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Buffer administration during CPR promotes cerebral reperfusion after return of spontaneous circulation and mitigates post-resuscitation cerebral acidosis

Xiaoli Liu, Ala Nozari, Sten Rubertsson, Lars Wiklund *

Uppsala University Hospital, Department of Surgical Sciences/Anesthesiology and Intensive Care, SE-751 85 Uppsala, Sweden

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Abstract

To explore the effects of alkaline buffers on cerebral perfusion and cerebral acidosis during and after cardiopulmonary resuscitation (CPR), 45 anaesthetized piglets were studied. The animals were subjected to 5 min non-interventional circulatory arrest followed by 7 min closed chest CPR and received either 1 mmol/kg of sodium bicarbonate, 1 mmol/kg of tris buffer mixture, or the same volume of saline ($n = 15$ in all groups), adrenaline (epinephrine) boluses and finally external defibrillatory shocks. Systemic haemodynamic variables, cerebral cortical blood flow, arterial, mixed venous, and internal jugular bulb blood acid–base status and blood gases as well as cerebral tissue pH and PCO_2 were monitored. Cerebral tissue acidosis was recorded much earlier than arterial acidaemia. After restoration of spontaneous circulation, during and after temporary arterial hypotension, pH in internal jugular bulb blood and in cerebral tissue as well as cerebral cortical blood flow was lower after saline than in animals receiving alkaline buffer. Buffer administration during CPR promoted cerebral cortical reperfusion and mitigated subsequent post-resuscitation cerebral acidosis during lower blood pressure and flow in the reperfusion phase. The arterial alkalosis often noticed during CPR after the administration of alkaline buffers was caused by low systemic blood flow, which also results in poor outcome.

Keywords: Cardiac arrest; CPR; Acidosis; Buffer; Cerebral blood flow; Cerebral oxygenation

Resumo

Estudaram-se 45 leitões anestesiados para avaliar os efeitos de tampões alcalinos na perfusão e acidose cerebral durante e após reanimação cárdio-pulmonar (RCP). Os animais foram sujeitos a paragem cardíaca, durante 5 minutos sem intervenção, após o que se seguiram 7 minutos de compressões torácicas e 1mmol/kg de bicarbonato de sódio, 1mmol/kg de mistura tampão tris ou o mesmo volume de soro fisiológico ($n = 15$ em todos os grupos), bólus de adrenalina e finalmente desfibrilação externa. Monitorizaram-se as variáveis hemodinamicas sistémicas, o fluxo sanguíneo cerebral cortical, o estado gasométrico e ácido-base do sangue arterial, venoso e do bolbo da jugular, bem como o Ph e PCO_2 tecidular cerebral. A acidose tecidular cerebral foi registada muito mais cedo que a acidemia arterial. Depois de restabelecida a circulação espontânea, durante e após hipotensão arterial temporária, o pH no sangue do bolbo da jugular interna e no tecido cerebral, bem como o fluxo sanguíneo cortical eram mais baixos nos animais que receberam soro fisiológico do que nos que receberem tampão alcalino. A administração de tampão durante RCP promoveu a reperfusão cerebral cortical e mitigou a acidose cerebral post-reanimação subsequente durante a fase de reperfusão com baixa pressão arterial e baixo fluxo. A alcalose arterial muitas vezes notada durante a RCP após administração de tampões alcalinos foi causada por baixo fluxo sanguíneo sistémico, que também se associou a mau prognóstico.

Palavras chave: Paragem cardíaca; RCP; Acidose; Tampão; Fluxo sanguíneo cerebral; Oxigenação cerebral

* Corresponding author. Tel.: +46-18-611-48-51; fax: +46-18-55-93-57
E-mail address: lars.wiklund@anestesi.uas.lul.se (L. Wiklund).

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Resumen

Se estudiaron 45 cerditos anestesiados, para estudiar los efectos de taponadores alcalinos sobre la perfusión cerebral y la acidosis cerebral durante y despues de reanimación cardiopulmonar (RCP).Los animales fueron sometidos a un paro circulatorio no intervencional seguido de 7 minutos de RCP cerrada y recibieron ya fuera 1 mmol/kg de bicarbonato de sodio, 1 mmol/kg de mezcla tampón de tri, o el mismo volumen de solución salina ($n = 15$ en todos los grupos), recibieron bolos de adrenalina y finalmente descargas de desfibrilación externa. Se midieron variables hemodinámicas sistémicas, flujo cerebral cortical, estado ácido – base y gases en sangre arterial, venoso mezclado, y del bulbo yugular interna ; al tiempo que se monitoreaba PH y PCO_2 de tejido cerebral. La acidosis tisular cerebral se registró mucho antes que la acidemia cerebral. Después del retorno a circulación espontánea, durante y después de la hipotensión arterial transitoria, el PH en sangre del bulbo de la yugular interna y en el tejido cerebral, al igual que el flujo sanguíneo cerebral cortical fue menor en los animales con solución salina que en los animales que recibieron tampones alcalinos. La administración de tampones durante la RCP promovió la reperfusión cerebral cortical y mitigó la acidosis cerebral subsecuente postresucitación durante la fase de reperfusión con baja presión y flujo. La alcalosis arterial frecuentemente encontrada durante la RCP después de la administración de tamponesera causada por flujo sanguíneo sistémico bajo, que también lleva a malos resultados.

Palabras clave: Paro cardíaco; RCP; CPR; Acidosis; Tampón; Flujo sanguíneo cerebral; Oxigenación cerebral

1. Introduction

During cardiac arrest and cardiopulmonary resuscitation (CPR) a combined hypercarbic and metabolic acidosis rapidly develops [1]. In the ischaemic tissues, carbon dioxide is generated by the reaction of anaerobically produced H^+ with ambient, mostly intracellular, bicarbonate ions. An increase in carbon dioxide production combined with a significant decrease in its removal through the lungs [2] results in a rapid increase in extracellular and intracellular PCO_2. The anaerobic metabolism also leads to the accumulation of lactate, H^+ and K^+ ions, in particular, with an accompanying metabolic acidosis [3]. Since the disruption in acid–base homeostasis is associated with cellular and systemic dysfunction, including an increased defibrillation threshold and decreased myocardial contractility [4,5], it is believed that correction of acidosis with alkaline buffers might improve the outcome after cardiac arrest. This is also supported by the finding that severe acidosis during ischaemia leads to biochemical events that trigger cerebral tissue damage after restoration of spontaneous circulation (ROSC) [6]. Correction of severe intracellular acidosis after cardiac arrest might therefore attenuate secondary brain injury mechanisms including the compromised cellular calcium metabolism, free radical accumulation and pH-related alterations in gene expression and endonuclease activation [7,8]. The lack of convincing evidence in support of a beneficial effect, and an adverse effect of bicarbonate therapy found in some reports [9,10], have, however, caused considerable controversy regarding the use of alkaline buffers during CPR. Indeed, sodium bicarbonate has even been suggested to result in an aggravation of the intracellular acidosis by means of an increased CO_2 production resulting from its effect on the carbonic acid–bicarbonate buffering mechanism [9–11].

