5. IS IT RELIABLE TO REFRESH A REVERSED CIRCUIT WITH MINIMAL FLOW FOR STABLE OXYGENATION?

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Abstract

Minimal flow anesthesia (MFA) is associated with better preservation of airway moisture and less heat loss. Decreased gas waste also reduces costs. The total amount of vaporized anesthetics is reduced and the risk for unnecessary work place contamination is decreased as well as the amount released into the atmosphere and subsequent impact on the global ecosystem. But low fresh gas flow (FGF) means increased rebreathing of exhaled gases. Thus, some risk of hypoxic gas mixture formation appears. Carrier gas composition acquires high importance. If pure oxygen is used as a carrier gas, adequate oxygenation for patient must be ensured. However pure oxygen delivering rises arterial oxygen partial pressure. So, we have to consider the degree of hyperoxemia. Using oxygen and air mixture as a carrier gas gives us possibility of maintaining blood oxygen level in more physiologic range, but in case of MFA, steady oxygen concentration in breathing circuit is not guaranteed, especially with fixed flow. The aim of present review is to update information about safety of MFA as a method ensuring stable oxygenation. Not using nitrous oxide accelerates the process of shortening high flow phases. Ensuring sufficient denitrogenation and the avoidance of volume imbalances are only of secondary importance. As a result of rapid reduction to a low fresh gas flow, considerable cost saving can be expected. Using fixed minimal flow gives us the possibility to take the advantages of rebreathing systems right from the start. Minimal fixed FGF needs high FiO_2 of the carrier gas to ensure steady inhaled oxygen concentration ($FinspO_2$) during long term anaesthesia. Effect of high FiO_2 on respiratory system and clinical outcome is being debated. Finding appropriate balance between the FiO_2 of the carrier gas and the $FinspO_2$ is challenging. Minimal fixed flow anesthesia (0.5 L/min) is safe if pure oxygen is used as a carrier gas. Using oxygen/air mixture as a carrier gas includes some risks of $FinspO_2$ dropping. Patients' age and body size can be used as the prognostic factors to prevent significant decreasing of $PinspO_2$. Fixed MFA needs more time for inhala-tional agent to achieve desired alveolar concentration. Less soluble agents are more suitable for MFA.

Keywords: minimal flow anesthesia, oxygen concentration, carrier gas

Introduction

Low and minimal flow anesthesia are characterized by the significantly decreased rate of fresh gas flow (FGF), which is fed into the breathing gas system. If FGF is lower than minute ventilation, the exhaled gases are returned to the patient via closed or semi-closed rebreathing systems after CO_2 has been chemically bonded. As a result of this process, the rebreathing volume consecutively increases with a reduction in FGF and the excess gas volume is continually reduced. In minimal flow anesthesia (MFA), the FGF is reduced to 0.5 L/min. Reducing the FGF is associated with several benefits: Enhanced preservation of temperature and humidity, cost savings through more efficient utilization of inhaled anesthetics. In modern clinical practice, when inhalational anesthesia is performed using a rebreathing system, the FGF should always be as low as possible. This is the only way in which the emission of excess anesthesia gases can be reduced to a minimum and the advantages of improved respiratory gas conditioning achieved. The total amount of vaporized anesthetics is reduced and thus risk for unnecessary work place contamination is decreased as well as the amount released into the atmosphere and subsequent impact on the global ecosystem.

Fresh gas composition may consist of oxygen, oxygen/air or oxygen/nitrous oxide. The use of nitrous oxide (N_2O) may be seen as somewhat more complicated, considering the need for more vigilant control of circle gas composition. An alternative and potentially safer technique is to use pure oxygen or oxygen/air mixture. The use of oxygen as the sole fresh gas essentially eliminates the risk for a hypoxic gas mixture. Nitrogen constitutes a major part of ambient air and thus in the airways and its accumulation in reversed circuit needs to be considered in association with low/minimal flow anesthesia. Decrease in oxygen concentration is the result of its uptake from the inspired gas and further dilution by accumulated gases in reversed circuit. The uptake of oxygen from the inspired gas is related to physiological requirements, which are dependent on body size and metabolic needs. Dilution of gases in the reversed circle system by nitrogen can be minimized by an effective denitrogenation of the gaseous compartment during induction. Baum recommended high initial fresh

gas flow for denitrogenation. But this recommendation especially refers to the inhalational anesthesia when a carrier gas mixture contains nitrous oxide. High flow phase may be shortened when air/oxygen mixture is used as a carrier gas. The use of pure oxygen will result in high oxygen concentrations, improving the patients' safety by increasing the pulmonary oxygen reservoir and preventing the development of hypoxic gas mixtures within the breathing system. However pure oxygen delivering will rise arterial oxygen partial pressure (PaO_2). So, we have to consider the degree of hyperoxemia. Using oxygen/air mixture as a carrier gas gives us possibility of maintaining blood oxygen level in more physiologic range. According to Jan A. Baum, using oxygen and air mixture as a carrier is a gold standard. But in case of low FGF, steady oxygen concentration in breathing circuit is not guaranteed, especially with fixed FGF flow. If the carrier gas does not contain any N_2O, the patient only takes up oxygen and an adequate amount of volatile agent. Thus, a higher volume of excess gas is available in N_2O-free MFA, resulting in an improved gas filling of the breathing system and hence a significant decrease in the risk of accidental gas volume deficiency. It must be ensured during the initial distribution phase that the fresh gas volume supplied is not lower than the gas losses caused by individual gas uptake and system leakages. This considerably facilitates the performance of MFA in routine clinical practice. If, however N_2O is not used at all, no nitrogen wash-out is required and N_2O wash-in is not needed. Thus, the duration of the initial phase is determined only by the time needed to establish the agent alveolar concentration required to guarantee a sufficient anesthetic depth. As a result of rapid reduction to a low FGF, considerable cost saving can be expected. This is due to the fact that according to current investigations, 60 to 70% of volatile anesthetics consumption takes place during the first ten minutes of the wash-in phase.

Discussion

Hendrickx and colleagues in their randomized clinical study aimed to determine the effect of different air/oxygen mixtures and fresh gas flows (FGF) on the relationship between the FiO_2 and $FinspO_2$ in a circle system. The authors concluded, that when air/oxygen mixtures are used with low and especially minimal flow techniques in a circle system, $FinspO_2$ becomes lower than the FiO_2 with FGF ≤ 2 L/min. The relative proportion of O_2 in the FGF has to be increased accordingly.

In 2008 Hendrickx and De Wolf published an extensive review of the pharmacokinetics of inhaled anesthetics and their use with low FGF. They stated that the focus should be shifted to “what combination of delivered concentration and FGF can be used to attain the desired alveolar concentration.”

Some authors recommend to start with high FGF to reduce wash-in time and then switch to low or minimal flow,. Other authors prefer “equilibration point” for switching to the low/minimal flow,.

Arslan and colleagues tried to answer the question: Are high FGF rates necessary during the wash-in period in low-flow anesthesia (LFA)? They compared the efficiency, safety and the consumption of desflurane in LFA using constant FGF (1 L/min) and conventional LFA using high FGF (4 L/min) during the wash-in period. Wash-in was accomplished with 1 L/min FGF (FiO_2 0.5) and 18 % desflurane in group 1; and by 4 L/min FGF (FiO_2 0.5) and 6 % desflurane in group 2. Throughout the surgery, the vaporizer was adjusted to maintain 0.6 to 0.8 MAC. They concluded, that the efficiency of anesthesia in both the first hour and in total was higher in group 1 ($P < 0.001$) and it is safe, more efficient and economical to use 1 L/min FGF during the wash-in period in LFA.

