SUBMITTED 2 NOV 21
REVISION REQ. 21 NOV 21; REVISION RECD. 30 DEC 21
ACCEPTED 9 DEC 21
ONLINE-FIRST: JAN 2022
DOI: https://doi.org/10.18295/squmj.1.2022.002

Cold Bubble Humidification of Oxygen

Old habits die hard

Sugata Dasgupta,[1] Shrestha Ghosh,[2] *Atanu Chandra[2]

Departments of [1]Critical Care Medicine and [2]Internal Medicine, RG Kar Medical College and Hospital, Kolkata, India
**Corresponding Author's e-mail: chandraatanu123@gmail.com*

'Chains of habit are too light to be felt until they are too heavy to be broken.'- Warren Buffett

Introduction

Oxygen therapy is a widely used treatment modality, which when administered correctly can be life-saving. Published data have demonstrated that a large proportion of doctors and nurses have been unable to accurately follow the proper methods for administration of oxygen.[1, 2] Administration of oxygen through cold bubble humidifiers is a generic approach in acute respiratory failure due to a whole host of causes, especially in poorly resourced health systems. This article attempts to systematically discredit the age-old practice of cold bubble humidification by questioning the norm of prescribing 'moist oxygen' to all patients irrespective of oxygen flow rate. To establish our views, we have elucidated the concepts of low-flow and high-flow oxygen therapy, the physiology and physics of humidification, and the risks of infections associated with cold bubble humidifiers. Finally, we have concluded that cold bubble humidifiers, scientifically, are unable to meet the physiological needs of the upper airway, thereby, rendering them far inferior to heated humidifiers.

Low flow and high flow oxygen

Oxygen delivery systems have always remained a critical component of patient care, in hospital and otherwise.[3]Devices for delivery of medical oxygen can be broadly categorized on the basis of rates of oxygen flow, into high-flow and low-flow devices. The required flow rate is determined for individual patients on the basis of their peak inspiratory flow rate, which in turn is dependent on each patient's pre-existing respiratory ailment.

Low-flow oxygen therapy devices are also known as variable performance devices.[4] These devices deliver a variable fractional inspired concentration of oxygen (FiO_2) according to the variations in minute ventilation (variations in tidal volume, respiratory rate and inspiratory flow) of a patient. The final delivered FiO_2 is the result of mixing of variable amounts of inhaled room air although the device delivers 100% oxygen to the upper airway. Severely breathless adult patients often generate inspiratory flows of greater than 40-60L/minute. As the low flow devices usually supply oxygen at flow rates (maximum 15L/min in India) lower than the dyspnic patient's inspiratory demand, a variable amount of room air is required to achieve the required flow. Therefore, FiO_2 of inspired air varies substantially. Examples of commonly used low-flow or variable performance oxygen therapy devices are nasal cannulae, simple face masks and partial rebreathing and non-rebreathing reservoir masks.[5]

High-flow or fixed performance devices, such as air entrainment masks, large volume nebulisers and high-flow nasal cannulae (HFNC), provide oxygen at flow rates adequate enough to meet the inspiratory demands of the patient.[5,6] These devices blend 100% oxygen with room air to produce a final inspired gas with the desired FiO_2 and provide an inspiratory flow high enough to exceed any tidal volume, respiratory rate and inspiratory flow a breathless patient might usually generate, thereby preventing dilution of FiO_2 by entrained room air. Therefore, high-flow, fixed-performance devices deliver a predictable FIO_2. The delivered concentration and flow of oxygen affect the final FiO_2 and they can be controlled independently in some devices. However, direct caregivers should be cautious that even with these devices, the FiO_2 can be reduced if the inspiratory flow of an occasional severely dyspnic patient exceeds the device's total flow output. With the emergence of the COVID-19 pandemic, the potential of HFNC as an alternative to standard oxygen therapy and non-invasive ventilation (NIV) has been revisited with special interest across the globe. Guy *et al* in a monocentric study concluded that HFNC was effective in managing COVID-19 patients in ICU setting.[7] A study of moderate to severe COVID-19 patients by Geng *et al* suggested that administration of HFNC reduced the rate of intubation and improved the clinical outcome in type 1 acute respiratory failure.[8] High flow nasal cannulae are always used with heated humidifiers.

Concept of physiological humidification: absolute and relative humidity

The importance of the upper airway is often understated. However, it holds special significance with regards to understanding the processes behind physiological humidification of inspired air. Besides the upper airway, the trachea provides countercurrent mechanism for heat and moisture exchange during breathing, and hence plays an important role in heating and humidifying inspired gas.

Understanding the concept of humidity, and the ways to measure it, is beneficial in a discussion pertaining to the physiology of humidification of inspired gas.[4] Humidity is quantified in two ways. Absolute humidity (expressed in g/m^3) is defined as the mass of water vapor present per unit volume of gas at any given temperature and pressure.[9]Relative humidity is a comparative measurement, describing the ratio between the mass of water vapor present in a given volume of air to the mass of water vapor required to completely saturate said volume of air, at a particular temperature. It is expressed in percentage (%).[4]

The nose is the site of maximal heat and moisture exchange, such that a gradient of heat and absolute humidity is achieved down the upper airway.[10]The normal temperature, relative humidity and absolute humidity of inspired gas at the airway opening are about 22°C, 50% and 10 g/m^3 respectively. After normal heating and humidification mechanisms in the intact upper respiratory tract, these values reach 29-32°C, 95% and 28-34 g/m^3 in the oropharynx and 32-36°C, 100% and 34-40 g/m^3 in the trachea. On reaching the lungs, the inspired gas is fully saturated with water vapor at body temperature (37°C, 100% relative humidity, 44 g/m^3 absolute humidity).[11] The point at which this occurs is called the isothermic saturation boundary (ISB), which is approximately 5 cm distal to the carina at the level of third generation airways.[4]

Nasal mucosa is kept warm and moist by secretions from goblet cells and mucous glands, such that when inhaled air passes through the path created between the turbinates, incoming air is warmed by convection. Liquid moisture from epithelial lining evaporates by utilizing latent heat of vaporization to add to the humidity of inhaled air. Heat and moisture exchange is crucial to maintaining mucociliary function, as ciliary motility is drastically reduced, airway irritation increases and pulmonary secretions become viscid and inspissated when exposed to cold, dry air.[12]Respiratory heat loss occurs during exhalation, as latent heat is released when water vapor from saturated exhaled air condenses in the upper airways. Thus, the airways are prepared for another cycle of heating and humidification of inspired air.

Physics of humidification

Humidifiers form an important limb of oxygen delivery systems. A variety of devices are available to achieve ideal humidity levels that are as close to the physiologic requirement as possible. Based on their mechanism of action, humidifiers are divided into active and passive types.[9] Active humidifiers such as bubble and pass-over humidifiers add water or heat or both to the inspired gas. Passive humidifiers e.g. heat and moister exchangers (HME) use exhaled heat and moisture to humidify inspired gas. A nebulizer produces an aerosol, a suspension of water particles in gas, for humidification.

Bubble humidifiers are one of the most common humidifiers used in India. These are water containers in which gas is forced to escape through a tube placed at the bottom.[13] The gas bubbles collect moisture while journeying to the water surface and pass through an outlet connected to an oxygen delivery device. A number of factors govern the amount of water vapor gained through this process. Lower flow rates allow longer contact time between the gas and water, thereby increasing humidity. The higher is the flow through a bubble humidifier, the lower is the water vapor content and temperature of the gas leaving the device. Flow rates of more than 10L/min usually result in decreased contact time and inability to achieve required absolute humidity. Absence of a diffuser also lowers humidity. Diffusers break larger gas bubbles into smaller ones, increasing the surface area and, thus, enabling greater gas-liquid interaction. Moreover, a heat source provides latent heat of vaporization required to maximize humidification of gas.

More often than not, especially in resource limited setups, there is an absence of a heat source. The resultant use of cold bubble humidification renders an absolute humidity of only 10-20 g/m^3 at standard room temperature against the physiological requirements of at least 34 g/m^3 in trachea and 44 g/m^3 below carina at the isothermic saturation boundary (ISB). A comparison of various humidifiers shows that while cold bubble humidifiers and HMEs drastically fail to provide 100% saturation at 37° C and heated water baths just meet the requisite levels, heated Bernoulli nebulizers as well as ultrasonic nebulizers more than surpass the mark.[14]

Infections associated with cold bubble humidifiers

Respiratory tract infections are the commonest type of healthcare-associated infections (HAI).[15]Elderly, immunocompromised or critically ill subjects are particularly susceptible to the nosocomial infections caused by several bacteria and fungi. Equipments used for respiratory care such as nebulizers, ventilators and humidifiers may act as potential vehicles for transmission of those organisms, though their exact role in causation of HAI is still a matter of debate. Humidifiers may serve as a reservoir of several microorganisms, as the fluids inside them may be contaminated by different bacteria and fungi. Some of the organisms may also multiply in the stagnant water. The organisms gain access inside the host by two ways- firstly, from the aerosolization in the room and secondly, through direct delivery to the airways.[16]Moreover, many gram-positive and gram-negative bacteria can form biofilms over medical devices; among them some of the important organisms are *Staphylococcus aureus*, *Enterococcus faecalis*, *coagulase negative Staphylococcus*, *Klebsiella pneumonia and Pseudomonas aeruginosa*.[17]

La Fauci V *et al* conducted a study by collecting water samples from disposable and reusable oxygen humidifiers from different wards and processed them for microbial analysis.[18]They found a very high rate of microbial contamination in samples from reusable oxygen humidifiers in comparison to the disposable ones. The contamination rate in the reusable oxygen humidifiers was more than 50% and most relevant pathogens were *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Another hospital-based study conducted by Jadhav S et al showed that colonization rates of the oxygen humidifier chambers of portable cylinders and pipelines by bacteria and fungi were 75% and 87% respectively.[16] *Aspergillus Spp.* was the commonest among the fungal isolates. Among the gram negative bacteria, several multi-drug resistant organisms such as *Klebseilla pneumonia*, *Pseudomonas spp.*, *Acinetobacter spp and Escherechia coli* were isolated.

Recommendations

Jadhav *et al* demonstrated the importance of disinfection by documented reduced colonization rates of 15% and 12% for fungi and bacteria respectively after maintenance of hand hygiene and disinfection of humidifier chambers with 70% ethanol.[16]Overall, to prevent microbial growth, sterile water instead of tap water is recommended along with regular thorough cleaning and changing of humidifiers. However, with stretched resources, especially during the on-going pandemic, meticulous implementation of such practices may prove to be difficult. Hence, revisiting the rationale behind routine usage of humidified oxygen over ‘dry (without usual cold bubble humidification)’ oxygen is reasonable. Non-humidified and non-heated air-oxygen mixtures can lead to increased airway resistance, dry up upper airway mucosa leading to reduced muco-ciliary clearance, cause airway mucosal inflammation and damage, and increase the amounts of energy expended by patients to warm and humidify the delivered gas.[19] Cold bubble humidifiers are unable to add the necessary amount of humidification and heat needed to prevent the above mentioned complications. Over the years, several studies have validated that there is little difference in clinical outcome and symptom severity between patient groups using humidified and non-humidified oxygen.[20, 21]

British Thoracic Society (BTS) guidelines do not recommend routine humidification of oxygen when delivered under low flow (1-4 L/min) unless upper airways are bypassed, as in intubated or tracheotomised patients.[22]Higher flows of oxygen (>4 L/min) can cause upper airway discomfort due to dryness, although most patients may be able to tolerate it. Maintenance of adequate hydration of all patients receiving supplemental oxygen remains most essential. The guidelines also suggest administering normal saline nebulisation for liquefying viscid secretions, further negating requirement of oxygen humidification.

Furthermore, high-flow oxygen therapy if needed should be provided with heated humidifiers as opposed to cold bubble humidifiers which are highly ineffective. Studies by Santana *et al* and Franchini *et al* support that cold bubble humidifiers fail to provide any additional humidity to nasal mucosa when compared to non-humidified oxygen therapy.[23,24] Humidification of inspired oxygen can only be considered in patients who complain of excessive nasal dryness associated discomfort. However, topical application of water based lubricants can be a reasonable solution to this complaint.[4]In published guidelines on oxygen therapy in pediatric patients, available evidence has not supported the use of heated or unheated humidification with low flow oxygen delivery.[25, 26]

Conclusion

With the growing need for oxygen administration due to COVID-19 infection, the importance of heating and humidification with oxygen administration should be reaffirmed. However, the issue is universal and not associated only with COVID-19 infection. Cold water chamber humidifier has been rendered redundant in the light of better technology, for it is unable to provide adequate humidification required by the respiratory tract. Moreover, evidence suggests that humidification is not mandatory in patients on oxygen therapy with any of the low flow delivery devices, as described earlier. Furthermore, it is imperative that cold bubble humidifiers are acknowledged as a breeding ground of infections, especially in resource stretched scenarios due to difficulty in regular cleaning and maintenance. Hence to conclude, a cold bubble humidifier cannot humidify to the levels required. Its usage should be abandoned as it offers no significant added advantage over room air and increases potential infection risk.

