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Effect of Fractional Inspiratory Oxygen Concentration on Perioperative Liver Injury and Lung Imaging

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Abstract

Objectives: To maintain gas exchange and avoid desaturation during anesthesia, oxygen supplementation is frequently used. Nonetheless, there is an ongoing discussion on the ideal fractional inspiratory oxygen concentrations (FiO_2) concentration, with practices ranging from 30% in Europe to 100% in the US. While preventing hypoxia, high FiO_2 levels can have unfavorable effects, including absorption atelectasis, which may affect liver function in the postoperative period. The purpose of this study was to investigate how perioperative liver injury is affected by varying FiO_2.

Methods: A total of 159 patients aged 18-65 years who underwent procedures lasting more than an hour were included in the study. Three groups of patients - one for each intraoperative FiO_2 concentration - were given 34%, 50%, and 70% of the total. Pre- and postoperative measures of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and international normalized ratio (INR) were used to evaluate liver function. In this prospective trial design, participants with a history of liver disease or other aggravating circumstances were not allowed to participate. Pre- and postoperative chest X-rays were compared.

Results: There were no statistically significant variations in the ALT and AST values of the groups according to the analysis. In contrast to the other groups, the group that received 70% FiO_2 had much lower INR levels. This implies that increased FiO_2 concentrations may have a protective effect against liver function, especially in individuals with impaired liver function. No significant pathological differences were detected between preoperative and postoperative chest X-ray findings.

Conclusion: According to the study findings, patients who require liver-protective medication or have poor liver function may benefit more from high FiO_2 concentrations after surgery. Although there was no indication of liver damage caused by hyperoxia, more investigation using larger samples and longer follow-up is recommended to validate these results.

Keywords: Liver, fractional inspiratory oxygen concentrations, liver failure, general anesthesia, imaging

Introduction

Pre-, during-, and post-anesthesia oxygen supplementation at concentrations above the standard atmospheric 21% is routinely used to prevent desaturation and mitigate the disruption of gas exchange caused by the residual effects of anesthetic and analgesic drugs during airway management. The ideal concentration of this additional oxygen is debatable, and regional variations exist in practice. In the US, oxygen concentrations can reach as high as 100%, whereas in Europe, a 30% concentration is typical.[1] Publications in the literature have shown a strong correlation between postoperative cardiac damage and low intraoperative fraction of inspired oxygen (FiO_2) values.[2] Similar to low FiO_2 levels, high FiO_2 levels can have a major impact on clinical outcomes. One of the negative consequences of elevated FiO_2 levels is absorption atelectasis.[3] During the perioperative phase, surgical site infections are critical. To aid in the prevention of these infections, the World Health Organization recommends setting the perioperative FiO_2 concentration to 80%.[4] Typically, the FiO_2 concentration is maintained between 30% (low) and 80% (high) to minimize the negative effects of high oxygen therapy and prevent hypoxia.[5]

Hypoxemia or ischemia due to other causes can particularly cause liver tissue damage, especially following reperfusion.[6,7] Tissue damage can also result from hyperoxia because it produces free oxygen radicals.[8]

In order to determine the ideal FiO_2 levels for patients with impaired liver function or those in need of liver-protective medication, this study aimed to examine the impact of different FiO_2 concentrations on perioperative liver injury.

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Methods

The investigation was planned as an observational prospective study that would be conducted in the operating room of our institution. The study was approved by Erzincan Binali Yıldırım University's Clinical Research Ethics Committee (approval number: 2022-08/5, approval date: 22.12.2022). All patients who collaborated provided written informed consent. According to G-Power analysis, the study comprised 159 patients, aged 18-65, who were categorized as American Society of Anesthesiologists (ASA) 1, 2 and 3 and underwent surgical procedures at the Mengücek Gazi Training and Research Hospital that took more than an hour to complete between January 1 and June 30, 2023. Exclusion criteria were a history of drug allergies, liver disease, drugs that affect the liver, pregnancy, electrolyte imbalances, organ failure, liver dysfunction, kidney dysfunction, obesity, cachexia, refusal to participate, or inability to cooperate.

One day before the procedure, all patients received information regarding the study protocol and procedures, and written informed consent was obtained. Preoperative chest X-rays were taken from the patients. Patients were taken to the operating room on the day of the procedure, and venous access was performed as usual through the left antecubital fossa. Peripheral oxygen saturation, non-invasive blood pressure monitoring, and three-channel electrocardiography were performed.

Based on intraoperative FiO_2 values, patients were divided into three groups: 34% (Group A), 50% (Group B), and 70% (Group C). A number of preoperative tests were noted, including international normalized ratio (INR), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). General anesthesia was induced in all patients using 0.6 mg/kg of rocuronium, 1 mcg/kg of fentanyl, and 2 mg/kg of propofol. Remifentanil was infused at a rate of 0.5-1 mcg/kg/min, and 2% sevoflurane was infused at a rate of 4 L/min to maintain anesthesia. Groups A, B, and C were given oxygen-medical air mixtures with different FiO_2 concentrations: 34%, 50%, and 70%, respectively. At the end of the operation, anesthetic gases and remifentanil were discontinued, and the patients were transferred to extubation using 100% oxygen. Atropine (0.015 mg/kg) and neostigmine (0.04 mg/kg) were given. All patients underwent blood sampling for AST, ALT, and INR after extubation. After surgery, patients were moved to the postoperative recovery area. Atelectasis, effusion, infiltration, consolidation, and edema were investigated on preoperative and postoperative chest X-rays. Patients with aldrete scores >9 were moved to the ward after the scores were recorded at 5, 10, and 30 minutes. Postoperative chest X-rays were obtained from the patients in the ward. The preoperative and postoperative test results were compared, and the collected blood samples were examined.

Statistical Analysis

IBM Statistical Package for the Social Sciences (SPSS) Statistics 25.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. For normally distributed variables, descriptive statistics are presented as mean±standard deviation; for non-normally distributed variables, they are presented as median (minimum-maximum); and nominal variables are presented as frequency (%).

The significance of mean differences between the two groups was evaluated using the t-test, whereas differences in medians were evaluated using the Mann-Whitney U test. ANOVA was used to assess mean differences in comparisons involving more than two groups, and the Kruskal-Wallis test was employed to assess median differences. Both Fisher's exact test and Pearson's chi-square test were used to assess nominal variables.

When the distribution was non-normal, the Spearman correlation test was used to evaluate the relationship between continuous variables; when the distribution was normal, the Pearson correlation test was employed.

Results were considered statistically significant at a p value of <0.05.

Using one-way ANOVA and an effect size (Cohen's f) of 0.25 for the comparison of AST, ALT, and INR values among the three groups, the sample size calculation required 159 individuals. Type 1 Error (α) was set at 0.05 and Power (1-β) was set to 0.80. There was a constant participant count in each group.

Results

The study included 167 individuals with ASA classes 1, 2, and 3 who were aged 18-65 years. Two patients were omitted because of FiO_2 changes caused by desaturation, and six patients were excluded because their surgeries took less than an hour to complete. After the removal of these individuals, the study was concluded, including the 159 participants who were initially scheduled. All patients underwent blood sampling for ALT, AST, and INR measures 1 h prior to surgery and again 1 h following the conclusion of the procedure and the patients' ward transfer. The outcomes were noted and examined.

Of the participants in the study, 62% were female. The mean age of the patients was 43.32±15.20 years. The average duration of the surgeries was measured at 122.45±59.57 minutes.

Pre- and postoperative ALT, AST, and INR values in each group are summarized in Table 1.

When the preoperative and postoperative ALT results were compared, A vs. B: p=0.605, A vs. C: p=0.262, and B vs. C: p=0.545 showed no statistically significant differences were observed between the groups. The postoperative ALT results of all three groups were statistically significantly (p<0.05) lower than their preoperative ALT measurements (Figure 1).

There were no statistically significant differences between the groups when the preoperative and postoperative AST findings were analyzed

Table 1. Pre- and postoperative ALT, AST, and INR levels according to groups

	Preoperative			Postoperative		
	ALT	AST	INR	ALT	AST	INR
Group A	25.11±20.28	29.17±36.35	0.99±0.06	22.04±17.50	29.62±33.23	1.10±0.12
Group B	23.60±16.05	23.32±9.24	1.02±0.07	20.64±15.42	22.89±9.68	1.12±0.25
Group C	21.49±10.95	22.06±7.57	1.00±0.06	19.36±9.97	21.92±9.12	1.06±0.13

ALT: Alanine aminotransferase, AST: Alanine aminotransferase, INR: International normalized ratio

(A vs. B: p=0.123; A vs. C: p=0.070; B vs. C: p=0.784). There was no statistically significant difference (p=0.960) between the preoperative and postoperative AST results among all groups were taken into account (Figure 2).

There were no statistically significant differences between Groups A and Group B (p=0.295) or between Groups A and Group C (p=0.278) according to the examination of the INR values. In contrast to Group C, Group B's INR value was statistically considerably higher ($p<0.05$). Postoperative INR values were significantly higher than preoperative INR values when all groups were taken into account ($p<0.05$). Although all three groups had considerably higher postoperative INR values than preoperative values, Group C's increase was less noticeable than the other groups' (Figure 3).

No significant pathological findings were detected on preoperative and postoperative chest X-rays in any group. Examples of preoperative and postoperative chest X-rays are shown in Figure 4.

Discussion

To determine the ideal FiO_2 concentration for patients with borderline liver capacity or those in need of liver-protective medication, we examined the effects of several FiO_2 concentrations (34%, 50%, and 70%) on perioperative liver damage. Our findings showed that during the anesthetic process, there was no statistically significant difference in the AST and ALT levels among the various FiO_2 concentrations. In contrast to the other groups, higher FiO_2 concentrations were linked to more favorable INR findings. Therefore, we deduced that patients requiring liver-protective medicine or those with borderline liver function could benefit more from increased FiO_2 levels.

Chronic liver dysfunction significantly elevates perioperative risk. In Europe, 26 cases of cirrhosis occur every 100,000 people. As with all patients, patients with chronic liver disease may require surgery for a variety of reasons. Surgical patients with liver illness have worse morbidity and mortality rates than the general population; in patients with decompensated liver disease, these rates can reach 11.6%.[9-14]

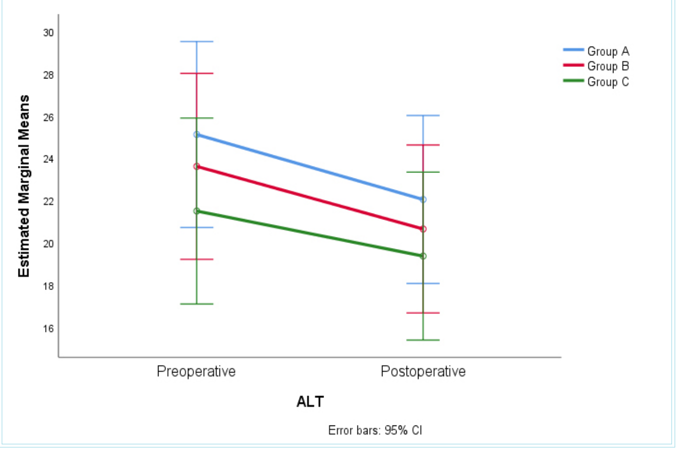

Figure 1. Pre- and postoperative ALT levels

ALT: Alanine aminotransferase, CI: Confidence interval

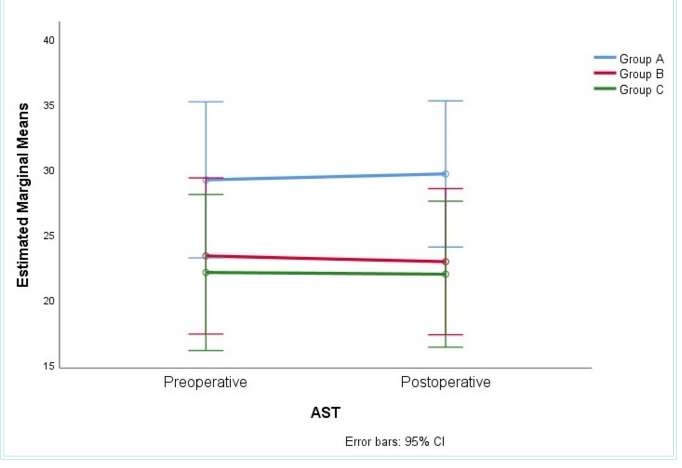

Figure 2. Pre- and postoperative AST levels

AST: Alanine aminotransferase, CI: Confidence interval

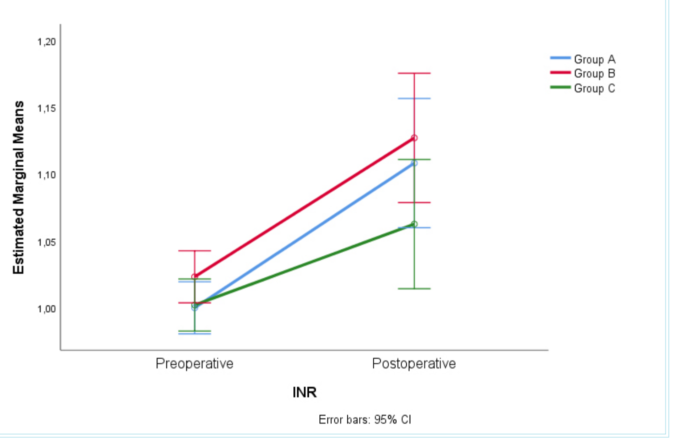

Figure 3. Pre- and postoperative INR levels

INR: International normalized ratio, CI: Confidence interval

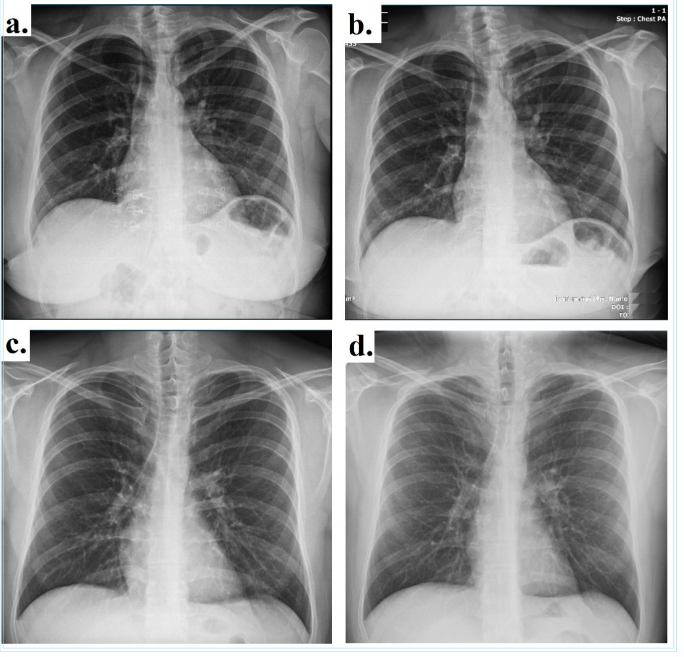

Figure 4. (**a**) Preoperative chest X-ray of a 54-year-old female patient. (**b**) Postoperative chest X-ray of the same patient. (**c**) Preoperative chest X-ray of a 27-year-old male patient. (**d**) Postoperative chest X-ray of the same patient

Worldwide, perioperative oxygen is the standard treatment for general anesthesia. The normal oxygen content in Europe is approximately 30%; however, in the US, it can range from 30% to 100%. Regarding the ideal oxygen concentration for perioperative oxygen treatment, opinions differ. According to recent research, keeping oxygen support at 80% is adequate to prevent perioperative problems.[15-18] In our study, we divided the patients into three groups and monitored them with oxygen support at FiO_2 levels of 34%, 50%, and 70%, respectively.

