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Original Article

The Cardiovascular Changes Induced by Inspired Oxygen Fraction in Patients Undergoing on-pump Coronary Artery Surgery

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Background: The inspiratory gas during open heart surgery with on-pump technique usually consists of 100% oxygen without any N2O because the risks of bubble embolism during these procedures. We sought to establish whether the cardiovascular effects of increased FiO2 are also present in cardiac surgery patients.
Patients and Methods: The present study was a randomized double- blind clinical trial on sixty adult patients (40-70 years) with the cardiac ejection fraction (EF) of more than 40% and ASA II or III undergoing elective on-pump coronary artery bypass. They received either a mixture of 50% O2 with 50% air (case group=30) or 100% oxygen (control group=30) throughout the anesthesia. Data were analyzed by SPSS software using t-test and Q-square as well as non parametric tests wherever appropriate.
Results: The mean values of systolic, diastolic and mean blood pressure as well as HR and CI were similar in the case and control groups ($p>0.05$) at all times of measurement. The mean PaO2 was significantly higher in the control group ($p<0.05$). The mean pH was statistically higher in the control group but not clinically noticeable. The control group required more inotropic drug support than the case group (16 vs. 8 patients respectively). Likewise, the mean venous pressure was higher in the control group compared with the case group.
Conclusions: Exposing patients during and after coronary artery surgery to hyperoxia induced significant hemodynamic changes which required more extensive studies with invasive CI measurements and larger groups.

Key words: Hyperoxia, cardiac surgery, FiO2, cardiac index

Introduction

One of the important points in open heart surgery is preventing air bubble embolism in cardiac chambers and arteries, however this process cannot be completely prevented.[1] In this connection, for most cardiac surgeries nitrous oxide (N_2O) is not used during anesthesia because it can enhance volume of air bubble which may enter cardiovascular system and eventually increases the risk of air emboli in sensitive organs like brain.[1] As mentioned

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above instead of using a combination of oxygen and nitrous oxide it is better to use 100% oxygen.

High inspired oxygen fraction is accompanied by many dangerous side effects. High inspired O_2 consumption in healthy volunteers causes lung injuries whose grading cannot be determined directly. Instead, an indirect method based on specific findings can establish oxygen dose dependent poisoning.[1] It is forbidden to use O_2 at 100% concentration ($Fio_{2=}$ %100) for more than 12 hours ,at 80% concentration for more than 24 hours and at 60% concentration for more than 36 hours. Nevertheless chronic consumption of oxygen at concentrations lower than 50% has no adverse effects on cardio-pulmonary function or gas exchange, although the reasons for such dose and time dependant toxicity is generally unclear.[2]

The most prominent symptoms of oxygen toxicity in healthy individuals are respiratory distress and substernal discomfort which is started with mild stimulations in carina and some time accompanied by attacks of cough. Upon further stimulations the pain is aggravated with more frequent coughs followed by deep inspirations. These symptoms progress to dyspnea , cough attacks and reduction of vital capacity with 100% oxygen after 12 hours.[3] In this situation recovery of mechanical function usually occurs after 12 to 24 hours and even more than 24 hours in some patients. Continued poisoning affects pulmonary compliance and blood gas.[4] Three steps are involved in pathologic staging of pulmonary lesions. These include tracheobronchitis: encountered in 12 hours or up to one week, interstitial pulmonary edema occurring within days and pulmonary fibrosis which may happen after one week.

Respiratory depression is another oxygen poisoning adverse effect which may be aggravated by drugs or disease. In a case of respiratory depression by relieving hypoxemia with increasing FIO2 hypercapnia ensues, but hypoxemia may not necessarily follow.

Absorptive atelectasis is an additional oxygen poisoning side effect.[6] The excessive consumption of oxygen by neonates causes retrolenthal fibroplasias which is an abnormal retinal vessel proliferation in premature neonates.[1] Prematurity is the most sensitive factor for this phenomenon (gestational age <7 months or neonatal body weight<1000g). This risk is particularly high when the neonate is exposed to $FIO_2 \geq$ 80 mmHg for more than 3 hours. This problem may happen up to 44th weak of life.[1] If ductus arteriosus remains patent (PDA), arterial blood sample should be obtained from right hand radial artery, because lower extremities and umbilical arterial samples have lower Pao_2 compared with the arterial blood which is passed through ophthalmic circulation.[1] Oxygen poisoning mechanism is very complex, but at a glance it is due to an interaction with cellular metabolism. The most important are oxygen free radicals which interact with surfactant systems.[6] FIO_2 100% cause's nitrogen gradient in high perfusion tissues, eventually discharge nitrogen tissues and finally cause absorptive atelectasis.[1-6] In some studies, it was shown that using 100% inspiratory oxygen in normobaric condition (normal atmospheric pressure) in conscious and healthy volunteers causes cardiovascular depression and undesired hemodynamic effects.[7,11-13] In one study, it was shown that Fio2 100% during anesthesia may cause overt hemodynamic change and depression of cardiovascular parameters.[8] Using Fio_2 95% in children with congenital

heart disease, showed reduced cardiovascular and hemodynamic parameters.[9] Except one report, undesired effects of Fio2 100% on cardiovascular indices during coronary artery bypass surgery (CABG) was not observed in any of these studies.[10] At present in heart surgery centers FIO_2 100% is used during anesthesia. In this study, we compared the effects of FIO_2 and a mixture of O2 and air (50%+50%) on cardiovascular parameters in patients undergoing CABG.