Bahar, S. and co-authors in their study aimed to evaluate the efficacy and practicability of fixed low flow (1 L/min FGF FiO_2 0.5) during both the wash-in and maintenance periods of desflurane anesthesia. After endotracheal intubation, FGF was reduced to 1 L/min and the desflurane vaporizer was set at 18%. The time from opening the vaporizer to end-tidal desflurane concentration reaching 0.7 MAC was recorded. The average MAC 0.7 time was 2.9±0.5 min. MAC and BIS values at the start of the surgery were 0.7 (0.6–0.8) and 39±8.5 respectively. No individual patient had a BIS value above 60 throughout the surgery. Hemodynamic variables were stable and inhaled oxygen concentration ($FinspO_2$) did not fall below 30% in any patient. The authors demonstrated that LFA without use of initial high fresh gas flow during the wash-in period is an effective, safe and economic method which is easy to perform.

Horwitz and Jakobsson compared desflurane with sevoflurane by fixed low and minimal flow techniques. Patients were randomized to receive either desflurane or sevoflurane to maintain anesthesia with one of the two fixed FGF 0.5 L/min or 1 L/min FGF both with oxygen in air (FiO_2 0.5) throughout anesthesia. Within each of the four groups, they recorded the time from opening the vaporizer until the Etaa concentration reached 1 and 1.5 MAC. With fixed 0.5 l/min minimal flow time to reach 1 MAC anesthetic concentration was 8.5±1.7 min for desflurane and 15.2±2.4 min for sevoflurane $P < 0.01$.

Jiwook Kim with colleagues aimed investigate the change in $FinspO_2$ in LFA using oxygen and medical air. A total of 60 patients scheduled for elective surgery with an ASA physical status I or II were enrolled and randomly allocated into two groups. Group H: FGF 4 L/min (FiO_2 0.5). Group L: FGF 1 L/min (FiO_2 0.5). Oxygen and inhalation anesthetic gas concentration were recorded for 180 min at 15 min interval. In group H, the $PinspO_2$ did not change significantly during anesthesia was kept at about 45%. In group L, the $FinspO_2$ during the first 15 min was 40.2 ± 2.0%. After 1 h, $FinspO_2$ was 37.3 ± 2.6% and after 120min 35.4 ± 4.0%. For individual patients, the lowest $FinspO_2$ during 180 min was 44% in group H and 26% in group L. One of the 30 patients in group L showed a reduction in the $FinspO_2$ to < 30%. The patient was 180 cm in height and 95 kg in weight, and the $FinspO_2$ began reducing below 30% after 60 min of anesthesia, which continued to 26% until the end of surgery. The authors concluded, that LFA with 1 L/min FGF ensured to maintain $FinspO_2$ at 30% or more for 180 min in patients under 90 kg.

In our study, We hypothesized, that fixed minimal fresh gas flow (0.5L/min) composed with medical air and oxygen (FiO_2 0.8) might decrease $FinspO_2$ more intensively compared with a pure oxygen as a carrier gas. The focus of our study was to test fixed minimal flow (0.5 L/min) with FiO_2 0.8 during off-pump coronary arterial grafting operations (≥ 3 h) as a safe method ensuring adequate oxygenation. We were interested, if it would be sufficient to keep $FinspO_2 \geq 0.4$. For safety reasons we appointed this preliminary margin (0.4) and if $FinspO_2$ dropped below it, FiO_2 was raised up to 1.0 to improve oxygenation. We did two parallel 2 arm trial for isoflurane and sevoflurane anesthesia separately. As we used fixed minimal flow, we were interested to study “wash-in” time for both inhalational anesthetics. 208 patients were randomly equally distributed into four parallel groups (two controls and two trials separately for sevoflurane and isoflurane anesthesia) with 1:1 allocation ratio (52 patients in each). The patients in the control groups were receiving pure oxygen as a carrier gas and the patients in the trial groups were receiving oxygen / air mixture (FiO_2 0.8). We used fixed MFA (0.5L/min) for both Sevoflurane and Isoflurane groups. We studied how oxygen uptake data correlated with $FinspO_2$ dropping. Minimal $FinspO_2$ values were compared between groups. We tried to reveal the independent factors that might have an effect on oxygen uptake. The independent predictors, that might affect on oxygen uptake were tested by multiple logistic regression. Patients' age, sex, body surface area (BSA), preoperative cardiac ejection fraction (EF), operation duration and the inhalational anesthesia agent were used as the independent predictors. Fixed MFA 0.5L/min with fresh gas FiO_2 0.8 was not found as safe enough to ensure adequate oxygenation during long term operations. In 30 patients (16 patients from isoflurane and 14 patients from sevoflurane groups) $FinspO_2$ dropped below preliminary margin (0.4). Those patients were excluded from trial groups and transferred into the subgroup “dropped-out”. So, 74 patients (36 patients in sevoflurane group and 38 patients in sevoflurane group) were retained in trial groups. Minimal mean FinspO2 value was 48.3 ± 3.7 % in isoflurane and 48.5 ± 4.7% in sevoflurane group. None of the patients from control groups were excluded. $FinspO_2$ remained high in all cases of control groups. We found fixed MFA 0.5L/min with pure oxygen fresh gas (FiO2 1.0) as the safe method avoiding oxygen concentration dropping in breathing circuit. Minimal median $FinspO_2$ (%) value was 75.5 [73–77] in isoflurane control group and 75 [73–77] in sevoflurane control group. In trial groups minimal $FinspO_2$ value highly correlates with average oxygen uptake. Pearson correlation r = - 811; $p < 0.001$. In trial groups $FinspO_2$ was significantly low than in control groups P<001. (Figure 1)