Tris buffer mixture (Tbm = Tribonat®), a mixture of tris buffer, acetate, sodium bicarbonate and phosphate, that was introduced in 1985, has been shown to correct the extracellular and intracellular acidosis without elevation of arterial PCO_2 [12]. In a recent clinical study, however, the authors failed to demonstrate beneficial effects on outcome after cardiac arrest [13]. The design of the latter study was discussed in an editorial in *Resuscitation* [14] where the wide and non-significant confidence interval of odds ratios (benefit of buffering: 0.43–1.41, difference between groups admitted to ICU: −0.06 to 0.06) and the high proportion of short dispatch-response intervals and the little need for buffering was highlighted. Furthermore, outcome was defined in the same study as being 'admitted to the ICU' or being 'discharged from the hospital' and thus the effects of buffer treatment on neurological outcome was not evaluated or discussed. One remaining issue therefore would be if buffering possibly could influence CPR negatively or even produce a deterioration in cerebral reperfusion.

The existing paradox of buffer treatment during CPR necessitates further exploration of the pharmacodynamic properties of these drugs as well as the pathophysiology of tissue and systemic acidosis in association with circulatory arrest. In a pig model of experimental CPR, we intended to evaluate the effects of Tbm and sodium bicarbonate (Bic) as compared to saline (Sal) on haemodynamics and cerebral blood flow and oxygenation as well as on systemic and cerebral tissue acid–base status during CPR and after ROSC. In order to achieve a fair comparison of the buffers and to compensate for the relatively higher osmolarity of the buffer solutions as compared to normal saline, the control group was to be treated with hypertonic saline (800 mosm/l). Our hypothesis was that the three treatments would cause no difference in the study variables.

2. Materials and methods

2.1. Animal preparations

Forty-five domestic piglets of both sexes with a mean body weight of 25.5±2.2 kg (mean±SD) were studied. All animals were kept fasting overnight, but had free access to water. The experimental protocol was approved by the Institutional Review Board for Animal Experimentation in Uppsala. Anaesthesia was induced with an intramuscular injection of Zoletil® (tiletamine and zolazepam, Reading, France) 6 mg/kg, Romupum® (xylazine, Bayer, Germany) 2.2 mg/kg and atropine 0.04 mg/kg, and with an intravenous injection of morphine 20 mg. Anaesthesia was maintained with an intravenous infusion of 8 mg/kg/h of pentobarbital (Apoteket, Sweden) and 0.25 mg/kg/h of pancuronium (Organon, Netherlands). Water losses were compensated with a bolus infusion of 30 ml/kg of acetated Ringer's solution during the first hour of the preparation after which a solution of glucose 25 mg/ml and electrolytes (Rehydrex med glukos® 25 mg/ml, Fresensius Kabi, Uppsala, Sweden) was infused continuously at a rate of 10 ml/kg/h to maintain a pulmonary artery wedge pressure of 7–10 mmHg. A tracheostomy was performed and the animals were mechanically ventilated (Servo ventilator 900C, Siemens-Elema, Solna, Sweden) with a 70/30 mixture of N_2O/O_2 during preparation. Minute ventilation was adjusted to maintain arterial PCO_2 within the range of 34–41 mmHg (4.5–5.5 kPa) and PEEP was set at 5 cmH_2O.

Three burr holes were made in the frontal bone. A laser-Doppler flow probe was placed (Periflux laser-Doppler flow meter Pf2b, Perimed, Stockholm, Sweden) [15–17] through one burr hole, which was positioned 1 cm from the coronal suture to the right nasal direction, for continuous measurement of cerebral cortical blood flow in direct contact with the surface of the right frontal cortex. Through another burr hole (left parietal region) a multiparameter fiberoptic sensor (Paratrend-7, Biomedical Sensors LDT, High Wyconbe, UK) [18–20] was inserted into the brain, for measurement of cerebral tissue PCO_2 and pH. Through the third hole (opposite the second hole), a Camino probe (Camino M420, Camino Laboratories, San Diego, CA) was inserted into the subarachnoid space approximately 1 cm lateral to the Paratrend probe in order to measure intracranial pressure.

A pulmonary artery catheter (Viggo Spectramed 7 French) was inserted through the right external jugular vein for pressure monitoring and sampling of mixed venous blood. A catheter was also inserted into the right atrium (7 French) for drug administration and CVP monitoring. A 20 Gauge catheter was advanced into the aortic arch via a branch of the right external carotid artery for arterial pressure monitoring and blood sampling. Another catheter was inserted cranially into the left internal jugular bulb for blood sampling. The animals in which ROSC was not achieved underwent necropsy in order to detect any pre-existing illness or organ damage.

2.2. Measurements

Haemodynamic variables, including lead II ECG recording, systemic arterial blood pressure, right atrial pressure and pulmonary artery pressure, were continuously monitored and recorded (Simens Sirecust 128, Siemens Medical Eleconics Inc., Danvers, MA). The coronary perfusion pressure (CPP) was calculated as the difference between the diastolic aortic pressure and the right atrial pressure measured simultaneously. Samples of arterial blood, pulmonary arterial blood and internal jugular bulb blood were taken for gas analysis (ABL 300, Radiometer, Copenhagen, Denmark). The cerebral perfusion pressure (Cere PP) was calculated as the difference between the mean arterial pressure reading and the highest value of either the intracranial pressure or the mean central venous pressure. The cerebral cortical blood flow was continuously recorded every 5 s and expressed as percent of baseline using a laser-Doppler flowmeter [15,16,21]. The cerebral oxygen extraction ratio was calculated as the ratio between arterial–jugular bulb oxygen content difference and arterial oxygen content $((CaO_2-CjO_2)/CaO_2)$.