Patients and Methods

In a randomized double-blind clinical trial study , range age patients from40-70 years, cardiac output (CO) greater than 40%, ASA(American Society of Anesthesia)II ,III and body mass index (BMI) <30% were scheduled for elective CABG. With the statistical formula shown below the total volume of sample was estimated as 60 patients which were divided into two 30 patient groups (cardiac index scattering $s^2= (0/5)^2$ and the lowest valuable difference between two means in comparison was d=0.15. The place of study was hospital heart medical center. After preparation patients underwent general anesthesia with 5mg/kg thiopental, fentanyl 3µ/kg, pancuronium (0.1mg/kg) and lidocaine (1.5mg/kg)..Maintenance of anesthesia performed by isoflourane 1-1.5% and during pump with midazolam and fentanyl infusion. Patients randomized into two groups of case and control. In case group during anesthesia a combination of 50% oxygen and 50% air was used during surgery. In control group, we used only oxygen at 100% concentration. In the stage of prepump, after pump, before entering recovery room and 2 hours after surgery systolic diastolic and mean arterial pleasure HR, central vanes pressure (CVP), arterial oxygen pressure (Pao2) arterial pH, arterial O_2 saturation (Sao2) and cardiac index (CI) were measured and recorded at the end of surgery. Patients were assessed for inotropic support requirements and duration of pump connection. Cardiac index measured through a non invasive cardiac output technique. In this study questionnaires were used for collection of data. Data were analyzed by version14 SPSS software, t-test and Chi- square as well as repeated measurement ANOVA. IF sample group was not normal non- parametric tests like Huynh-feldt test were used. Significance was defined as P<0.05. Data interpreted as Mean ± standard deviation (SD).

Table 1. Comparison of data between case and control groups

Data topics	Case	Control	P value
Age(year)	59 (6)	58 (7)	0.9
Height(cm)	165 (8)	168 (5)	0.85
Weight(kg)	77 (6)	75 (8)	0.18
Operation time(min)	257 (54)	254 (52)	0.24
Pump time (min)	140 (27.2)	144 (29.7)	0.4

Data are shown as mean (standard deviation)

Results

As shown in Table-1, there were no differences found between the two groups with regard to age, sex, on-pump time, operation time and body mass index and preoperative ejection fraction (EF) (P>0.5). In this study 30 patients received 100% oxygen during surgery. they were evaluated systolic, diastolic, mean arterial pressure, cardiac index, arterial blood pH, arterial oxygen saturation(Sao_2), arterial oxygen pressure (Pao2) , HR , and central venous pressure(CVP) in 4 steps consisting of pre-pump , after pump, before entering recovery room and 2 hours after recovery admission. Also the duration of pump connection and need for intropic positive drugs during

Table 2. Comparison of mean (SD) arterial PH, oxygen pressure and CVP in time interval's of measurement between case and control groups

		Case	Control	P value*
Arterial PH (mmHg)	Pre Pump	7.4 (0.05)	7.4 (0.05)	0.01
	After pump	7.4 (0.07)	7.5 (0.050	
	Before entering recovery room	7.4 (0.07)	7.4 (0.10)	
	Two hours after operation	7.29 (0.05)	7.29 (0.05)	
Central venous pressure (CVP) (mmHg)	Pre Pump	7.4 (1.9)	7.9 (2.6)	<0.001
	After pump	7.5 (1.4)	8.9 (2.4)	
	Before entering recovery room	7.6 (1.7)	9.9 (2.6)	
	Two hours after operation	7.7 (1.9)	8.9 (2.6)	
Arterial oxygen pressure	Pre Pump	194.1 (26.8)	285.6 (50.7)	<0.001
	After pump	180.1 (27.1)	406.7 (51.6)	
	Before entering recovery room	174.1 (27.4)	286.6 (50.7)	
	Two hours after operation	148.2 (42.90	144.4 (41.9)	

* Non parametric test of Huynh feldt

operation in this group was compared with the other 30 patients who received a combinations of 50% oxygen and 50% air during operation. There was no significant relationship (P>0.05) between case and control groups for systolic and diastolic blood pressure, cardiac Index , HR , and Sao2 mean values. However there were significant differences (P<0.05) in regard to arterial pH, Pao2 and need for positive inotropic drugs and CVP correlation (Tables 2).