The multiple logistic regression was done with the method “Forward LR”. Only BSA (B = 38.7; p = 0.002) and patient's age (B = 0.47; p = 0.004) were retained into final regression model as independent predictors. We transformed BSA as the continuous variable into the ordinal variable by making subcategories: BSA <2.0; BSA = [2.0–2.1]; BSA = [2.1–2.2]; BSA = [2.2–2.3]; BSA>2.3. Each of the 30 patients, that were dropped out from the trial groups, reached preliminary low margin of oxygenation (FinspO2 0.4) at different times (85 ± 18.5 min) after applying fixed MFA. Tested by Survival Cox regression, we found out that patients with BSA >2.3 (B; 5.2) had much higher chance of leaving the group, that is 183 (Exp.B) times that of those with BSA <2.0 ($p < 0.001$). For the patients with BSA [2.2–2.3]; [2.1–2.2]; [2.0–2.1] that chances were 59 (Exp.B) p < 001; 23(Exp.B) p = 0.004; 11(Exp.B) p = 0.035 respectively. (Figure 2)

Body oxygen consumption depends on several factors. More body size requires more oxygen. Patients retained in the trial groups had less BSA, then the “dropped-out” patients (1.93 ± 0.16 m2 vs 2.26 ± 0.18 m2) P < 0.001. In the elder patient oxygen uptake may be less because of reduced

metabolism. The “dropped-out” patients were younger, then the patients retained in the trial groups (58 ± 7 years vs 69 ± 8 years) P < 0.001. According to the curve built by logistic regression, for the patients aged less than 55 years the probability of being “dropped-out” exceeds 75 %. Oxygen consumption proportionally is related to the cardiac output. However, hemodynamic profile of retained and dropped-out patients was similar. The dosage of the medication affecting HR and MAP was similar as well. The trial groups received 100 ml nitrogen per minute (0.5 l/min FG x 0.2). Nitrogen accumulation is considerable factor during long term operations. Operation time may also be the contributor for oxygen concentration dropping in the breathing circuit. The subgroup “dropped-out” and the trial groups had almost the same operation time (234 ± 38 min vs 232 ± 36 min P = 0.780).

We concluded, that MFA (0.5 L/min) is safe if pure oxygen (FiO_2 1.0) is used as the carrier gas during off-pump coronary artery grafting operations lasting more than 3 hours. Using oxygen/air mixture (FiO2 0.8) as a carrier gas includes some risks for younger patients with high BSA. Minimal fixed 0.5 L/min flow anesthesia with FiO_2 0.8 may not be suitable for the patients younger than 55 years and with BSA more than 2.0.

