea and measured polarographic oxygen tension in arterial blood every minute for 5 minutes. This experiment was performed under two conditions, one with endotracheal tube left open to room air versus connected to an oxygen reservoir bag. The study concluded that hypoxia can be avoided in respiratory arrest for specific periods of time through apnoeic oxygenation. Cardiopulmonary effects of apnoeic oxygenation were studied by Fraioli[15] in 1973. They quantified the degree of fall of PaO_2 and rise in $PaCO_2$ during AO, observed a slight decrease in FRC during the process of AO and recorded arrythmias at the same time (only PVCs were observed). Importantly, they observed that rate of desaturation during AO was dependent on ratio of FRC to body weight. The provision of AO at different flow rates were reported by Mackenzie et al in a study on dogs in 1991.[16]

The physiology of apnoeic oxygenation

With cumulative contributions from the above studies, the current understanding about the mechanism of AO is as follows. During regular breathing, where the volume of oxygen entering the blood from alveoli is nearly equal to the amount of CO_2 moving out of blood into alveoli. During apnoea, in contrast, though 250 ml/minute of oxygen moves from the alveoli to the blood, in the opposite direction, only 8-20 ml/minute of CO_2 moves from blood into the alveoli.[17] The rest of the CO_2 produced in the tissues gets buffered.[18] Due to this discrepancy, the alveolar pressure becomes sub-atmospheric and draws the air from pharynx to alveoli through passive diffusion. By giving apnoeic oxygenation, the pharyngeal space is filled with an oxygen rich reservoir which in its turn moves in and fills the lungs and helps to improve arterial oxygen saturation and prolong the safe apnoea time.

Summary of evidence for apnoeic oxygenation from paediatric emergency room or ICU studies

The studies performed in the cohort of paediatric patient undergoing emergency intubations in the emergency department (ED) or ICU are largely in the form of quality improvement (QI) initiatives undertaken by units to incorporate the practise of AO for presumably reducing the risk of adverse events. Some studies conducted in this context are summarised in table 1.

Discussion :

Due to the obvious physiologic advantage of continued oxygenation during apnoea in reducing the risk of hypoxemia and prolonging safe apnoea time, the high risks associated with hypoxemia during an emergency intubation, demonstrated efficacy in other cohorts under more controlled conditions, as well as the ease of application of the technique without reported adverse events, AO can be proposed as a standard of care in paediatric emergency intubations. Though evidence for efficacy of this practise has not been strictly demonstrated in high quality large randomised control trials (RCT) conducted in the paediatric population in the ED/ICU setting, work in adults and in the paediatric anaesthetic cohort is supportive.[26-29]

Several methods of providing apnoeic oxygenation have been described in adult literature, including nasal prongs, high flow nasal cannula (HFNC), nasopharyngeal catheter, endotracheal and endobronchial catheters and laryngoscope with oxygen channel incorporated in the design of the blade.[30] While the pros and cons of each method are debatable and not demonstrated in children in comparative studies, the simplest and the most common method used has been the nasal cannula. Flow rates have varied in different studies, but approximately 5 L/min for infants, 10 L/min for children < 10 years and 15 L/min for older children > 10 years have been used more commonly[19, 23-25] and can be suggested. Flow rates and delivery technique require standardisation. Though, generally flow rates through nasal cannulae are limited to 6 L/min for lack of humidification, this may not be a practical impediment to use for short periods of time. Practically, if respiratory support in the form of HFNC is already being provided immediately prior to intubation, it may be useful to continue the same for pre as well as apnoeic oxygenation for RSI with FIO_2 increased to maximum allowed, though again, comparative studies of high versus low flow systems have not been performed. Simple nasal cannula is generally not an impediment to bag and mask ventilation in modified RSI, should that become necessary, but the HFNC cannula may be more difficult in this regard and should be removed if proving so. Furthermore, risk of gastric distension may be theoretically increased with AO, though this particular aspect has not been studied. It is again important to practically have two sources of oxygen during any emergency intubation, one for apnoeic oxygenation and the other connected to AMBU bag so that precious time is not wasted for changing the oxygen from one delivery method to another during an emergency. Multiple factors may come to consideration in assessing the risk of hypoxemia during an emergency intubation including the number of attempts, experience of the provider, adequacy of pre-oxygenation, presence of comorbidities like obesity, difficulty of the airway in both anatomic and physiologic terms etc. But it may be postulated that apnoeic oxygenation may be useful across the spectrum of paediatric intubations, with greater usefulness in more difficult contexts.

There may be several hindrances to the regular incorporation of this practise in routine care.[24] Lack of awareness of the practise, resistance to incorporating new practices, difficulty in remembering to provide in the context of an intense high-risk situation, perceived ease of intubation and reduced risk of hypoxemia, unanticipated difficulty in the context of selective usage, lack of standardisation of delivery technique, can all contribute to underutilisation. Therefore, as the above quoted studies have demonstrated, performing a QI initiative with a multipronged approach to improving utilisation can be highly effective in incorporation as a standard of care.

