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Hyperoxia Early After Hospital Admission in Comatose Patients with Non-Traumatic Out-of-Hospital Cardiac Arrest

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Background: The clinical effect of hyperoxia in patients with non-traumatic out-of-hospital cardiac arrest (OHCA) remains uncertain. We therefore initiated this study to find out whether there is an association between survival and hyperoxia early after return of spontaneous circulation (ROSC) in OHCA patients admitted to our hospital.

Material/Methods: All OHCA patients admitted to our hospital between 1 January 2008 and 30 June 2015 were identified by analysis of our central admission register. Data from individual patients were collected from patient health records and anonymously stored on a central database.

Results: Altogether, there were 280 OHCA patients admitted to our hospital between 1 January 2008 and 30 June 2015, including 35 patients (12.5%) with hyperoxia and 99 patients (35.4%) with normoxia. Comparison of these 2 groups showed lower pH values in OHCA patients admitted with normoxia compared to those with hyperoxia (7.10±0.18 *vs.* 7.21±0.17; p=0.001) but similar rates of initial lactate (7.92±3.87 mmol/l *vs.* 11.14±16.40 mmol/l; p=0.072).

Survival rates differed between both groups (34.4% *vs.* 54.3%; p=0.038) with better survival rates in OHCA patients with hyperoxia at hospital admission.

Conclusions: Currently, different criteria are used to define hyperoxia following OHCA, but if the negative effects of hyperoxia in OHCA patients are a cumulative effect over time, hyperoxia < 60 min after hospital admission as investigated in this study would be equivalent to a short period of hyperoxia. It may be that the positive effect of buffering metabolic acidosis early after cardiac arrest maintains the negative effects of hyperoxia in general.

MeSH Keywords: Blood Gas Analysis • Cardiopulmonary Resuscitation • Hyperoxia • Out-of-Hospital Cardiac Arrest

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Background

The current guidelines of the European Council of Resuscitation (ERC) emphasize the use of 100% oxygen during out-of-hospital cardiac arrest, but to titrate the inspired oxygen concentration after return of spontaneous circulation (ROSC) to maintain the arterial blood oxygen saturation in the range of 94–98% [1]. This recommendation aims to avoid hypoxia as well as hyperoxia during the early post-cardiac arrest phase, as several animal studies have indicated that hyperoxia early after ROSC might cause oxidative stress and harm post-ischemic neurons [2]. However, all human data have been derived from intensive care unit registries, with conflicting results on the potential impact of hyperoxia after resuscitation from cardiac arrest [3]. As such, the clinical impact of hyperoxia for non-traumatic out-of-hospital cardiac arrest (OHCA) patients remains uncertain and further studies in other patient collectives have been recommended [4,5]. We therefore initiated this study to determine whether there is an association between survival and hyperoxia early after ROSC in OHCA patients admitted to our hospital.

Material and Methods

Patient data collection

We identified all victims of non-traumatic out-of-hospital cardiac arrest who were admitted to our hospital between 1 January 2008 and 30 June 2015 by analysis of our central admission registry. Patient data were collected from the health records and anonymously stored on a central database. The study adhered to all criteria of the WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects [6].

Statistical analysis

Statistical analysis was done using SPSS 23.0 (IBM, Armonk, NY, USA) and we expressed continuous variables as the mean ± standard deviation and comparisons of categorical variables among groups were conducted using the chi-square test or Student's t-test. P-values ≤0.05 were defined as statistically significant.

Results

Patient population

Altogether, there were 280 OHCA patients admitted to our hospital between 1 January 2008 and 30 June 2015. Of these, we excluded 21 patients (7.5%) who regained consciousness before hospital admission and breathed spontaneously, 61 patients (21.8%) who were admitted under continued resuscitation efforts, 40 patients (14.3%) who had no documented arterial blood gas analysis during the first 60 min after hospital admission, and a further 24 patients (8.6%) with hypoxia (Figure 1).