The “wash-in” time up to 1.2 MAC in our study was about 10.5 min for sevoflurane and about 16 min for isoflurane. The patients undergoing cardiac surgery after tracheal intubation need to be prepared before the operation is started. This preparement includes central lines incertion, preoperative transesophageal cardiosonography and ect. During that period of time the patient is under anesthesia by the medications given intravenously at induction stage and alveolar concentration of inhalational anesthetic is being raised meanwhile. Although extra intravenous boluses may be administered as needed.

Summary

Decreasing of FGF is the significant trend in modern anaesthesiology. The benefits of MFA must be combined with consideration of the risk factors and reasonable balance of side effects. Minimal fixed FGF needs high FiO_2 to ensure steady $FinspO_2$ during long term anaesthesia. Effect of High FiO_2 on respiratory system and clinical outcome is being debated. Finding appropriate balance between the FiO_2 of a carrier gas and the $FinspO_2$ of an inhaled mixture is challenging. Fixed MFA (0.5 L/min) is safe if pure oxygen is used as a carrier gas. Using oxygen/air mixture as a carrier gas includes some risks of $FinspO_2$ dropping. Patients' age and body size can be used as the prognostic factors to prevent significant decreasing of $PinspO_2$. Fixed MFA needs more time for inhalational agent to achieve desired alveolar concentration. Less soluble agents are more suitable for MFA. During using minimal flow techniques continuous monitoring of the $FinspO_2$ and Etaa concentration are mandatory in order to ensure patient safety.

References

1. M. Brattwall, M. Warrén-Stomberg, F. Hesselvik, and J. Jakobsson, “Brief review: Theory and practice of minimal fresh gas flow anesthesia,” *Can. J. Anesth. Can. d'anesthésie*, vol. 59, no. 8, pp. 785–797, Aug. 2012, doi: 10.1007/s12630-012-9736-2.
2. J. A. Baum, “How to perform low flow anaesthesia without nitrous oxide,” in *Low Flow Anaesthesia with Dräger Machines*, 23558 Lübeck, Germany: Drägerwerk AG & Co. KGaA, 2015, pp. 44–64. [Online]. Available: https://www.draeger.com/%0Alibrary/content/rsp-curves-and-loops-booklet-9097339-en.pdf.
3. J. A. Baum, “The carrier gas in anaesthesia: nitrous oxide/oxygen, medical air/oxygen and pure oxygen,” *Curr. Opin. Anaesthesiol.*, vol. 17, no. 6, pp. 513–516, Dec. 2004, doi: 10.1097/00001503-200412000-00012.
4. J. A. Baum, *Low flow anesthesia, the theory and practice of low flow minimal flow and closed system anaesthesia*, 2nd ed. Melbourne: Butterwoth-Heinemann, 2001.
5. C. Hönemann and B. Mierke, “Low-flow, minimal-flow and metabolic-flow anaesthesia Clinical techniques for use with rebreathing systems,” pp. 1–104, 2015.
6. J. F. A. Hendrickx *et al.*, “Air-oxygen mixtures in circle systems,” *J. Clin. Anesth.*, vol. 13, no. 6, pp. 461–464, 2001, doi: 10.1016/S0952-8180(01)00303-8.
7. J. F. A. Hendrickx and A. De Wolf, “Special aspects of pharmacokinetics of inhalation anesthesia,” *Handb. Exp. Pharmacol.*, vol. 182, no. 182, pp. 159–186, 2008, doi: 10.1007/978-3-540-74806-9_8.
8. T. Mallik, S. Aneja, R. Tope, and V. Muralidhar, “A randomized prospective study of desflurane versus isoflurane in minimal flow anesthesia using 'equilibration time' as the change-over point to minimal flow,” *J. Anaesthesiol. Clin. Pharmacol.*, vol. 28, no. 4, pp. 470–475, 2012, doi: 10.4103/0970-9185.101916.
9. V. Chatrath, R. Khetarpal, D. Bansal, and H. Kaur, “Sevoflurane in low-flow anesthesia using 'equilibration point,'” *Anesth. Essays Res.*, vol. 10, no. 2, p. 284, 2016, doi: 10.4103/0259-1162.172343.