2.3. Experimental protocol

Preparation was completed, nitrous oxide was discontinued. The piglets were then ventilated with 30% O_2 in air and the arterial PCO_2 was adjusted to a range between 4.5 and 5.5 kPa (34–41 mmHg) and maintained for 1 h. Baseline values were obtained before ventricular fibrillation (VF) was induced by a transthoracic alternating current (AC) shock of 40–60 V (time point 0 min). Cardiac arrest was confirmed by VF on the ECG and a loss of systolic aortic blood pressure (below 25 mmHg). Mechanical ventilation was stopped at the same time. After 5 min of VF without any resuscitative efforts, closed-chest CPR was initiated and mechanical ventilation resumed with 100% O_2. The piglets were then randomized to receive 1 mmol/kg of tris buffer mixture (Tribonat®, Fresenius Kabi, Uppsala, Sweden, 0.5 mmol/ml) (Tbm group, $n=15$); 1 mmol/kg of sodium bicarbonate (Fresenius Kabi, Uppsala, Sweden, 0.6 mmol/ml) (Bic group, $n=15$), or, for the control group, 2 ml/kg of hypertonic saline (70 mg/ml) (Sal group, $n=15$), through the right atrial catheter after 3 min of CPR. 20 μg/kg of adrenaline (epinephrine) was administered as a bolus through the right atrial catheter after 1 and 6 min of CPR, respectively. The kind of buffer administered was blinded to those present in the laboratory.

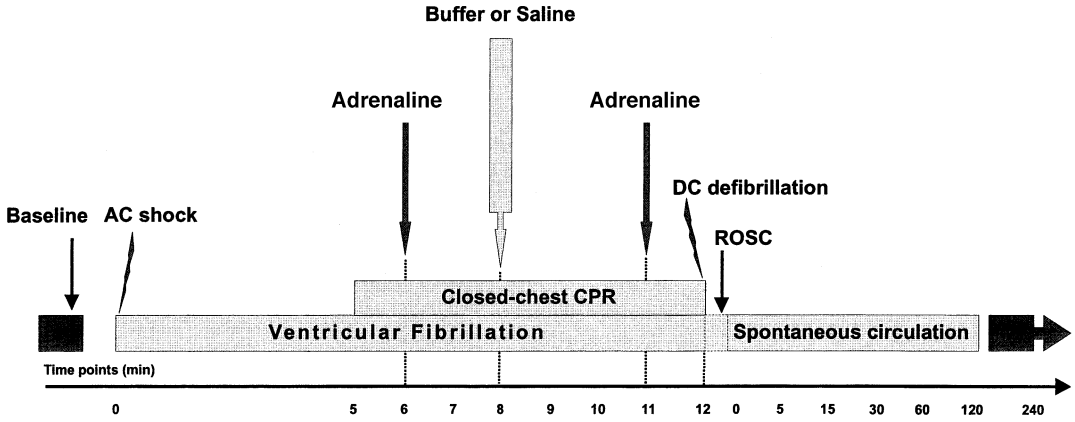

Fig. 1. Experimental protocol. At 3 min (8 min of ventricular fibrillator) from the beginning of CPR, the piglets were randomized to receive 1 mmol/kg of tris biffer mixture (Tbm); 1 mmol/kg of sodium bicarbonate (Bic) or 2 ml/kg of (Sal) hypertonic saline. After 7 min of CPR, external defibrillatory shocks were performed at an energy level of 200 J.

After 7 min of CPR, external defibrillatory shocks were administered at an energy level of 200 J (Fig. 1). If ROSC was not accomplished after three defibrillatory shocks, a third bolus injection of the adrenaline (20 μg/kg) was administered. DC shocks were applied at the same energy level during a maximum period of 5 min. ROSC was defined as a pulsatile rhythm with a systolic aortic blood pressure greater than 60 mmHg for at least five consecutive minutes. CPR was discontinued if ROSC was not achieved during this time. After 5 min of spontaneous circulation, FiO_2 was reset to 0.3. Haemodynamic values, cerebral cortical blood flow, cerebral tissue pH and PCO_2 were recorded continuously, during CPR, and 5, 10, 15, 30, 45, 60, 90, 120, 180 and 240 min after ROSC. Arterial, mixed venous and internal jugular bulb blood gases and pH were measured at baseline, after 2 and 4 min of CPR, and 5, 15, 30, 45, 60, 90, 120, 180, 240 min after ROSC.

2.4. Statistics

All data are expressed as means ± SD. For repeated measures, analysis of variance (ANOVA) was used to identify significant mean differences among the three treatment groups over time. Exploratory post hoc tests were applied to indicate the significant mean difference between the groups if ANOVA showed statistically significant differences. Logistic regression analysis was applied to analyze possible differences in survival among the groups (survival as the dependent variable, group and CPPs at 7 min as independent variables). A probability level of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Restoration of spontaneous circulation

In the Sal group ROSC was achieved in13 piglets out of 15, and in the Trib group in 12 out of 15, whereas ROSC was achieved in only five out of 15 piglets in the Bic group ($P = 0.006$). At autopsy we found no organ damage or abnormalities that could explain these differences. The difference was partly explained by the fact that the blood pressure and CPP were already somewhat lower in the Bic group before administration of the buffers ($P = 0.03$), but in addition, after due statistical consideration of this fact (logistic regression) the rate of ROSC was found to be lower ($P = 0.046$) in the Bic group. This means that the odds ratio for a non-ROSC in a pig receiving bicarbonate and having the same CPP as the other piglets in the present investigation was approximately nine, but with a wide confidence interval (1.04–78.90). In contrast to the animals achieving ROSC, there was lower arterial blood pressure and CPP and there was no significant arterial pressure increase after adrenaline administration in the animals not achieving ROSC. After administration of the buffer, arterial and pulmonary arterial pH were greater ($P = 0.0005$) (arterial 7.64 ± 0.22 vs. 7.39 ± 0.1, and pulmonary arterial 7.24 ± 0.8 vs. 7.16 ± 0.5) and pulmonary arterial PCO_2 tended to be lower ($P = 0.131$) in non-ROSC cases than in animals achieving ROSC (9.8 ± 1.2 vs. 10.4 ± 1.0 kPa).