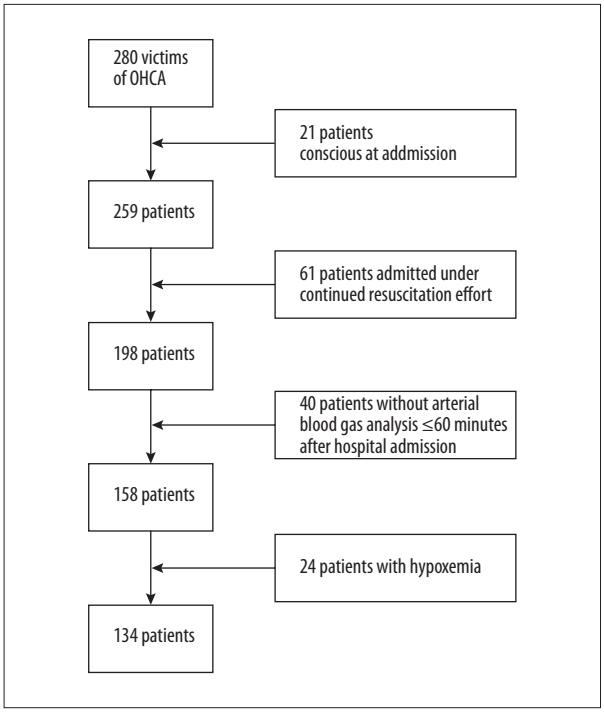

Figure 1. Of a total of 280 OHCA patients admitted to our hospital during the study period, 134 patients were included in this study.

Differences between OHCA patients with normoxia or hyperoxia at hospital admission

During the first 60 min after hospital admission, 99 patients presented with normoxia and 35 patients with hyperoxia. There were no differences between the groups with regard to sex ratio (61.6% male *vs.* 60.0% male; p=0.866), age (68.47±13.87 years *vs.* 69.8±14.05 years; p=0.629), rate of witnessed arrest (67.7% *vs.* 77.1%; p=0.479, bystander resuscitation (46.5% *vs.* 51.4%; p=0.195), or initial shockable rhythm (34.3% *vs.* 48.6%, p=0.159). Furthermore, patients with normoxia or hyperoxia showed comparable rates of endotracheal tube use (68.7% *vs.* 85.7%; p=0.051), the number of required defibrillations (1.95±3.32 shocks *vs.* 2.30±3.17 shocks; p=0.603), and the dose of epinephrine (2.39±2.77 mg *vs.* 1.89±2.22 mg; p=0.334). Upon hospital admission, measurements of systolic blood pressure (120.19±37.75 mmHg *vs.* 121.69±39.52 mmHg; p=0.843), heart rate (91.86±25.17 beats per min *vs.* 88.89±25.29 beats per min; p=0.551) auricular body temperature (35.39±1.34°C *vs.* 35.29±1.16°C; p=0.708), and APACHE II scores (37.00±4.27 *vs.* 35.30±4.41) [7] yielded comparable

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Table 1. Comparison of victims from OCHA admitted with normoxia or hyperoxia in the first blood gas analysis after hospital admission.

	Normoxia (n=99)	Hyperoxia (n=35)	p
Male gender	61 (61.6%)	21 (60.0%)	0.866
Age (years)	68.47±13.87	69.8±14.05	0.629
Witnessed arrest	67 (67.7%)	27 (77.1%)	0.479
Bystander CPR[1]	46 (46.5%)	18 (51.4%)	0.195
Initial shockable rhythm	34 (34.3%)	17 (48.6%)	0.159
Endotracheal tube	68 (68.7%)	30 (85.7%)	0.051
Number of defibrillator shocks	1.95±3.32	2.30±3.17	0.603
Preclinical dose of epinephrine (mg)	2.39±2.77	1.89±2.22	0.334
Systolic blood pressure at admission (mmHg)	120.19±37.75	121.69±39.52	0.843
Heart rate at admission (/minute)	91.86±25.17	88.89±25.29	0.551
Auricular body temperature at admission (°C)	35.39±1.34	35.29±1.16	0.708
APACHE II score [7]*	37.00±4.27	35.30±4.41	0.056
STEMI[2]	18 (18.2%)	8 (22.9%)	0.630
Coronary angiography	55 (55.6%)	19 (54.3%)	0.366
Percutaneous coronary intervention (PCI)	32 (32.3%)	13 (37.1%)	
RIVA[3]	14 (14.1%)	6 (17.1%)	
RCX[4]	5 (5.1%)	1 (2.9%)	0.431
RCA[5]	9 (9.1%)	3 (8.6%)	
Multi vessel intervention	4 (4.0%)	3 (8.6%)	
Targeted temperature management (TTM)	58 (58.6%)	19 (54.3%)	0.614
First arterial pH value	7.10±0.18	7.21±0.17	0.001
First arterial lactate (mmol/l)	7.92±3.87	11.14±16.40	0.072
Survival until hospital discharge	34 (34.3%)	19 (54.3%)	0.038