10. M. Arslan *et al.*, "Are high fresh gas flow rates necessary during the wash-in period in low-flow anesthesia?", *Kaohsiung J. Med. Sci.*, vol. 36, no. 10, pp. 834–840, Oct. 2020, doi: 10.1002/kjm2.12251.
11. S. Bahar *et al.*, "Low-flow anaesthesia with a fixed fresh gas flow rate," *J. Clin. Monit. Comput.*, vol. 33, no. 1, pp. 115–121, Feb. 2019, doi: 10.1007/s10877-018-0135-2.
12. M. Horwitz and J. G. Jakobsson, "Desflurane and sevoflurane use during low-and minimal-flow anesthesia at fixed vaporizer settings," *Minerva Anestesiol.*, vol. 82, no. 2, pp. 180–185, 2016.
13. J. Kim, D. Kang, H. Lee, S. Ryu, S. Ryu, and D. Kim, "Change of inspired oxygen concentration in low flow anesthesia," *Anesth. Pain Med.*, vol. 15, no. 4, pp. 434–440, 2020, doi: 10.17085/apm.20055.
14. I. Begashvili, M. Kiladze, C. Ejibishvili, and G. Grigolia, "Minimal fixed flow anesthesia for off-pump coronary artery bypass surgery: A parallel randomized trail," *Heliyon*, vol. 9, no. 11, p. e22181, Nov. 2023, doi: 10.1016/j.heliyon.2023.e22181.

Figure 1. FinspO_2(%) at start and end points of operations in the trial and the control groups

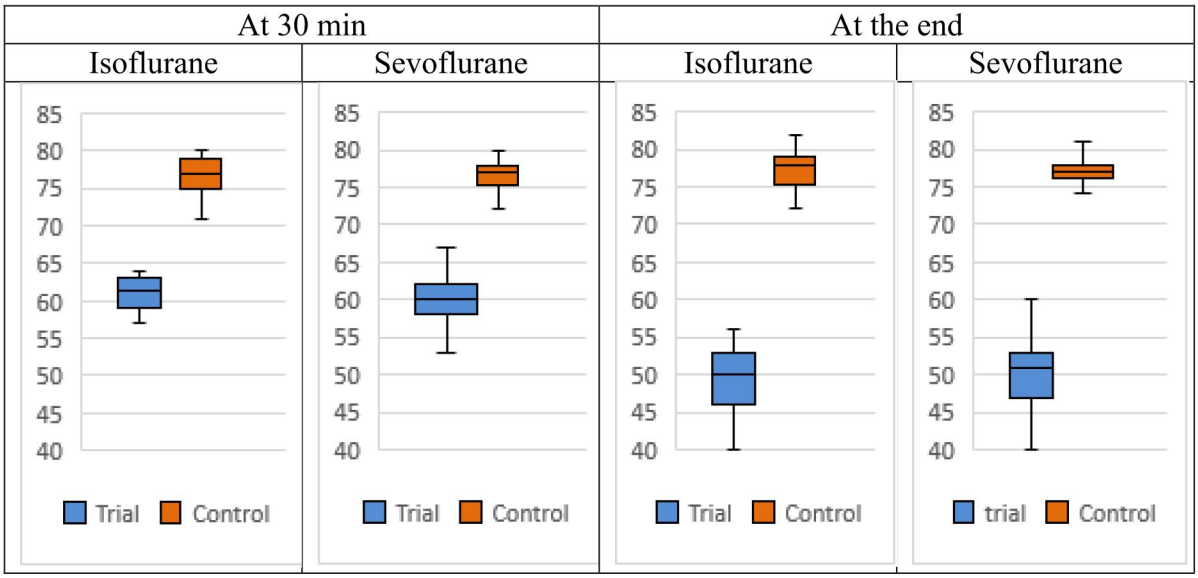

Figure 2. Survival function for BSA subcategories