3.2. Systemic haemodynamic variables

There were no haemodynamic differences among the three groups at baseline. During CPR mean arterial

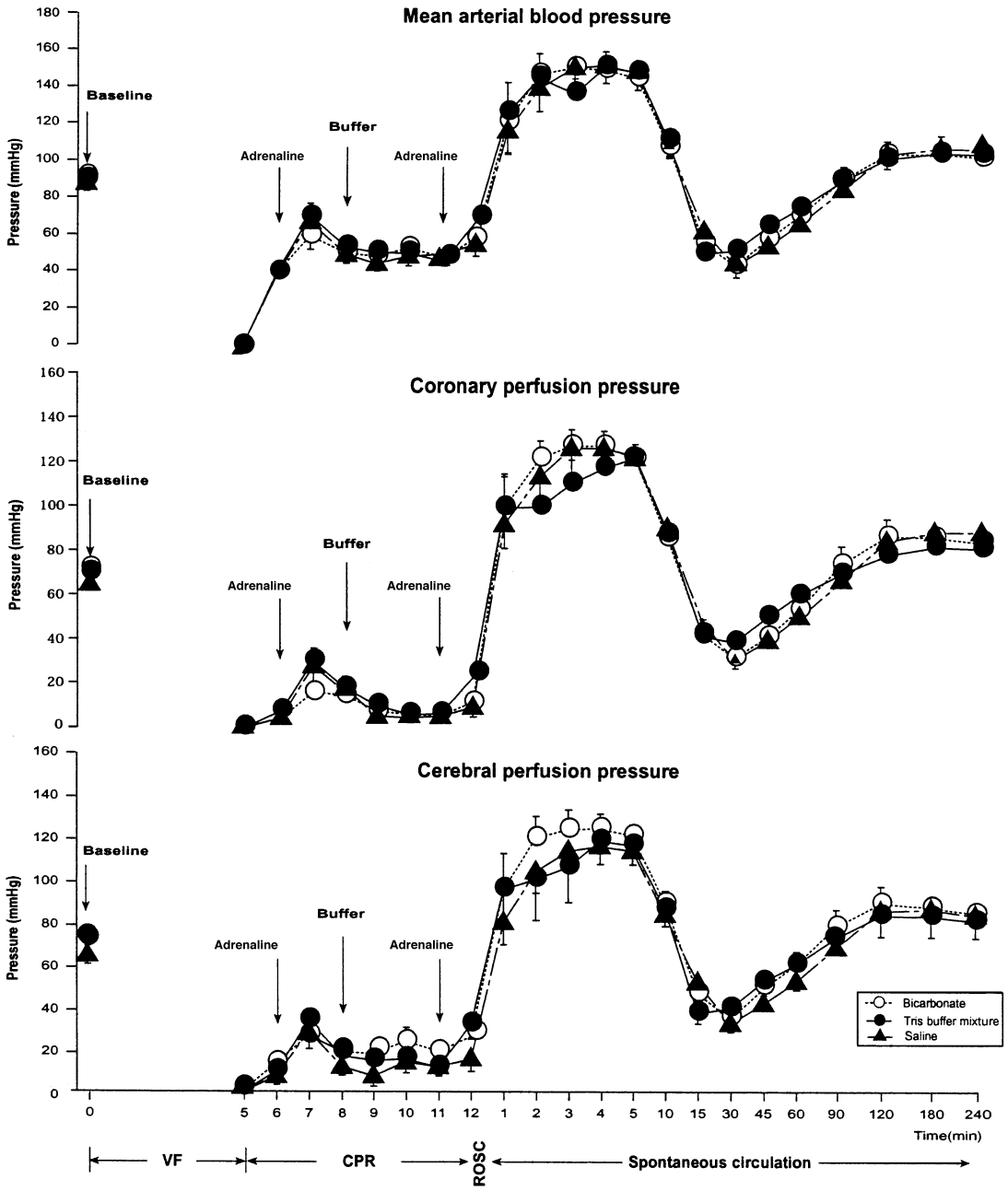

Fig. 2. Mean arterial blood pressure, coronary perfusion pressure and cerebral perfusion during CPR and after ROSC expressed as means ± SD. ○, Bic group; ●, Tbm group; ▲, Sal group.

blood pressure (MABP) was lower than baseline (50%) in all three groups without any differences among groups (Fig. 2). Administration of adrenaline increased the MABP, CPP and CerePP, with a greater effect after the first administration compared to the second. During the first 10 min after ROSC there was an overshoot of the MABP (140%) as well as the CPP (130–140%) and CerePP (130%), after which these pressures decreased again during the period 15–60 min after ROSC and returned subsequently to baseline values in all three groups without any differences among the groups. After ROSC, heart rate and cardiac output paralleled the MABP.

3.3. Arterial and pulmonary arterial pH and PCO_2

Five minutes of VF and 2 min of CPR did not cause a systemic arterial acidaemia in any of the groups. In contrast, there was a pulmonary arterial acidaemia after 5 min of circulatory arrest. Two minutes after administration of buffer there was a significant difference between the buffered and the Sal groups in arterial and