1. CPR – cardiopulmonary resuscitation; 2. STEMI – ST elevation myocardial infarction; 3. RIVA – Ramus interventricularis anterior; 4. RCX – Ramus circumflexus; 5. RCA – right coronary artery; * APACHE II scores were calculated in 88 patients with normoxia and 33 patients with hyperoxia; in 13 patients the APACHE scores could not be calculated due to missing body temperature measurement at hospital admission.

results. There were no differences in the percentage of OHCA patients who presented with ST elevation myocardial infarction (STEMI) (18.2% *vs.* 22.9%; p=0.630), patients who were treated with coronary angiography (55.6% *vs.* 54.3%; p=0.366), or who received percutaneous coronary intervention (PCI) (32.3% *vs.* 37.1%; p=0.431). Also, targeted temperature management (TTM) was used at similar rates (58.6% *vs.* 54.3%; p=0.614).

There were lower pH values in OHCA patients admitted with normoxia compared with those with hyperoxia (7.10±0.18 *vs.* 7.21±0.17; p=0.001), but there were similar rates of initial lactate (7.92±3.87 mmol/l *vs.* 11.14±16.40 mmol/l; p=0.072). Survival rates differed between the groups (34.4% *vs.* 54.3%; p=0.038), with better survival rates in OHCA patients with hyperoxia at hospital admission (Table 1).

Discussion

We performed this study to determine the clinical effect of hyperoxia in OHCA patients. In light of the ongoing discussion about the prognostic value of early hyperoxia following OHCA,

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we wanted to investigate in another patient population whether there is an association between survival and hyperoxia in OHCA patients admitted to our hospital.

Previous studies mostly reported the negative effect of hyperoxia on survival in patients following stroke, traumatic brain injury, and (partly) in those resuscitated from cardiac arrest [3,8]. We were surprised to find even better survival rates in OHCA patients admitted with hyperoxia when compared with normoxia in our patient collective. In an attempt to explain this observation, we have to refer to the fact that different criteria have been used in different studies to define hyperoxia in terms of the PaO_2 value, the time of assessment, and predetermined cutoffs; this lack of consistency has also been criticized by Damiani et al. [8]. Even though most authors define hyperoxia as PaO_2 ≥300 mmHg [9–12], the optimal time of assessment has not been defined. Kilgannon et al., for example, reported that arterial hyperoxia is independently associated with increased in-hospital mortality compared with either hypoxia or normoxia [9]. Like us, they used PaO_2 values based on the first arterial blood gas analysis in a collective of non-traumatic out-of-hospital cardiac arrest patients older than 17 years. However, they included all non-traumatic OHCA patients with arterial blood gas analysis performed within 24 h after arrival [9], whereas we only included those patients with arterial blood gas analysis within 60 min after hospital admission. Elmer et al. suggested a shorter time interval and excluded patients if no arterial blood gas was available within 4 h after ROSC [13]. However, their patient collective combined out-of-hospital cardiac arrest patients and in-hospital cardiac arrest patients, and they excluded patients who died within 24 h after return of spontaneous circulation, which, in our opinion, may be misleading, because OHCA patients who die after hospital admission do not survive the first 2 days [14]. In any case, Elmer et al. presented 2 important observations. First, they described a cumulative effect of hyperoxia over time with each hour of exposure to severe hyperoxia (PaO_2 >300 mmHg) associated with an OR of 0.84 (95%CI 0.72–0.98) for survival to discharge. Second, they showed an association between moderate or probable hyperoxia (PaO_2 101–299 mmHg) and improved organ function at 24 h [13].

Understanding the negative effects of hyperoxia in victims of OHCA as a cumulative effect over time would help to explain our findings. Hyperoxia ≤60 min after hospital admission, as investigated in this study, would be equivalent to a short period of hyperoxia consisting of the sum of minutes needed to transport a patient after ROSC to the hospital in an urban region and the time interval between hospital admission and blood gas analysis. Therefore, it may be that the positive effect of buffering metabolic acidosis early after cardiac arrest maintains the negative effects of hyperoxia in general [15].

Therefore, and with regard to previously published data that describe the impossibility of titrating oxygen in the pre-hospital period following OHCA without inducing phases of too low oxygen saturation in a high percentage of patients [16], we conclude that hyperoxia during the first minutes after ROSC might be acceptable. Nevertheless, the exact period of time in which hyperoxia might be tolerable remains unclear. We also call attention to the limitation that this was a retrospective, single-center trial.

Conclusions

A general recommendation to avoid hyperoxia following OHCA might be too imprecise, as it does not fully consider the different stages of post-cardiac arrest treatment. We highly recommend further studies to test whether post-arrest oxygen exposure has to be targeted according to different time intervals after cardiac arrest or to specific patient subpopulations.

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