Different pH Strategies Effect Plasma Renin Activity During Cardiopulmonary Bypass

AÇIK KALP AMELİYATLARINDA UYGULANAN PH YÖNTEMLERİNİN PLASMA RENİN AKTİVİTESİ ÜZERİNE ETKİLERİ

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Summary

The effects of different pH management strategies on plasma renin activity (PRA) and renal functions were studied in man during hypothermic cardiopulmonary bypass (CPB). 40 male patients undergoing elective coronary artery bypass surgery were studied. The patients were randomly selected into pH-stat and Alpha-stat pH management groups. At pH-stat group CO 2 was added to the gas flow to the oxygenator so that pCOj was maintained at 40mmHg, during hypothermic CPB. At Alpha-stat group only O2 was added. PRA, Creatinine clearance, fractional excretion of sodium, renal failure index, mean urine output, mean arterial pressure (MAP), central venous pressure (CVP) and left atrial pressure (LAP) were measured at six different times. The increase in PRA at pH-group was higher than Alpha-group (5.72±2,J and 4.00±J.5 hgr/ml respectively) after CPB; (4,99±l,4 and 3,68±1,8 hgr/ml) in 5th measurement; (4,98±I,3 and 3,33±I,7 hgr/ml) and in the last measurement (p=0.02, p<0.05, p-0.01, respectively). MAP was significantly higher in the pH group than those of in the Alpha group in third (68,9±8,6 and 58,6±5,1 inmHg, p=0.001) and fourth (83.2±11,7 and 73.0±4,6 inmHgp=0.01) measurements. There were no differences in the other renal functional parameters between the groups. The pH management strateg)' of hypothermic cardiopulmonary bypass doesn't effect the primary renal functions but causes significant increases in PRA and MAP.

Key **Words:** Alpha-stat, pH-stat, Cardiopulmonary bypass, Rennin

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Özet

Bu çalışmada açık kalp ameliyatı sırasında uygulanan pH yöntemlerinin plasma renin aktivitesi ve böbrek fonksiyonları üzerine etkisinin olup olmadığı araştırıldı. Koroner bypass ameliyatına alınan 40 erkek hasta çalışmaya alındı. Hastalar alfa-stat ve pH-stat yöntemleri uygulanmak üzere gelişigüzel iki gruba ayrıldı. pH-stat grubunda ameliyat süresince pC0₂ 40 mmHg'de sabit kalacak şekilde, pompaya C0₂ eklendi. Alfa-stat grubunda ise sadece O7 verildi. Plasma renin aktivitesi (PRA), kreatinin klirensi, fraksiyone Na atımı, renal yetmezlik indeksi, ortalama idrar miktarı, ortalama sistemik kan basıncı, santral venöz basınç ve sol atrium basıncı parametre olarak alındı. pH-stat grubunda PRA 'nm daha yüksek olduğu görüldü. Bu değerler dördüncü ölçümde pH-stat grubunda 5.72±2.1 ngr/ml iken alfa-stat grubunda 4.00±1.5 ngr/ml; beşinci ölçümde 4.99±1.4 ve 3.68±1.8 ngr/ml ve son ölçümde 4.98±1.3 ve 3.33±1.7 ngr/ml olarak bulundu (sırasıyla p—0.02, p<0.05 ve p=0.01). Ortalama sistemik kan basınçları pH-stat grubunda anlamlı olarak yüksekli. Basınç değerleri üçüncü ölçümde 68.9±8.6 ve 58.6±5.1 mnıHg (p=0.001); dördüncü ölçümde 83.2±11.7 ve 73.0±4.6 mm-Hg (p=0.01) olarak ölçüldü. Diğer böbrek fonksiyon parametrelerinde gruplar arasında anlamlı bir farklılık görülmedi. Açık kalp ameliyatlarında uygulanan pH-stat yöntemi böbrek fonksiyonlarını etkilememekte ancak PRA ve ortalama sistemik basıncın yüksek olmasına yol açmaktadır.

Anahtar Kelimeler: Alpha-stat, pH-stat, Cardiopulmonary bypass, Rennin

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The pH of the arterial blood increases 0.015 pH Units for every degree Celsius decrease in body temperature (1). The pH-stat strategy is achieved by the addition of CO_2 into the gas flow to the oxygenator, whereas 100% O_2 is generally satisfactory to achieve Alpha-stat.

Optimal pH management during CPB has been discussed widely. All debates has been focused on the resulting cerebral perfusion and the implications for postoperative neurological outcome (2,3). Both the pH-stat and Alpha-stat strategies have theoretic disadvantages. The pH-stat strategy may re-

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suit in loss of cerebral autoregulation. Increasing cerebral blood flow beyond metabolic requirements, the pH-stat strategy may lead to an increased potential risk for microembolisation and brain edema, also results in less cerebral flow and a shift to the left of the oxyhemoglobin dissociation curve (4). Contrary to this study, there is another opinion that the oxyhemoglobin dissociation and whole-body oxygen consumption were not significantly different between two strategies (5).