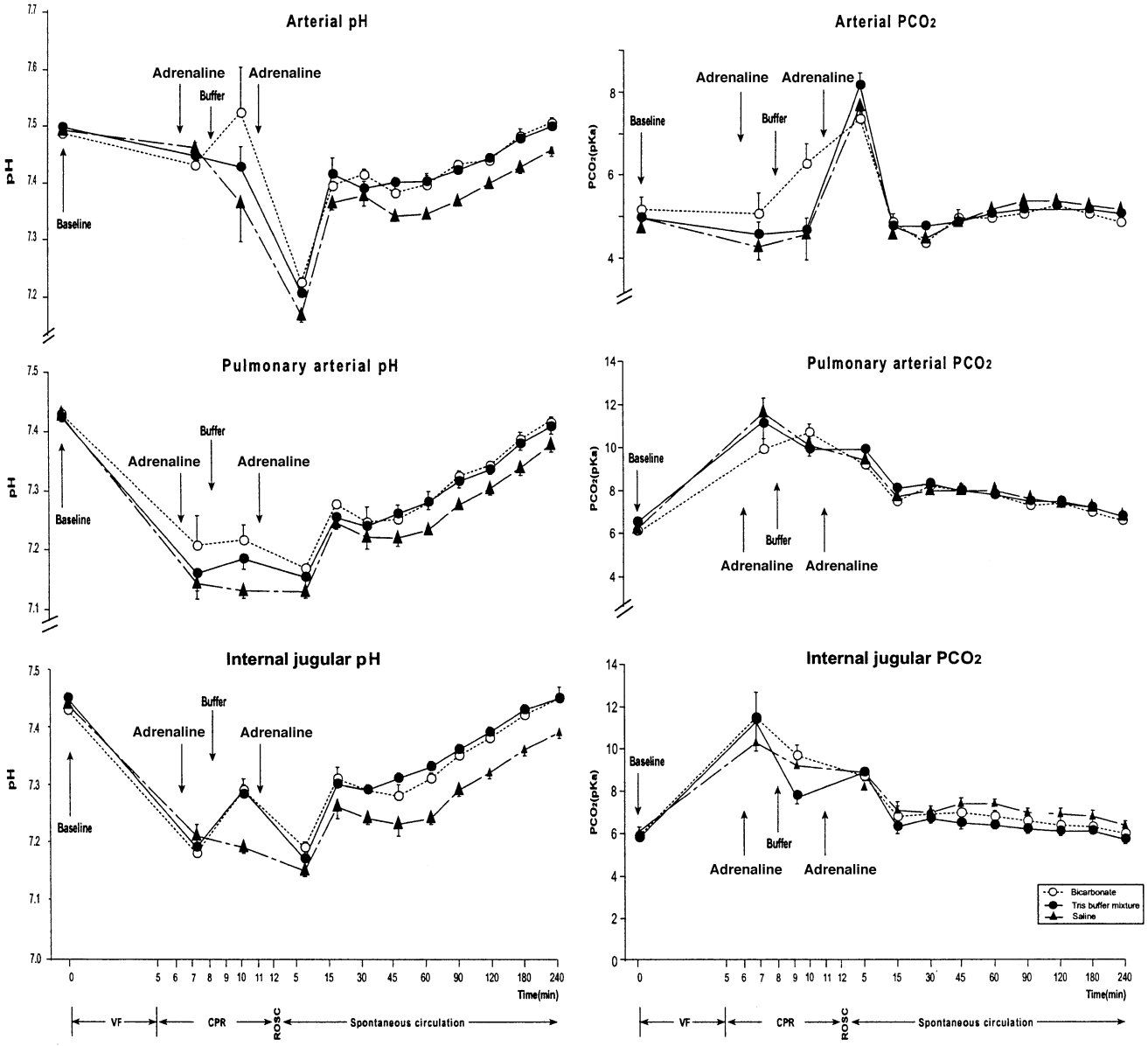

Fig. 3. Arterial, pulmonary arterial and internal jugluar vernous blood pH and PCO_2 at different time points during CPR and after ROSC. The data are expressed as means ± SD. ○, Bic group; ●, Tbm group; ▲, Sal group.

pulmonary arterial pH and PCO_2 (Fig. 3). Whereas Bic increased both arterial and pulmonary arterial pH and PCO_2, Tbm increased pulmonary pH but not arterial pH or the arterial and pulmonary arterial PCO_2. Arterial PCO_2 in the Tbm group was virtually identical with that in the Sal group. After ROSC maximum arterial and pulmonary arterial acidaemia were recorded after 5 min, significantly more so in the Sal group. Thereafter arterial and pulmonary arterial pH and PCO_2 were restored to control levels but the arterial and pulmonary arterial pH in the Sal group remained significantly lower than in the other two groups throughout the protocol.

3.4. Internal jugular bulb pH and PCO_2

Internal jugular bulb pH decreased continuously during VF and CPR except during the immediate period after buffer administration when it increased temporarily in the Tbm and Bic groups, as compared with Sal group ($P < 0.001$). Meanwhile, internal jugular bulb PCO_2 decreased in all three groups, more so in the Tbm group ($P < 0.001$, compared with the Bic and Sal groups). However, no difference was found in the pH and PCO_2 between the groups at 5 min after ROSC (Fig. 3). Thereafter internal jugular bulb pH made a slow recovery, reaching baseline values 240 min after ROSC

in the Bic and Tbm groups, with the Sal group lagging significantly behind. The internal jugular bulb PCO_2 in the three groups returned to baseline values 15 min after ROSC.

3.5. Cerebral cortical blood flow

As expected, this blood flow was zero during VF. During CPR the cerebral cortical blood flow was 20–60% of baseline values, the flow in the Tbm group being greater ($P < 0.001$) than in the other groups. Administration of adrenaline increased this blood flow approximately from 25 to 50% of baseline values in all the groups. During CPR this blood flow was somewhat greater in the Tbm group than in the other groups. During the first 5–10 min after ROSC the cerebral cortical blood flow increased to 120–160% (120% in the Sal group vs. 150–160% in the other groups, $P < 0.001$) of baseline values (Fig. 4). After this (10–30 min after ROSC, although somewhat earlier in the Sal group) a decreased cerebral cortical blood flow was recorded during the arterial hypotensive period (60–80% of baseline in all groups). 1 h after ROSC the cerebral blood flow had leveled-off at approximately 80% of baseline in all groups.

3.6. Cerebral oxygen extraction ratio

This variable increased markedly during CPR. After administration of adrenaline and buffer it tended to decrease, somewhat earlier in the Tbm group ($P = 0.09$). Five minutes after ROSC the cerebral oxygen extraction ratio (Fig. 5) reached its minimum, after which it exhibited a second peak during the arterial hypotension 15–60 min after ROSC. Thereafter the cerebral oxygen extraction ratio decreased again but remained somewhat lower in the Tbm group than in the Sal group ($P = 0.04$), with the Bic group exhibiting an intermediate ratio. In contrast to the Sal and Bic groups where this variable remained slightly above the control level ($P = 0.07$), in the Tbm group it returned to baseline values at 90 min.