Authors' Contributions

SD and SG prepared the manuscript with adequate planning and execution. SD and AC contributed to review of literature, critical revision of content and final approval of manuscript. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgement

We are extremely grateful to Dr Farhad N Kapadia; MD, FRCP, DA, EDIC; Consultant physician and intensivist, Hinduja Hospital, Mumbai, Maharashtra, India for providing valuable inputs regarding this topic.

References

1. Budinger GRS, Mutlu GM. Balancing the risks and benefits of oxygen therapy in critically ill adults. Chest. 2013 Apr;143(4):1151-1162. doi: 10.1378/chest.12-1215. PMID: 23546490; PMCID: PMC3616683.
2. Cousins JL, Wark PAB, McDonald VM. Acute oxygen therapy: a review of prescribing and delivery practices. Int J Chron Obstruct Pulmon Dis. 2016 May 24;11:1067-75. doi: 10.2147/COPD.S103607. PMID: 27307722; PMCID: PMC4888716.
3. Hardavella G, Karampinis I, Frille A, Sreter K, Rousalova I. Oxygen devices and delivery systems. Breathe (Sheff). 2019 Sep;15(3):e108-16. doi: 10.1183/20734735.0204-2019. PMID: 31777573; PMCID: PMC6876135.
4. Hess DR. Humidity and Aerosol Therapy. In: Respiratory Care: Principles and Practice.2nd ed. Jones and Bartlett Learning, 2012. p.303-36

5. Kallstrom TJ; American Association for Respiratory Care (AARC). AARC Clinical Practice Guideline: oxygen therapy for adults in the acute care facility--2002 revision & update. Respir Care. 2002 Jun;47(6):717-20. PMID: 12078655.
6. Renda T, Corrado A, Iskandar G, Pelaia G, Abdalla K, Navalesi P. High-flow nasal oxygen therapy in intensive care and anaesthesia. Br J Anaesth. 2018 Jan;120(1):18-27. doi: 10.1016/j.bja.2017.11.010. PMID: 29397127.
7. Guy T, Créac'hcadec A, Ricordel C, Salé A, Arnouat B, Bizec JL, *et al*. High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. Eur Respir J. 2020 Nov 12;56(5):2001154. doi: 10.1183/13993003.01154-2020. PMID: 32859678; PMCID: PMC7453734.
8. Geng S, Mei Q, Zhu C, Yang T, Yang Y, Fang X, *et al*. High flow nasal cannula is a good treatment option for COVID-19. Heart Lung. 2020 Sep-Oct;49(5):444-5. doi: 10.1016/j.hrtlng.2020.03.018. PMID: 32295710; PMCID: PMC7151489.
9. Plotnikow GA, Accoce M, Navarro E, Tiribelli N. Humidification and heating of inhaled gas in patients with artificial airway. A narrative review. Rev Bras Ter Intensiva 2018;30(1):86–97. doi: 10.5935/0103-507X. 20180015.
10. Shelly MP. The upper airway--the forgotten organ. Crit Care. 2001;5(1):1-2. doi: 10.1186/cc971. PMID: 11178219; PMCID: PMC137263.
11. Gross JL, Park GR. Humidification of inspired gases during mechanical ventilation. Minerva Anestesiol. 2012 Apr;78(4):496-502. PMID: 22269929.
12. Kilgour E, Rankin N, Ryan S, Pack R. Mucociliary function deteriorates in the clinical range of inspired air temperature and humidity. Intensive Care Med. 2004 Jul;30(7):1491-4. doi: 10.1007/s00134-004-2235-3. PMID: 15024566.
13. McNulty G, Eyre L. Humidification in anaesthesia and critical care, *BJA Education*, Volume 15, Issue 3, June 2015, Pages 131–35, doi: 10.1093/bjaceaccp/mku022
14. Davis PD, Parbrook GD, Kenny GNC. Humidification. In: Basic Physics and Measurement in Anaesthesia. 4th ed. Oxford: Butterworth-Heinemann Ltd, 1995. p.146-57
15. Haque M, Sartelli M, McKimm J, Abu Bakar M. Health care-associated infections - an overview. Infect Drug Resist. 2018 Nov 15;11:2321-2333. doi: 10.2147/IDR.S177247. PMID: 30532565; PMCID: PMC6245375.
16. Jadhav S, Sahasrabudhe T, Kalley V, Gandham N. The microbial colonization profile of respiratory devices and the significance of the role of disinfection: a blinded study.