Conclusion :

Though new research is necessary to provide high quality evidence for efficacy in the specific context of paediatric emergency intubation, multiple studies have demonstrated safety and trends toward reduced risk of hypoxemia. Standardisation of delivery methods and flow rates needs more study. We can however conclude that apnoeic oxygenation is an easily applied, well tolerated technique with minimal adverse effects to help improve the safety of paediatric emergency intubations.

Authors/year of publication/n (sample size)	Study design	Method of providing apneic oxygenation	Outcomes
Mortimer et al[19]/2016/44 (58 intubation attempts)	Prospective case series	Nasal cannula, 5 L/min for <4 years, 10 L/min for 4 to 12 years, and 15 L/min for 12 to 18 years	AO was well tolerated in critically ill children and was not associated with adverse events.
Long et al[20]/2017/117 (46 post and 71 pre implementation of QI initiatives)	Prospective quality improvement study	AO using positive airway pressure/ PEEP via face mask/t-piece, and nasal cannula oxygenation during laryngoscopy.	Fewer hypoxic adverse events in post intervention cohort, all occurring only with multiple attempts. (multiple interventions designed to improve peri-intubation outcomes performed including AO)
Vukovic et al[21]/2018/149	Observational study	4 L/min for < 2 years, 6 L/min for 2-12 years, 8 L/min for > 12 years	Apneic oxygenation is an easily-applied intervention associated with decreases in hypoxemia during pediatric intubation. Nearly 50% of children not receiving AO experienced hypoxemia
Overmann et al[22]/2018/305	Retrospective observational study	Simple nasal cannula: 2 L/min for < 3 years, 4 L/min for 3-8 years, 6 L/min for > 8 years	AO was not associated with a lower risk of desaturation during RSI
Napolitano et al[23]/2019 / 1373 (661 pre- and 712 post implementation of AO)	Prospective pre-post observational study. Implementation of AO as QI initiative in academic PICU	Regular nasal cannula : 5 L/min for infants < 12 months, 10 L/min for children from 1–7 year, 15 L/min for children above 8 years	Moderate and severe oxygen desaturation fewer in post implementation phase with AO. It is feasible to implement AO as a QI intervention in an academic PICU.

Jen Heng Pek et al[24]/2020/47 (22 pre and 25 post QI implementation)	Prospective QI study	Nasal cannula: 5 L/min for < 1 year, 10 L/min for 1–10 years, and 15 L/min for > 10 years	Successful implementation of care bundle to incorporate AO as standard of care for pediatric emergency intubations
Napolitano, Polikoff et al[25]/2023/ 6549 (2554 pre and 3995 post implementation phase)	Prospective multicentric QI interventional study	Nasal cannula: 5 L/min for < 1 year, 10 L/min for 1–7 years, and 15 L/min for =8 years	Use of AO was associated with lesser tracheal intubation associated adverse events, but this result may be explained by patient, practise and provider factors.

Table 1 : Summary of evidence for apneic oxygenation from pediatric emergency room or ICU studies

References :

1. Hughes G. First do no harm; then try to prevent it. Emerg Med J. 2007 May; 24(5):314.
2. Scott A, Chua O, Mitchell W, Vlok R, Melhuish T, White L. Apneic Oxygenation for Pediatric Endotracheal Intubation : A Narrative Review. J Pediatr Intensive Care. 2019 Sep;8(3):117-121.
3. Mort TC. The incidence and risk factors for cardiac arrest during emergency tracheal intubation: a justification for incorporating the ASA Guidelines in the remote location. J Clin Anesth. 2004 Nov; 16(7): 508-16.
4. Lyons C, Callaghan M. Uses and mechanisms of apnoeic oxygenation : a narrative review. Anaesthesia. 2019 Apr;74(4):497-507.
5. Hook M. An account of an experiment made by Mr. Hook, of preserving animals alive by blowing through their lungs with bellows. Philosophical Transactions of the Royal Society of London 1666; 2: 539-40.
6. Volhard F. Überkünstliche Atmungdurch Ventilation der Trachea und eineeinfache Vorrichtungzurrhyth mischenkünstlichen Atmung. Münchener Medizinische Wochenschrift 1908;55.
7. Meltzer SJ, Auer J. Continuous respiration without respiratory movements. J Exp Med 1909; 11:622–5.
8. Draper WB, Whitehead RW, Spencer JN. Studies on diffusion respiration: alveolar gases and venous blood pH of dogs during diffusion respiration. Anesthesiology. 1947 Sep;8(5):524-33.
9. Bartlett RG Jr, Brubach HF, Specht H. Demonstration of aventilatory mass flow during ventilation and apnea in man. J Appl Physiol. 1959 Jan;14(1):97-101.
10. Frumin MJ, Epstein RM, Cohen G. Apneic oxygenation in man. Anesthesiology. 1959 Nov-Dec;20:789-98.
11. Nahas GG. Influence of low oxygen tension on pulmonary circulation after temporary arrest of ventilation in curarized dogs. J Appl Physiol. 1956 Nov;9(3):352-8.
12. Weitzner SW, King BD, Ikezono E. The rate of arterial oxygen desaturation during apnea in humans. Anesthesiology. 1959 Sep-Oct;20:624-7.
13. Millar RA, Morris ME. Apneic oxygenation in adrenalectomized dogs. Anesthesiology. 1961 May-Jun;22:433-9.
14. Heller ML, Watson TR Jr, Imredy DS. Apneic oxygenation in man: polarographic arterial oxygen tension study. Anesthesiology. 1964 Jan-Feb;25:25-30.
15. Fraioli RL, Sheffer LA, Steffenson JL. Pulmonary and