3.7. Cerebral tissue pH and PCO_2

Cerebral tissue pH decreased from a baseline of 7.08 ± 0.09, 7.06 ± 0.17, 7.08 ± 0.17, to 6.56 ± 0.22, 6.54 ± 0.28, 6.66 ± 0.23, in the Tbm, Bic and Sal groups during VF ($P < 0.01$), respectively, with no differences among the groups. After administration of buffers or saline it decreased temporarily in the Sal group already before ROSC, while it was stable in the Bic and Tbm groups, and decreased markedly again in the Sal group during the arterial hypotensive period 15–60 min after ROSC, indicating a difference ($P = 0.02$) between the Bic and Tbm groups versus the Sal group 30–120 min after ROSC. Cerebral tissue PCO_2 increased markedly during CPR and during the period immediately after buffer administration (8–12 min after commencement of CPR) there was a difference ($P < 0.03$) between the Bic and Tbm groups, with the Sal group taking an intermediate position. After ROSC, cerebral tissue PCO_2

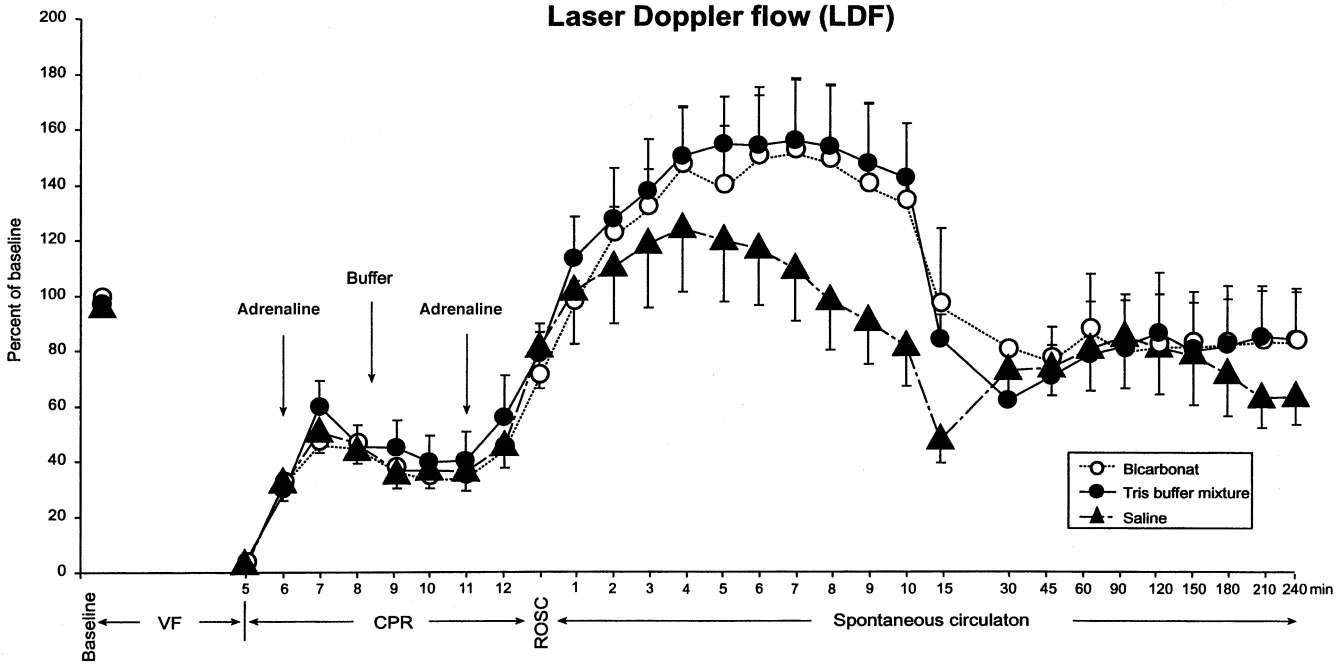

Fig. 4. Cerebral cortical blood flow during CPR and after ROSC. The values were expressed as means ± SD in percent of the baseline values. ○, Bic group; ●, Tbm group; ▲, Sal group.

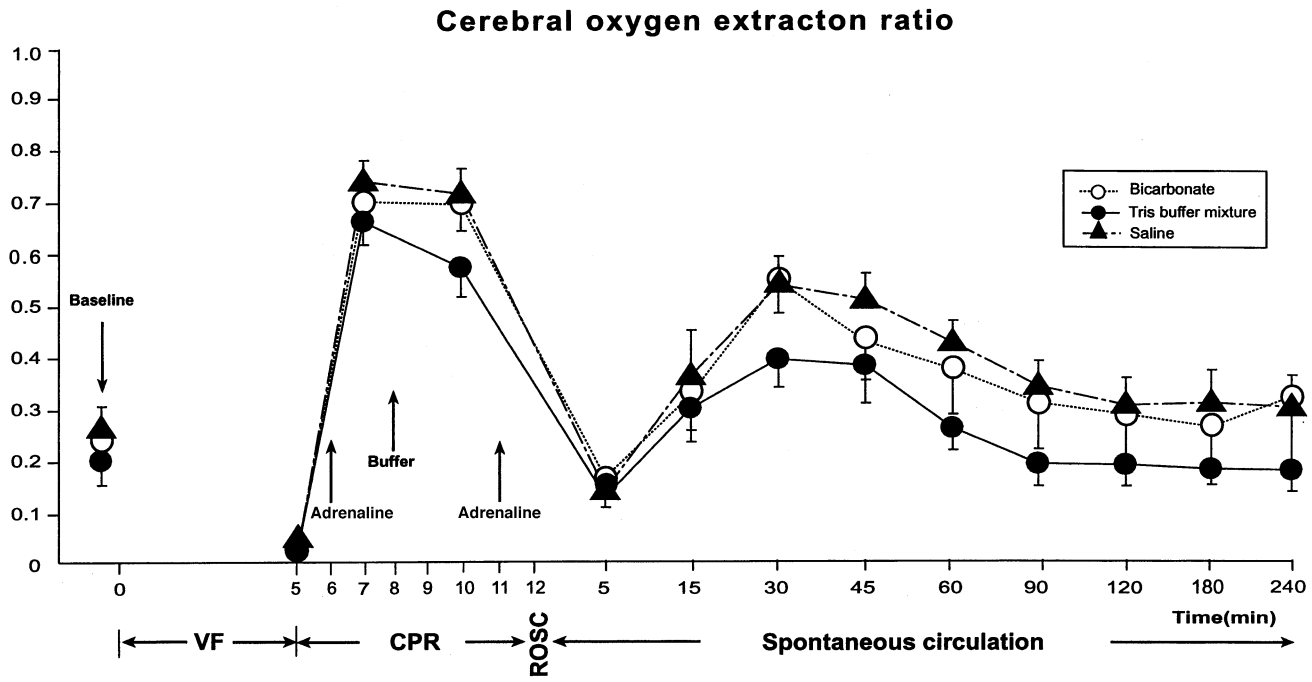

Fig. 5. Cerebral oxygen extraction ratio. The values were calculated according to the formula $((CaO_2 - CjO_2)/CaO_2)$ and expressed as means ± SD. ○, Bic group; ●, Tbm group; ▲, Sal group.

gradually decreased in the three groups, and leveled out at baseline values 15 min after ROSC (see Fig. 6).