J Clin Diagn Res. 2013 Jun;7(6):1021-6. doi: 10.7860/JCDR/2013/5681.3086. PMID: 23905094; PMCID: PMC3708189.

17. Khatoon Z, McTiernan CD, Suuronen EJ, Mah TF, Alarcon EI. Bacterial biofilm formation on implantable devices and approaches to its treatment and prevention. Heliyon. 2018 Dec 28;4(12):e01067. doi: 10.1016/j.heliyon.2018.e01067. PMID: 30619958; PMCID: PMC6312881.
18. La Fauci V, Costa GB, Facciolà A, Conti A, Riso R, Squeri R. Humidifiers for oxygen therapy: what risk for reusable and disposable devices? J Prev Med Hyg. 2017 Jun;58(2):e161-5. PMID: 28900356; PMCID: PMC5584085.
19. Fontanari P, Burnet H, Zattara-Hartmann MC, Jammes Y. Changes in airway resistance induced by nasal inhalation of cold dry, dry, or moist air in normal individuals. J Appl Physiol (1985). 1996 Oct;81(4):1739-43. doi: 10.1152/jappl.1996.81.4.1739. PMID: 8904594.
20. Wen Z, Wang W, Zhang H, Wu C, Ding J, Shen M. Is humidified better than non-humidified low-flow oxygen therapy? A systematic review and meta-analysis. J Adv Nurs. 2017 Nov;73(11):2522-33. doi: 10.1111/jan.13323. PMID: 28440960.
21. Poiroux L, Piquilloud L, Seegers V, Le Roy C, Colonval K, Agasse C, *et al*; REVA Network. Effect on comfort of administering bubble-humidified or dry oxygen: the Oxyrea non-inferiority randomized study. Ann Intensive Care. 2018 Dec 17;8(1):126. doi: 10.1186/s13613-018-0472-9. PMID: 30560440; PMCID: PMC6297119.
22. O'Driscoll BR, Howard LS, Earis J, Mak V. British Thoracic Society Guideline for oxygen use in adults in healthcare and emergency settings. BMJ Open Respir Res. 2017 May 15;4(1):e000170. doi: 10.1136/bmjresp-2016-000170. PMID: 28883921; PMCID: PMC5531304.
23. Santana LA, Bezerra SKM, Saraiva-Romanholo BM, Yamaguti WP, de Fátima Lopes Calvo Tibério I, Dos Santos TM, *et al*. Cold bubble humidification of low-flow oxygen does not prevent acute changes in inflammation and oxidative stress at nasal mucosa. Sci Rep. 2021 Jul 12;11(1):14352. doi: 10.1038/s41598-021-93837-x. PMID: 34253806; PMCID: PMC8275780.
24. Franchini ML, Athanazio R, Amato-Lourenço LF, Carreirão-Neto W, Saldiva PH, Lorenzi-Filho G, *et al*. Oxygen With Cold Bubble Humidification Is No Better Than Dry Oxygen in Preventing Mucus Dehydration, Decreased Mucociliary Clearance, and Decline in Pulmonary Function. Chest. 2016 Aug;150(2):407-14. doi: 10.1016/j.chest.2016.03.035. PMID: 27048871.

25. Napolitano N, Berlinski A, Walsh BK, Ginier E, Strickland SL. AARC Clinical Practice Guideline: Management of Pediatric Patients With Oxygen in the Acute Care Setting. Respir Care. 2021 Jul;66(7):1214-1223. doi: 10.4187/respcare.09006. PMID: 33790048.
26. WHO. Oxygen therapy for children: a manual for health workers. Geneva, Switzerland: World Health Organization (WHO); 2016.