cardiovascular effects of apneic oxygenation in man. Anesthesiology. 1973 Dec;39(6):588-96.

16. CF. Mackenzie, G. M. Barnas, J. Smalley, S. G. Park, J. Miller; Low and high flow tracheal insufflation of O2(trio) supports oxygenation in apneic dogs after ttx poisoning. Anesthesiology 1991; 75:A284.
17. Gleason JM, Christian BR, Barton ED. Nasal Cannula Apneic Oxygenation Prevents Desaturation During Endotracheal Intubation : An Integrative Literature Review. West J Emerg Med. 2018 Mar;19(2):403-411.
18. Weingart SD, Levitan RM. Preoxygenation and prevention of desaturation during emergency airway management. Ann Emerg Med. 2012 Mar;59(3):165-75.e1.
19. Mortimer T, Burzynski J, Kesselman M, Vallance J, Hansen G. Apneic Oxygenation during Rapid Sequence Intubation in Critically Ill Children. J Pediatr Intensive Care. 2016 Mar;5(1):28-31.
20. Long E, Cincotta DR, Grindlay J, Sabato S, Fauteux-Lamarre E, Beckerman D, Carroll T, Quinn N. A quality improvement initiative to increase the safety of pediatric emergency airway management. Paediatr Anaesth. 2017 Dec;27(12):1271-1277.
21. Vukovic AA, Hanson HR, Murphy SL, Mercurio D, Sheedy CA, Arnold DH. Apneic oxygenation reduces hypoxemia during endotracheal intubation in the pediatric emergency department. Am J Emerg Med. 2019 Jan;37(1):27-32.
22. Overmann KM, Boyd SD, Zhang Y, Kerrey BT. Apneic oxygenation to prevent oxyhemoglobin desaturation during rapid sequence intubation in a pediatric emergency department. Am J Emerg Med. 2019 Aug; 37(8):1416-1421.
23. Napolitano N, Laverriere EK, Craig N, Snyder M, Thompson A, Davis D, Nett S, Branca A, Harwayne-Gidansky I, Sanders R Jr, Shults J, Nadkarni V, Nishisaki A; National Emergency Airway Registry for Children (NEAR4KIDS) and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI). Apneic Oxygenation as a Quality Improvement Intervention in an Academic PICU. Pediatr Crit Care Med. 2019 Dec;20(12):e531-e537.
24. Pek JH, Tan HC, Shen G, Ong YG. Apneic Oxygenation for Emergency Intubations in the Pediatric Emergency Department-A Quality Improvement Initiative. Pediatr Qual Saf. 2020 Feb 13;5(2):e255.
25. Napolitano N, Polikoff L, Edwards L, Tarquinio KM, Nett S, Krawiec C, Kirby A, Salfity N, Tellez D, Krahn G, Breuer R, Parsons SJ, Page-Goertz C, Shults J, Nadkarni V, Nishisaki A; for National Emergency Airway Registry for Children (NEAR4KIDS) Investigators and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Effect of apneic oxygenation with intubation to reduce severe desaturation and adverse tracheal intubation-associated events in critically ill children. Crit Care. 2023 Jan 17; 27(1):26.
26. Taha SK, Siddik-Sayyid SM, El-Khatib MF, Dagher CM, Hakki MA, Baraka AS. Nasopharyngeal oxygen insufflation following pre-oxygenation using the four deep breath technique. Anaesthesia 2006; 61: 427-30.
27. Rudlof B, Hohenhorst W. Use of apneic oxygenation for the performance of pan-endoscopy. Otolaryngol Head Neck Surg 2013; 149: 235-9.
28. Patel A, Nouraei SA. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. Anaesthesia 2015; 70: 323-9.
29. Dias R, Dave N, Chhabria R, Shah H, Garasia M. A randomised comparative study of Miller laryngoscope blade versus Oxiport® Miller laryngoscope blade for neonatal and infant intubations. Indian J Anaesth. 2017 May;61(5):404-409.
30. Wong DT, Yee AJ, Leong SM, Chung F. The effectiveness of apneic oxygenation during tracheal intubation in various clinical settings: a narrative review. Can J Anaesth. 2017 Apr;64(4):416-427.