Despite improvements in CPB, anaesthesia and postoperative management, perioperative renal dysfunction still represents a significant and potentially lethal complication after cardiac operations. There is a disagreement about the renal effects of different pH management strategies. Some authors have suggested that Alpha-stat strategy improves some parameters of renal functions as opposed to pH-stat (6). Badner et al. published that differences in pH management during CPB doesn't influence renal function (7). The effect of pH management on PRA and renal functions have not been investigated extensively.

The aim of this study was to investigate PRA and the renal function at different pH management strategics during hypothermic CPB.

Methods

40 male patients undergoing elective coronary artery bypass surgery were randomly selected into pH-stat and Alpha-stat pH management groups. Criteria for exclusion from the study were diabetes mellitus, hypertension, concurrent diuretic therapy and renal function abnormalities. At the preoperative period creatinine clearance and the routine biochemical measurements were done. After induction of anaesthesia (I), at the beginning of CPB (II), when mild hypothermia (28°C) was achieved (III), after discontinuation of CPB (IV), and at the lst.(V) and 4th (VI) hours after operation was finished, simultaneous blood and urine samples were collected and pressure measurements were noted. Renal functions were assessed by measuring clearance of creatinine (CC), fractional excretion of sodium, renal failure index, plasma renin activity (PRA) and mean urine output (UO). All patients were cooled down to 28°C. At pH-Stat group $C0_2$ was added into the gas flow to the oxygenator so that $pC0_2$ was maintained at 40 mmHg and pH at 7.40. At Alpha-stat group only 100% 0_2 was given and pH of arterial blood increased to 7.50-7.55 without any intervention. Standard anaesthesia and CPB techniques were used for all patients by the same team. Electrocardiogram, radial artery blood pressure, central venous pressure and left atrial pressure were continuously monitored. After sternotomy was performed, left atrial pressure catheter was inserted directly to the left atrium percutanously. Arterial blood gas analysis was performed using AVL 995 Blood gas analyser (Switzerland), blood and urine electrolyte were measured by AVL 982 S Electrolyte analyser (Switzerland). PRA was measured by RIA method (Berthold 2111 Gama Counter, France). Fractional excretion of sodium (FENa) and renal failure index (RFI) were determined by using these formulas;

FENa= UNa/PNa-UCr/PCr X 100

RFI= UNa/UCr+PCr (U; Urine, P; Plasma Cr; Creatinine)

Statistics: Data was displayed as percents and mean±SD where appropriate. Student t-test and Fisher's Chi-square analysis were used for comparison of groups. A p value of <0.05 was considered to be statistically significant.

Results

Forty male patients undergoing elective CABG surgery were enrolled in the study. The characteristics of the patients arc listed in the Table 1. There were no statistically significant differences between the groups, with respect to patients' ages, aortic cross clamping times and duration of CPB. Clearance of creatinine, fractional excretion of natriunrand renal failure index were similar in both groups in all measurements. Mean urine output was

Table 1. The Characteristics of the Patients

	pH Group	Alpha Group	p
Age (year)	60.4J-6.1	53.3±9.6	NS
Clamping Time (min)	40±13	33±14	NS
CPB Time (min)	72±26	63±27	NS
Clearance (ml/min) (prcop)	69±7	72±6	NS
Clearance (ml/min) (postop)	72±9	74±10	NS

Clamping Time: Aortic Cross Clamping Time CPB: Cardiopulmonary Bypass
NS; Statistically Insignificant
Clcarancc(prcop); Clearance of Creatinine Measured Preopcrativcly
Clcarancc(postop); Clearance of Creatinine Measured Postoperatively

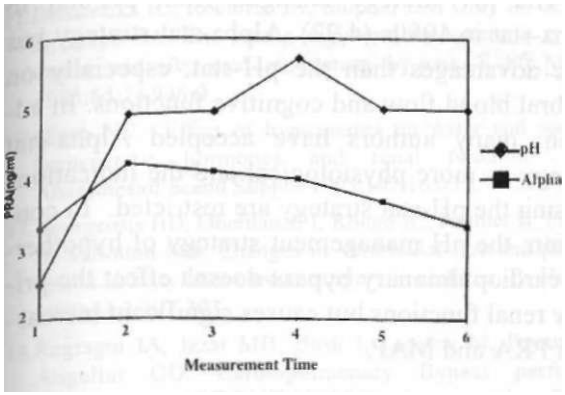

Figure 1. 3 th, 4th and 5th measurements are significant statistically. (p<0.02, p<0.05, p<0.01 respectively)

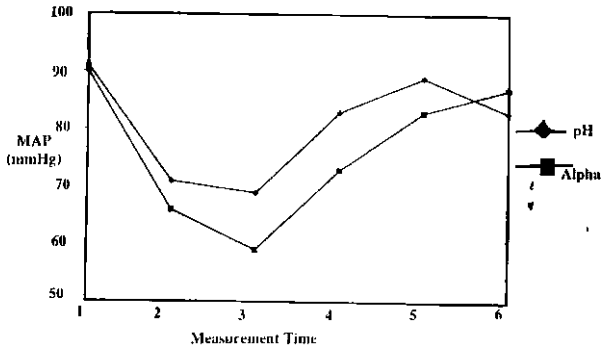

Figure 2. 3 th and 4th measurements are significant statistically. (p<0.001 p<0.01 respectively)