Discussion

This study was performed to show the effects of FIO2 fraction on hemodynamic and respiratory parameters of patients undergoing CABG. In mean arterial systolic blood pressure measurements which performed in 4 steps in case and control groups as mentioned above, there was no significant difference between two groups thus it was concluded that oxygen inspiratory fraction(FIO2) during CABG had no effects on systolic blood pressure. Stephan D, and colleagues study on 29 conscious volunteers after 1 hour of using 100% O2 there was no significant change in blood pressure without accurately mentioning the systolic blood pressure.[7] Their study was performed on young healthy conscious volunteers but the conclusion was similar to our study. There was also no significant difference found between diastolic blood pressure mean value measurements between case and control groups. On the other hand, inspired oxygen fraction had no effect on diastolic blood pressure (DBP) mean values during CABG.[7] There was no significant difference between these two groups in regard to mean arterial blood pressure. It was concluded that inspiratory O2 percentage had no effect on mean arterial blood pressure in a study carried out by Anderson and colleagues on ASA II,I patients. Pre-anesthetic O2 fraction of 100% caused no change in mean arterial blood pressure. Other data included mean heart rate which was performed as above in 4 steps and compared between two groups of case and control. After analyzing these data and regarding P=0.32, there was no significant difference between case and control groups for heart rate. Thus inspiratory oxygen fraction had no effect on heart rate during CABG.

Stephan. D and colleagues study heart rate measurements in healthy and conscious volunteers before and after 100% oxygen showed a significant reduction in these volunteers after oxygen delivery.[7] They did not state that their volunteers were healthy and conscious and time duration of oxygen consumption was one hour. In addition, the heart rate changes were compared with the same group. Warning and colleagues study on healthy volunteer's administration of 100% oxygen due to reduction heart rate.[11] Anderson and colleagues study on ASA I,II patients ,pre-anesthetic increase in inspiratory O2 fraction to 100% caused reduction heart rate and finally returning of fraction oxygen to base during anesthesia which caused increase heart rate.[8] Their study 100% oxygen had not used during anesthesia and inspired oxygen fraction was reduced from 1 to 0.3. On the other hand, our patients were ASAII and III and their heart rate was companied with their own primary heart rate These accounted for the difference between our results with the previous study. Additionally in this study central venous pressure was measured in 4 steps in two groups of case and control.

After comparison, the difference between two groups regarding to P=0.00 was not significant. This finding suggests that in patients undergoing CABG increasing inspired oxygen fraction elevated the central venous pressure. In none of the previous studies the effect of inspired oxygen fraction on CVP had been studied. Mechanism of increase in CVP in control group may be due to inotropic negative effects and in some degree decrease in cardiac output. Also in our study, mean arterial O2 saturation (SAO2) was measured compared in 4 steps of pre- pump, after pump , before entering recovery room and 2 hours after surgery in case and control groups. After comparison, considering P=0.4 ,there was no significant difference in case and control groups. On the other hand inspired O2 fractions had no effect on mean arterial O2 saturation (SAO2) during CABG. Furthermore, in our study, arterial pH was measured in 4 steps in two groups of case and control and the corresponding difference was significant. (P=0.01). On the other hand, an increase in FIO2, raised pH in patients during CABG, but this difference was not clinically prevalent. The mechanism of this decrease in arterial pH in case group which received 50% oxygen is mild hypoxia in tissues and subsequent mild acidosis in tissues and arterioles. In our study mean arterial oxygen was measured in case and control groups in 4 steps and the difference was significant. (P<0.001). On the other hand increase in FIO2 increased arterial O2 pressure in patients undergoing CABG. This parameter was not measured in previous studies. The prevalence of positive intoropic drugs used at the time of pump separation were measured and difference between case and control groups were significant (P=0.03). Patients receiving FIO2 100% during CABG had more isotropic positive requirements than the group receiving 50% oxygen during CABG. Thus in regard to our study, using 100% oxygen had negative isotropic effects on the heart and reduced cardiac index(CI) ,although the reduction in CI was not significant. This parameter was not measured in previous studies. Warning study, treating healthy volunteers with 100% oxygen caused CI reduction (P<0.05).[11] Harten and colleagues study giving100% oxygen to patients immediately after CABG caused CI reduction up to 10.6%.[10] It is worth mentioning that these patients had not received 100% O2 during CABG. Anderson study performed

on ASA I and II patients, increasing Fio2 up to 100% before surgery reduced CI which returned to its basal oxygen fraction value during increased CI.[8] However, our study was carried out on ASA II and III patients without any significant difference between case and control groups (P=0.3). In addition Anderson's study did not include 100% oxygen during anesthesia and their patients had no cardiovascular disease.

Conclusions: Our study measured CVP, arterial pH, arterial O2 pressure and isotropic positive requirement in patients undergoing CABG. The group which exposed to 100% oxygen (control group) had higher values compared with those receiving a combination of air and oxygen (control group). There was no significant difference in systolic blood pressure, diastolic blood pressure, HR, arterial oxygen saturation, CI and on-pump time duration between two groups. Findings of our study were different in some items from previous studies. It seems such dissimilarities arose from variations between studied groups and different times of oxygen exposure and parameters not measured in other studies. However more extensive investigations using larger groups of patients and more accurate methods are needed to establish effects of FIO2 on hemodynamic changes.. In ongoing studies it is advised to use more invasive methods of measurements to obtain more reliable results.

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