



Original Article

Diagnostic and prognostic values of cerebral oxygen saturations measured by INVOS™ in patients with ischemic and hemorrhagic cerebrovascular disease

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ARTICLE INFO

Keywords:

Stroke
Cerebrovascular disorders
Diagnosis
Diagnosis emergency department

ABSTRACT

Objectives: In this study it was aimed to investigate whether measurement of potential changes of cerebral oxygenation saturations due to ischemic or hemorrhagic cerebrovascular diseases have an early diagnostic and prognostic value.

Methods: Adult patients (≥ 18 years old) having acute ischemic or hemorrhagic stroke were included in the study. Patients under 18-year-old, those with incomplete data or suspicious diagnosis were excluded.

The cerebral oxygen saturations of the patients were compared with the healthy subjects. Patients were also grouped according to their clinical outcomes; good clinical status (group 1) and poor clinical status (group 2). These groups were compared according to the patients' cerebral oxygen saturations.

Results: The mean oxygen saturation of the patients and healthy people were similar ($59.48\% \pm 10.6$ versus $58.44\% \pm 9.6$). There was no difference between patients and healthy population according to cerebral oxygen saturations. Furthermore, mean oxygen levels were also similar between the hemisphere without lesion and with lesion in the patients group ($59.8\% \pm 11.8$ versus $59.2\% \pm 10.4$).

When the patients were grouped according to their clinical status, there were 30 patients in group 1 and 15 in group 2. The cerebral oxygen saturations of the hemisphere with lesion were similar between these groups and no statistical difference was observed ($59.2\% \pm 9.3$ versus $59.1\% \pm 12.6$, $p = 0.9$). There was also no statistical difference between the groups when delta oxygen levels of the affected and unaffected hemispheres of the groups were calculated ($0.9\% \pm 6.1$ versus $0.13\% \pm 8.4$, $p = 0.7$).

Conclusion: Results of this study revealed that there was no difference in cerebral oxygen saturations measured by near-infrared cerebral oximetry system between the patients with cerebrovascular disease and healthy population. Furthermore, our results did not support that the cerebral oxygen saturations may be used for determining the prognosis of the patients with cerebrovascular disease.

1. Introduction

Despite medical improvements, cerebrovascular disease (CVD) is still common at older ages and a leading cause of death and disability worldwide.^{1,2} It also places significant burden on the healthcare system and economy.^{3,4} Of the 10–15% of all stroke patients is hemorrhagic stroke which has poorer prognosis when compared with ischemic stroke. Computed tomography (CT), magnetic resonance imaging, and digital subtraction angiography are the imaging options for the diagnosis of patients with ischemic and hemorrhagic cerebrovascular diseases.⁵

Early diagnosis and immediate treatment of the stroke patients are essential for good clinical outcomes. In acute stroke, cerebral blood flow and cerebral metabolic rate of oxygen falling below threshold generally indicate irreversible tissue damage.⁶ Detection of impaired perfusion of the affected hemisphere of the patient having CVD with an invasive method would improve patient care quality.

In this study it was aimed to investigate whether measurement of potential changes of cerebral oxygenation saturations due to ischemic or hemorrhagic cerebrovascular diseases have an early diagnostic and prognostic value.

Peer review under responsibility of The Emergency Medicine Association of Turkey.

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<https://doi.org/10.1016/j.tjem.2019.01.001>

Received 30 November 2018; Received in revised form 9 January 2019; Accepted 9 January 2019

Available online 17 January 2019

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2. Methods

This prospective cross sectional study was conducted at the emergency department of a tertiary training and research hospital and approved by the local ethics committee (approval number 16129).

2.1. Participants

During the study period, adult patients (≥ 18 years old) having acute ischemic or hemorrhagic stroke with lateralized motor impairment was included in the study. All of the included patients had triage level I or II according to the Canadian Triage and Acuity Scale (CTAS) and they were evaluated in the critical care unit of the emergency department. Patients under 18-year-old, having CTAS level III or more (evaluated in other units of ED), the ones not having lateralized motor impairment, those with incomplete data or suspicious diagnosis, and those who did not agree to participate in the study, were excluded.

The cerebral oxygen saturations of the patients were compared with the healthy subjects. The healthy subjects were also the adults over age 18 with no complaints or symptoms which could be associated with ischemic and/or hemorrhagic cerebrovascular diseases.

Patients were also grouped according to their clinical outcomes; good clinical status (group 1) and poor clinical status (group 2). The patients who had died, observed in intensive care unit and the ones who needed surgical treatment were all included in the poor clinical status group. All other patients formed the good clinical status group. The cerebral oxygen saturations were compared between the groups to investigate whether poorer clinical status would worsen cerebral oxygenation.

2.2. Management of patients and collection of data

Cerebral oxygen saturation of all patients who were admitted to the emergency department with symptoms suggesting CVD as an initial diagnosis were measured as soon as possible by a near-infrared cerebral oximetry system at the time of admission. The cerebral oxygen saturations of both right and left hemispheres were not monitored continuously but a single measurement was done. The mean oxygen saturation was then calculated to be able to compare patients and healthy subjects through their whole cerebral oxygenations. After primary examination, cranial CT scan was performed on all patients having the initial diagnosis of CVD. Finally, diffusion MRI was performed to those whose cranial CT did not reveal hemorrhage. All diagnoses were confirmed by cranial CT and/or diffusion MRI according to a radiologist's report who was blinded to the study aims. Patient demographics (age, gender), arterial blood pressure measurement results, Glasgow Coma Scale scores (GCS), final diagnosis of the patients and the data of clinical outcomes (mortality, need of surgical treatment, intensive care unit observation) were noted.

2.3. Cerebral oxygen saturation measurement

Cerebral oxygen saturations were measured by the INVOS™ system, which is a near-infrared cerebral oximetry system. Although it was suggested by the manufacturer that a cerebral oxygen level of either $< 50\%$ or a 20% decline from the baseline may be a sign of ongoing clinical deterioration, some authors accepted a 5% decline from the baseline as a significant sign of neurological deterioration.⁷ In the present study, the authors of the study accepted a difference of cerebral oxygen saturations greater than or equal to 5% between the patients and healthy subjects as clinically significant. When comparing the cerebral oxygen saturations of the healthy hemisphere and the hemisphere with lesion of the patients, 5% difference was again accepted as the cut-off for the clinical significance.

2.4. Statistical analyses

Statistical analysis was performed via SPSS v25.0 for Mac OS X (Chicago, IL, USA). The normality of the data distribution was determined by the Kolmogorov–Smirnov test. Normally distributed continuous variables were expressed as mean \pm standard deviation, and tested with Student T test. The independent variables which were not distributed normally were tested with the Mann–Whitney *U* test and expressed as medians with interquartile ranges. Categorical variables were shown with the number of cases and percentages and were evaluated using Pearson Chi-square test. Statistical significance was assumed for $p < 0.05$.

3. Results

Forty-five patients with cerebrovascular disease were included in the study. Of these patients, 26 (57.8%) had ischemic stroke, while 19 (42.2%) had hemorrhagic stroke. The mean age of the patients was 69.7 ± 16.4 in patient group and 69.5 ± 16.4 in healthy control group. There was no statistical difference between the patients and the healthy subjects according to the gender and age (*p* values respectively; 0.8 and 0.9). Characteristics of the patients and control group were given in Table 1.

The mean cerebral oxygen saturations of the patients and healthy people were similar ($59.48\% \pm 10.6$ versus $58.44\% \pm 9.6$). Considering that at least 5% or more difference were expected to be able to define the difference as clinically significant, there was no difference between patients and healthy population according to cerebral oxygen saturations. Furthermore, mean oxygen levels were also similar between the hemisphere without lesion and with lesion ($59.8\% \pm 11.8$ versus $59.2\% \pm 10.4$).

When the patients were grouped according to their clinical status, there were 30 patients in good clinical status group (group 1) and 15 in

Table 1
Characteristics of the patients and control group.

	Patients	Healthy control group	P value
	N (%)	N (%)	
Age	69.7 ± 16.4	69.5 ± 16.4	0.9
Gender			
Female	26 (57.8)	28 (59.6)	0.8
Male	19 (42.2)	19 (60.4)	
Tension arterial (mmHg)			
SBP	159.4 ± 35.4	139.4 ± 27.3	0.003
DBP	87.9 ± 27.1	76.3 ± 16	
GCS	15^{13-15}		
Final diagnosis			
Ischemic stroke	26 (57.8)		
Hemorrhagic stroke	19 (42.2)		
Subarachnoid hemorrhage	10 (22.2)		
Subdural hemorrhage	5 (11.1)		
Epidural hemorrhage	1 (2.2)		
Intraparenchymal hemorrhage	11 (24.2)		
Cerebral oxygen saturations			
sO ₂ of the hemisphere without lesion	59.8 ± 11.8		
sO ₂ of the hemisphere with lesion	59.2 ± 10.3		
Delta sO ₂ (healthy side-effected side)	0.64 ± 6.9		
Mean sO ₂ ((Right hemisphere + left hemisphere)/2)	59.48 ± 10.6	58.44 ± 9.6	0.6

*GCS: Glasgow Coma Scale score, sO₂: saturation of oxygen, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

Table 2
Characteristics and cerebral oxygen saturations of the patients according to their clinical status.

	Group 1 (Good clinic group, 30 patients) N (%)	Group 2 (Poor clinic group, 15 patients) N (%)	P value
Age	68.2 ± 17.4	72.2 ± 14.1	0.3
Blood pressure (mmHg)			
SBP	155 (133.75–170)	175 (140–203)	0.07
DBP	80 (70–91.25)	80 (70–140)	0.4
GCS	15 (14.75–15)	12 ^{5–14}	< 0.001
Cerebral oxygen saturations			
sO ₂ of the hemisphere without lesion	60.1 ± 9.2	59.2 ± 16.2	0.8
sO ₂ of the hemisphere with lesion	59.2 ± 9.3	59.1 ± 12.6	0.9
Delta sO ₂ (healthy side-effected side)	0.9 ± 6.1	0.13 ± 8.4	0.7

*GCS: Glasgow Coma Scale score, sO₂: saturation of oxygen, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

the poor clinical status group (group 2). Of the group 2 patients, one of the patients died, 9 needed intensive care unit observation and 5 needed surgical treatment. The cerebral oxygen saturations of the hemisphere with lesion were similar between these groups and no statistical difference were observed (59.2% ± 9.3 versus 59.1% ± 12.6, $p = 0.9$). There was also no statistical difference between the groups when delta oxygen levels of the affected and unaffected hemispheres of the groups were calculated (0.9% ± 6.1 versus 0.13% ± 8.4, $p = 0.7$). Characteristics and cerebral oxygen saturation results of the patients according to their clinical status were given in Table 2.

4. Discussion

Early recognition of stroke symptoms is essential for seeking timely care.⁸ Evaluation of the stroke patients requires careful attention as the diagnosis of ischemic stroke can be made accurately on the basis of the clinical presentation and either a negative cranial CT in earlier presentations.^{9–11} So we need other new materials for detection of impaired perfusion of the cerebral tissue. According to our knowledge, this study was the first study investigated whether measurement of cerebral oxygen saturations have early diagnostic value. According to cerebral oxygen saturations, our results revealed no difference neither between patients and healthy population nor the hemisphere without lesion and with lesion in the patients. Furthermore, comparing the good and poor clinical status groups, no difference was observed between the groups and this result also showed that cerebral oxygen measurement by the INVOS™ did not also have a prognostic value in patients with CVD.

Cerebral oxygen saturations were used in several clinical scenarios.^{12–17} The majority of the studies measuring the cerebral tissue oxygen were mostly based on the monitoring the neonates and adult patients needed neurocritical care. In the meta-analysis by Xie et al., the prognostic value of cerebral oxygen measurement was confirmed, while the diagnostic value was not investigated. It was reported that adding brain tissue oxygen monitoring to the standard intracranial pressure/cerebral perfusion pressure-guided therapy improved long term outcomes in patients with traumatic brain injury.¹⁸ Oxygen measurement was confirmed but the diagnostic value was not investigated.

There are studies reporting that measuring regional cerebral oxygen saturations in the course of cardiopulmonary resuscitation facilitated prognostication of return of spontaneous circulation (ROSC) as well as neurological outcome.^{19,20} Although Schnaubelt et al., in their review, confirmed that higher cerebral oxygen saturations were correlated with increased rates of ROSC, they finally concluded that the discriminatory power of cerebral oxygen saturations to prognosticate favorable neurological outcome remains unclear.²¹

There are several articles in the literature studied the cerebral oxygen monitorization either in adults or in infants but we could not find any articles investigated its diagnostic value in patients with CVD.^{22,23} We believe that the present study has a unique value from the

point of being the first study investigating this subject.

5. