Original article

Effect of different dosages of nitroglycerin infusion on arterial blood gas tensions in patients undergoing on- pump coronary artery bypass graft surgery

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Background: On-pump coronary artery bypass graft (CABG) surgery impairs gas exchange in the early postoperative period. The main object on this study was evaluation of changes in arterial blood gas values in patients underwent on pump CABG surgery receiving different dose of intravenous nitroglycerin (NTG). **Materials and Methods:** sixty-seven consecutive patients undergoing elective on-pump CABG randomly enrolled into three groups receiving NTG 50 μg/min (Group N1, *n* =67), 100 μg/min (Group N2, *n* = 67), and 150 μg/min (Group N3, *n* = 67). Arterial blood gas (ABG) tensions were evaluated just before induction of anesthesia, during anesthesia, at the end of warming up period, and 6 h after admission to the intensive care unit. **Results:** Pao2 and PH had the highest value during surgery in Group N1, Group N2, and Group N3. No significant difference was noted in mean values of Pao2 and PH during surgery between three groups ($P > 0.05$). There was no significant difference in HCO_3 values in different time intervals among three groups ($P > 0.05$). **Conclusion:** our results showed that infusing three different dosage of NTG (50, 100, and 150 μg/min) had no significant effect on ABG tensions in patients underwent on-pump CABG surgery.

Key words: Blood gas analysis, coronary artery bypass, nitroglycerin

INTRODUCTION

Pulmonary function deterioration is the most frequent complication of on the pump coronary artery bypass graft (CABG) surgery in early postoperative phase.[1-4] It leads to impairment of gas exchange and prolonged extubation time.[5] On the other hand, respiratory dysfunction after cardiac surgery is the major cause of morbidity and mortality and increased duration of hospitalization.[6-8]

Occurrence of postoperative pulmonary problems is believed to be multifactorial. Some factors are patient dependent such as age, obesity, smoking[9] and others are surgical factors such as pain, general anesthesia, sternotomy, pleurotomy, medication, harvesting of the internal mammary artery, cardiopulmonary bypass, and alterations in lung and chest wall mechanics.[1,4,9-12]

It is thought that cardiopulmonary bypass induces many of these abnormalities by promoting an inflammatory response, increasing pulmonary endothelial permeability, and producing parenchymal damage.[13-16] Additionally, application of nitroglycerin – a potent vasodilator – in patients with coronary artery disease, reduces PO_2 by increasing perfusion in hypoventilated areas and antagonizing hypoxic pulmonary vasoconstriction. Considering undesirable effect of CABG on the respiratory function (producing ventilation-perfusion mismatch, pulmonary shunting, pulmonary edema) and the frequent usage of nitroglycerin infusion in these patients that can decrease PaO2 by pulmonary vasodilation and missing data regarding this issue, we designed this study to assess changes in arterial blood gas indices in patients receiving three different doses of intravenous nitroglycerin during on pump CABG surgery.

MATERIAL AND METHODS

After obtaining institutional approval from Ethic Committee of our University and taking written informed consent from patients, this randomized double- blinded clinical trial was performed on 67 consecutive patients, aged between 50 and 75 years, who candidate for elective on pump CABG surgery. All enrolled patients had ejection fraction more than 40%, negative history for diabetes, renal, respiratory, and hematologic disorders. No patients had coexisting disease. If technique

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of anesthesia or surgery was changed, the patient was excluded from the study.

The study drugs were prepared with an anesthesiologist in similar syringe with similar volume. The patients had normal ABG and spirometry before surgery.

Patients were assigned randomly into three groups receiving NTG 50 μg/min (Group N1, *n* =67), NTG 100 μg/min (Group N2, *n* = 67), and NTG 150 μg/min (Group N3, *n* = 67).

Anesthesia was induced by midazolam (0.1 mg/kg), etomidate (0.2 mg/kg), sufentanil (1 μg/kg), and pancuronium (0.1 mg/kg) for all patients.

Blood for arterial gas analysis (PH, PaO_2, $PaCO_2$, HCO_3), hemoglobin, and hematocrit was obtained in all patients at four points: just before induction of anesthesia, during anesthesia, at the end of warming up period and 6 h after admission to the intensive care unite (ICU).

Another anesthesiologist who was not aware from the study drug preparation recorded the data.

It was calculated that sample size of 67 patients in each group would have an 80% power to detect a 24% difference in the mean partial pressure of oxygen in the blood among three groups, with Alfa=0.05. Differences among three groups mean were compared using one-way analysis of variance (ANOVA) and posthoc comparisons at various points in time by using Bonferroni's type I error rate correction for multiple tests of significance. Categorical variables were analyzed by Pearson chi-square test and by Fisher's exact test when the anticipated number was less than 5. P less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 16.0 for Windows statistical package.

RESULTS

In our clinical trial, 67 patients were evaluated (mean age: 60.2 ± 10.29). Forty-one patients (61.2%) were male and 26 (38.8%) were female. All patients underwent on pump CABG surgery and the internal mammary artery was used for all. The flow diagram of randomized patients is shown in [Figure 1].

The mean duration of surgery was 3.4 ± 0.8 h. As mentioned in inclusion criteria, all patients had ejection fraction more than 40% and had no coexisting disease.

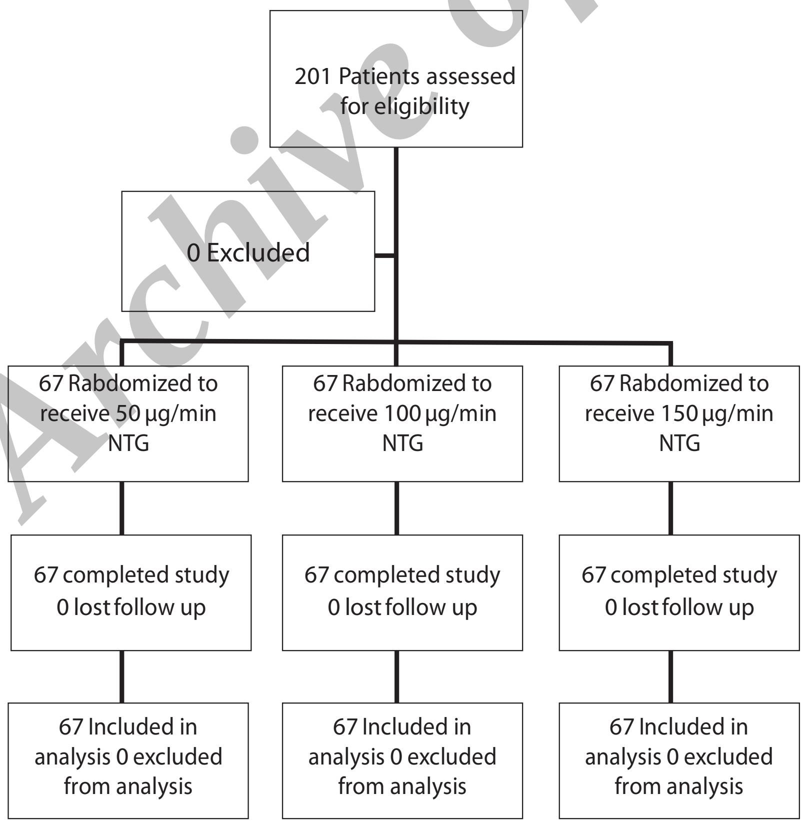

Figure 1: Flow diagram of randomized patients. NTG = nitroglycerin

Regarding to our results, Po_2 and PH had the highest value during surgery and in preoperative phase in all three groups, respectively. On the other hand, HCO_3 demonstrated subtle changes during all phases with no significant changes among three groups. Results are demonstrated [Figures 1–6].

DISCUSSION

Patients undergoing elective on-pump CABG enrolled in this study. Arterial blood gas status was evaluated in four different points in order to assess influence of different doses of intravenous nitroglycerin.

Patients' hemoglobin decreased during operation and the mean hemoglobin was lowest during operation (Hb: 7.09 ± 0.09 mg/dL) and hemoglobin changes were statistically significant during different phases of study with no significant difference among different groups. Furthermore, the highest hematocrit was detected in preoperative phase and its changes were statistically significant during different phases of study but not significant among different groups. It seems that blood loss during surgery is responsible for this phenomenon.

On the other hand, PO_2 was maximum during operation and decreased during warming up period and ICU admission but did not reached lower levels than first values.

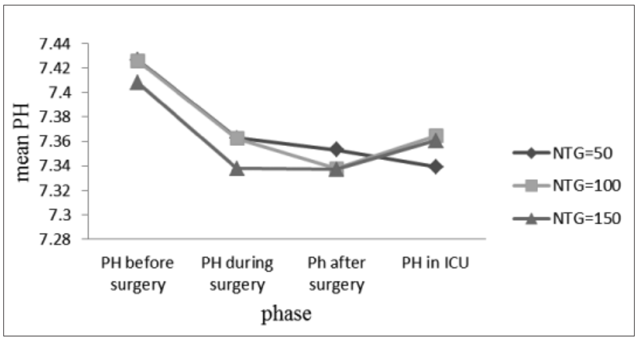

Figure 1: PH During different phases with different doses of intravenous nitroglycerin, NTG = nitroglycerin; ICU = intensive care unit; The unit of NTG dosage is microgram; pH = arterial pH

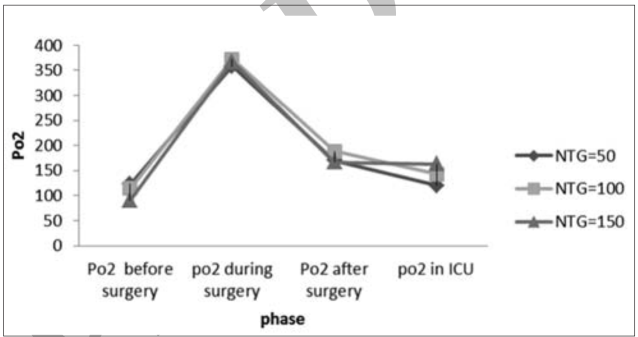

Figure 2: Po2 in different phases regarding different doses of NTG, NTG = nitroglycerin; ICU = intensive care unit; The unit of NTG dosage is microgram; Po2 = arterial Po2

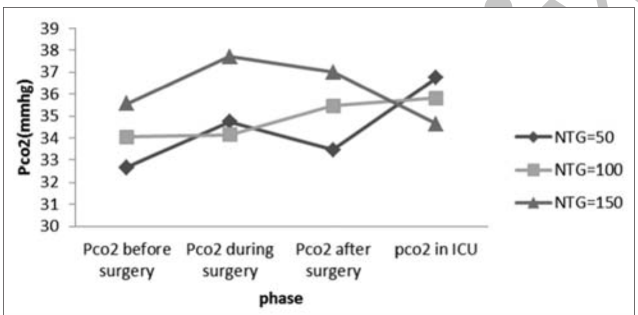

Figure 3: PCO2 during different phases with different doses of intravenous nitroglycerin, NTG = nitroglycerin; ICU = intensive care unit; The unit of NTG dosage is microgram; Pco2 = arterial Pco2

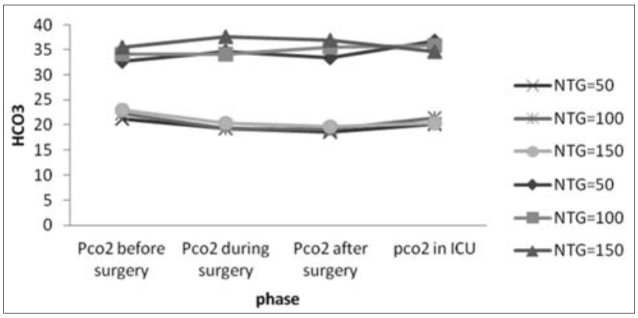

Figure 4: HCO3 during different phases with different doses of intravenous nitroglycerin, NTG = nitroglycerin; ICU = intensive care unit; The unit of NTG dosage is microgram; HCO3 = arterial HCO

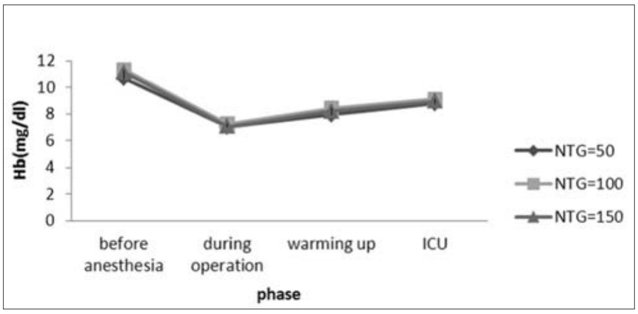

Figure 5: Hemoglubin (Hb) during different phases with different doses of intravenous nitroglycerin, NTG = nitroglycerin; ICU = intensive care unit; The unit of NTG dosage is microgram

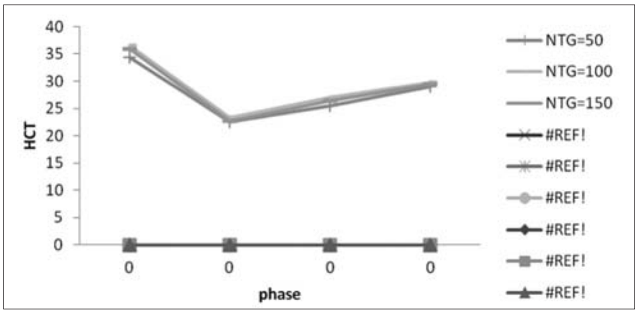

Figure 6: Hematocrit during different phases with different doses of intravenous nitroglycerin, NTG = nitroglycerin; ICU = intensive care unit; The unit of NTG dosage is microgram

Additionally, the mean arterial PO_2 was more than 90 mmHg in all groups, during all phases and no significant difference was found. It seems that hypoxemia did not take place during operation and early postoperative phase (first 6 h).

Considering our results, it seems that no prominent changes in ABG occur during the first few hour – 6 h in our study – after CABG, while previous studies, reported reduction in arterial PO_2 common following cardiac surgeries that persists for few weeks after surgery and is lowest on second day after operation then improves gradually.[17-23]

Masoumi *et al.*[24] in a clinical trial showed that applying different doses of intravenous NTG did not exert a significant influence on cardiac instability and the need for use of inotrope drugs. Their conclusion can be one of causes of our finding.

Singh and colleagues[19] showed that after CABC surgery, there is a marked decrease in Pa02. The decrease in Pa02 occurs usually on the second postoperative day and improves subsequently but remains below preoperative values on the eighth day postoperatively.

The decrease in PaO2 can be due to decrease in hematocrit and increased permeability pulmonary edema that noted in the postoperative period.[19]

Our study has two limitation: firstly, lack of data about the alveolar arterial gradient – an important factor for evaluating the postoperative respiratory function – may contribute to our results while in similar studies it is considered as a mainstay for determination of patient's ventilation system.

Secondly, 6 h is a short duration for evaluating patients for changes in ABG and hypoxemia so more studies is recommended with longer follow up time and more accurate measurements.

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