The literature does not contain any research on the connection between varying FiO_2 levels and liver injury. On the other hand, a study by Pedersen et al.[2] examined the development of myocardial damage in five patient groups undergoing surgery, with intraoperative FiO_2 values varying from 34% to 70%. The study revealed that myocardial damage occurred in tandem with an increase in FiO_2. Furthermore, increased FiO_2 levels were linked to a higher incidence of ischemic events, including myocardial infarction, according to a previous study. Wang et al.[6] demonstrated that ischemia and, in particular, subsequent reperfusion can cause liver damage due to reduced oxygen delivery. On the other hand, a different study conducted by Singer et al.[8] showed that hyperoxia might increase the production of reactive oxygen species, which may cause harm to organs and tissues. We found no evidence of statistically significant differences in ALT and AST levels between groups with increasing FiO_2 concentrations. Compared to the other groups, the group with 70% FiO_2 exhibited a noticeably lower INR increase. This result implies that FiO_2 levels can be advantageous for liver injury. We did not detect any evidence of liver damage related to hyperoxia because we did not exceed 70% FiO_2.

Study Limitations

The study we conducted has some limitations. Power analysis led us to include 159 patients in the study. Larger trials with more patients will yield more reliable results. Preoperatively and 24 hours after surgery, we assessed the ALT, AST, and INR levels. Long-term comparisons of the groups will be more accurate.

Conclusion

Our research concluded that, compared with the other groups, the liver benefited more from increased FiO_2 concentrations. We found that varying FiO_2 concentrations did not affect chest X-ray. Therefore, high FiO_2 concentrations may be more advantageous when liver-protective medication is needed or when liver capacity is questionable.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki (1975), as revised in 2013. The protocol was reviewed and approved by the Clinical Research Ethics Committee of Erzincan Binali Yıldırım University (approval number: 2022-08/5, approval date: 22.12.2022).

Informed Consent: Informed consent was obtained from all patients before the day of surgery.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.S., Concept: H.G.T., Design: H.G.T., Data Collection or Processing: F.S., Analysis or Interpretation: U.K., Literature Search: S.H., Writing: H.G.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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