4. Discussion

In the present study the arterial blood pressure and the coronary and cerebral perfusion pressures were significantly lower and did not increase after administration of adrenaline in the cases where ROSC was not achieved. These results, as well as the fact that arterial and mixed venous pH were lower and PCO_2 was greater in the animals achieving ROSC, confirmed previous findings of a correlation between arterial and mixed venous pH and systemic blood flow demonstrated by our group [12,22,23]. This means that systemic blood flow was lower in the non-surviving piglets and that this less satisfactory result was more common in the group receiving Bic during CPR. As low systemic blood flow means that there is a lower distribution volume for the buffers, this implies that although higher mixed venous pH and lower PCO_2 were associated with poor outcome, alkalosis was a result of lower systemic blood flow and the subsequent failure to induce ROSC and *not a cause of* the unsuccessful CPR. It is of great importance to point this out, especially as we have previously [23,24] maintained the opposite view. However, the results of the present investigation cannot explain why lower systemic blood flow, in spite of similar arterial blood pressure, was slightly more common after administration of Bic than after Tbm and Sal.

As a result of similar blood pressure and cerebral perfusion pressure in the three groups, and in spite of the finding of differences in arterial and internal jugular bulb pH and PCO_2 as well as brain tissue pH after administration of the buffers, the cerebral extraction ratio did not differ among the groups during CPR or the early phase of reperfusion after ROSC. In contrast, in conjunction with and after the arterial hypotension following 15–30 min after ROSC it became evident that the pH in internal jugular bulb blood and later in cerebral tissue lagged considerably behind resulting in (or from) a somewhat lower cerebral cortical blood flow and greater cerebral oxygen ratio in the Sal group. The background to this seems to be that the more intense cerebral reperfusion after ROSC was of a shorter duration and therefore possibly more incomplete in the Sal group which subsequently seems to have resulted in a protracted acidosis of the cerebral tissue and jugular venous blood. It is suggested that the shorter duration of the vigorous reperfusion in the Sal group might be due to a somewhat greater acidaemia and a subsequently less vigorous action of adrenaline [25,26].

By comparing the pH and PCO_2 in different compartments of the body, the distribution of a buffer can be elucidated (Fig. 7). Firstly, it must be noted that there was also a considerable rise in PCO_2 in the Sal group, most in brain tissue and least in the arterial blood. The maximum increase in cerebral tissue PCO_2 was recorded shortly after commencement of CPR, when a profound tissue acidosis was exhibited. Interestingly, the decrease in hydrogen ion concentration, as derived from the

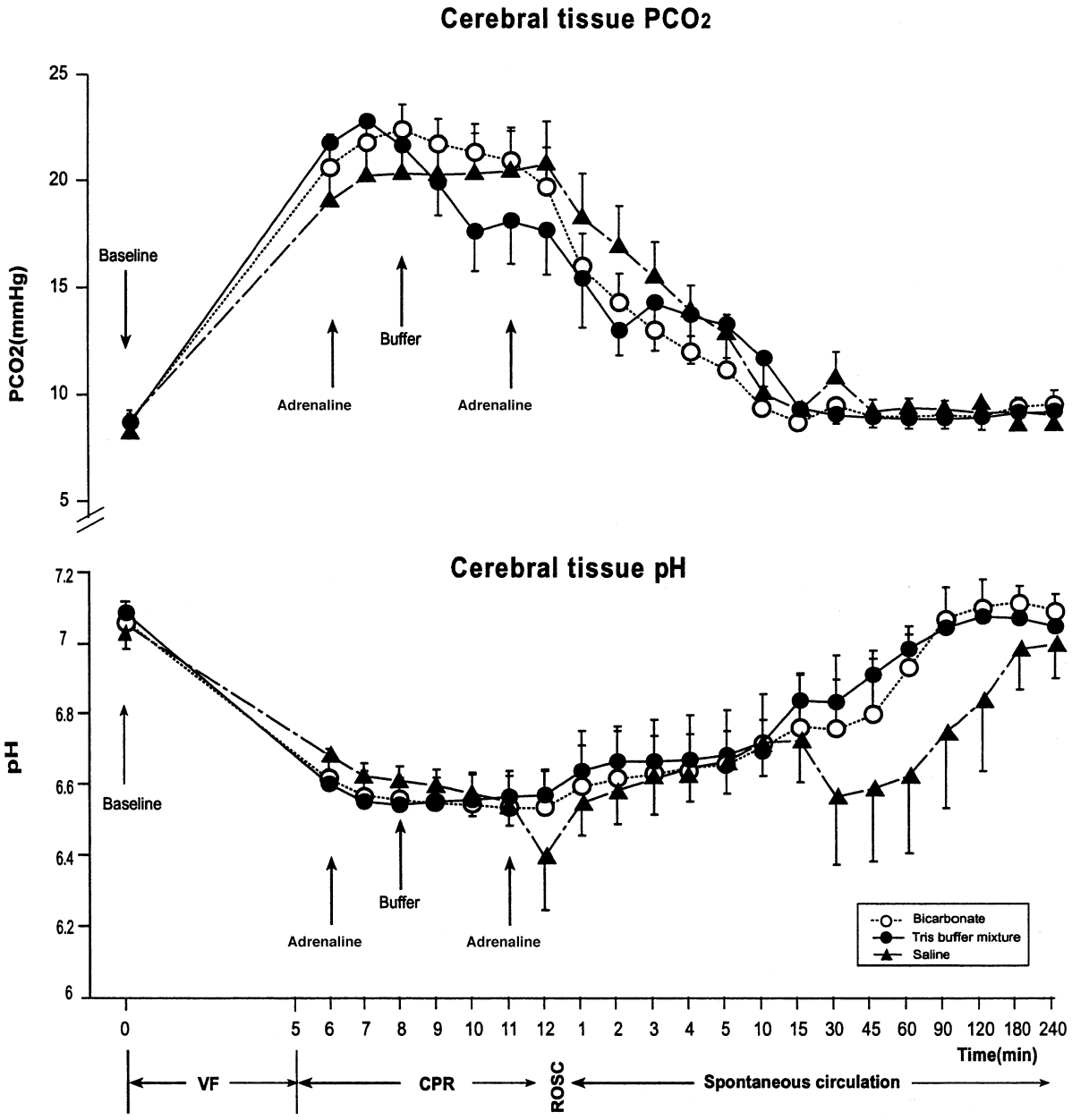

Fig. 6. Cerebral tissue pH (left) and PCO_2 (right) in the different time points during CPR and after ROSC expressed as means ± SD. ○, Bic group; ●, Tbm group; ▲, Sal group.