116±66 ml/h in the pH group and it was 161±51 ml/h in the Alpha-group. There were no statistically significant differences between groups. Figure 1 shows PRA of the groups at different times of measurements. Significant differences were found at 4th, 5th and 6th measurements. These values were (5.72±2.1 and 4.00±1.5 r|gr/ml respectively) after CPB; (4.99±1.4 and 3.68±1.8 t|gr/ml respectively) in 5th measurement; (4.98Ü.3 and 3.33±1.7 ?gr/ml respectively) in the last measurement (p=0.02, p<0.05, p=0.0T, respectively). Figure 2 shows MAP of the groups. MAP were found as 68.9±8.6 and 58.6±5.1 mmHg in the third measurements in pH and Alpha group respectively (p=0.001) and 83.2± 11.7 and 73.0±4.6 mmHg in the fourth measurements (p=0.0T).

Discussion

Although the effects of pH strategy on cerebral perfusion has been studied extensively, PRA (effects on heart and renal functions), using different pH strategies, had not been studied sufficiently and the results are controversial.

There are some studies that Alpha-stat strategy provides better renal functions compared with pH-stat (7). We noted increased urine output in the Alpha-stat group but it was statistically insignificant. This result is similar to that in the study of Michielan et al. They found no differences in fractional excretion of sodium and RFI, and believed that they couldn't claim superiority for Alpha-stat management (6).

In general, studies showed that in patients with normal preoperative renal function, the method of pH management doesn't effect perioperative renal function (8,9).

PRA increased significantly during CPB (10,11). Our findings are similar. Also, We noted significant difference between alpha-stat and pH-stat. Plasma renin is decreased in resting hypoxaemic conditions. Hypocapnic hypoxaemia in spontaneously breathing humans causes moderate increases in renal blood flow and only minor changes in GFR. In contrast, renal blood flow and GFR decreases during hypercapnic hypoxaemia (12). A positive correlation between PRA and postoperative percentage change of the left ventricular dimension was found (13). High PRA levels may responsible from hypertension, exist postoperatively. Also it may increase postoperative morbidity.

Creatinine clearance changes on CPB were reported previously, it increases during CPB (51 % at 28°C; 185% at 32°C; and 112% at 37°C) and returned to preoperative values in 24 hours postoperatively in all groups (14). We found similar results but we didn't have significant differences between groups.

The buffering capacity of the blood is effective at all temperatures and, at a constant $pC0_2$, is responsible for the linear change in blood pH with temperature. As temperature falls, therefore, a neutral pH is preserved by a rise in pH at a constant blood $pC0_2$ maintained by parallel $C0_2$ production and ventilation (15).

The constancy of pH is achieved by a marked increase in the total body content of $C0_2$ (16). Willford et al. reported that whole body and myocardial oxygen consumption rate decreased in both groups but more so in the Alpha-stat than in the pH-stat (1). According to Baraka oxygen delivery is not impaired during moderate hypothermic CPB independent of whether Alpha or pH strategy is used (5).

The reports about the effects of pH strategy on the heart functions and heamodynamics are controversial. We found significant increases in MAP and CVP at the pH-stat group. We didn't take seriously this result because a lot of various factors may effect both MAP and CVP. The effect of increased preload and afterload on the postoperative morbidity and mortality is negligible. But it may cause to subendocardial ischemia in patients who have multivessel diseases, low ejection fraction or left ventricular aneurysm. Constraining pH to 7.4 during hypothermia causes a degree of myocardial damage and limitation of cardioplegic protection which is avoidable by adjusting pH to maintain relative alkalinity as in ectoderms (17). Eton et al showed that neonatal heart function were resistant within the range of their study to changes in pH caused by changes in $C0_2$ tension during hypothermic perfusion and ischemia (15). A random study comparing the outcomes after Alpha-stat or pH-stat management during moderate hypothermic CPB in 316 patients undergoing CABG showed that cardiovascular morbidity and mortality were not affected by pH management (18). Another study showed that the only difference in hemodynamics was observed in mean pulmonary artery pressure and pulmonary artery resistance during hypothermia showing higher values in pH-stat animals (19). For the optimal myocardial function the Alpha-stat method is the method of choice.

The pH-stat method may result in loss of autoregulation in the brain. By increasing the cerebral blood flow beyond the metabolic requirements, the pH-stat method may lead to cerebral microembolisation and intracranial hypertension (20). In a patient group, Alpha-stat management is associated with a decreased incidence of cognitive dysfunction (21).

The pH strategy changed from pH-stat to Alpha-stat in 1980s (4,22). Alpha-stat strategy has more advantages than the pH-stat, especially on cerebral blood flow and cognitive functions. In addition, many authors have accepted Alpha-stat strategy as more physiological and the indications of using the pH-stat strategy are restricted. Jn conclusion, the pH management strategy of hypothermic cardiopulmonary bypass doesn't effect the primary renal functions but causes significant increases in PRA and MAP.

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