tissue pH, was of the same magnitude as the increase in PCO_2, indicating an association between these two variables and pointing out the importance of PCO_2 removal in the treatment of cerebral tissue acidosis. Although the effects of the buffers in arterial blood were small, the two buffer treatments seemed to exert protective effects on the cerebral tissue during the arterial hypotension 15–60 min after ROSC, when a tissue acidosis occurred only in the Sal group.

5. Conclusions

The present results indicate that the arterial alkalosis that is often seen during CPR after the administration of alkaline buffers is, at least in part, caused by low systemic blood flow, which also results in poor outcome regarding ROSC. Buffer administration during CPR promoted cerebral cortical reperfusion and mitigated the post-resuscitation cerebral acidosis observed during

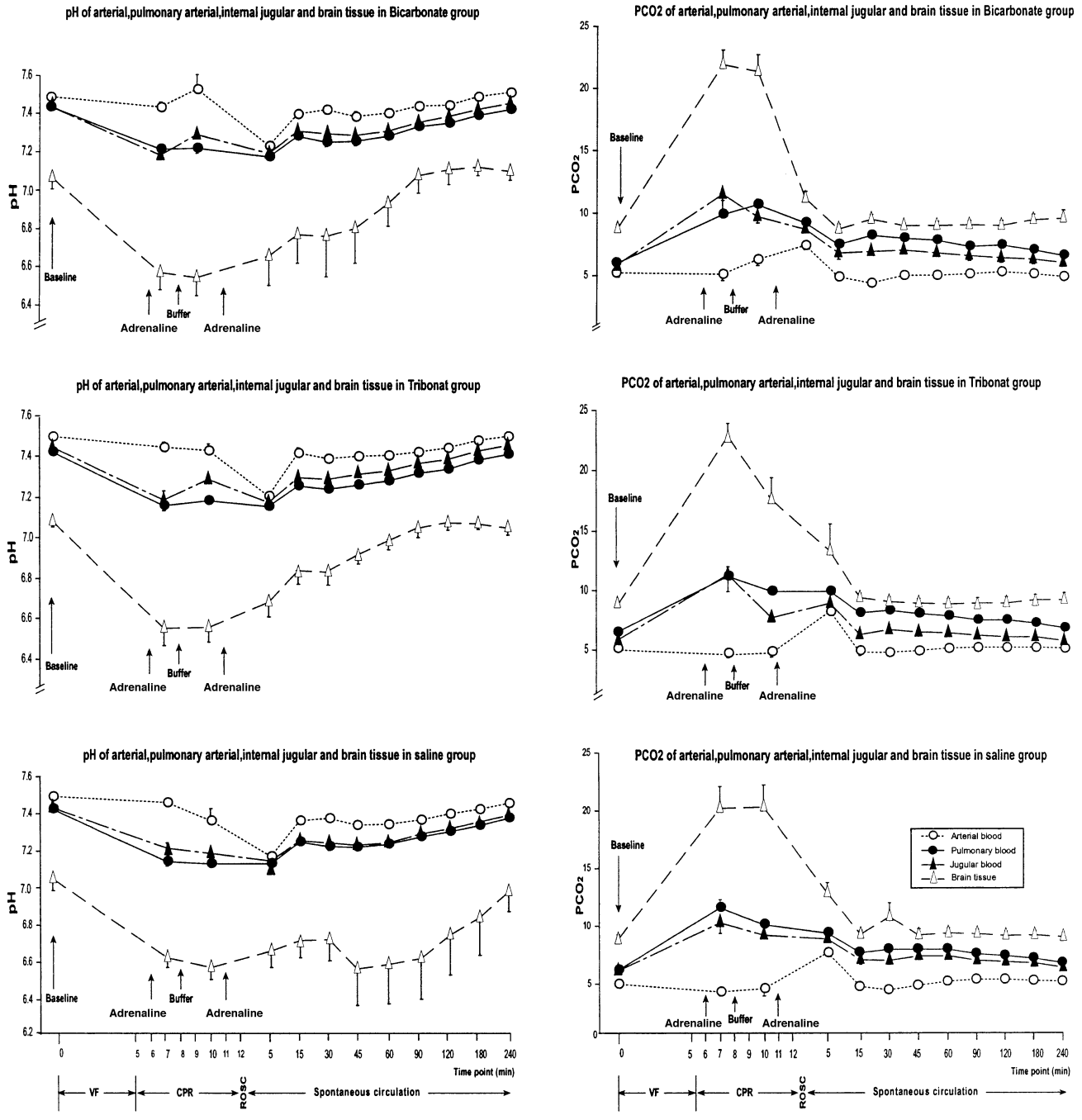

Fig. 7. The changes in PCO_2 and pH in different compartments of the body (arterial, pulmonary arterial, internal jugluar vernous blood and cerebral tissue) expressed as means $\pm$SD. ○, Arterial blood; ●, Pulmonary arterial blood; ▲, Jugluar vernous blood; △, Brain tissue.

the post-resuscitation hypoperfusion phase. Hence, it may be concluded that tris buffer mixture can be administered safely during CPR, without the risk deteriorating the resuscitability after a relatively short circulatory arrest and, in fact, even with positive effects on the post-resuscitative cerebral perfusion and tissue acidosis. Early administration of tris buffer mixture or hypertonic saline during CPR after a short cardiac arrest resulted in a better outcome regarding ROSC than after administration of bicarbonate.

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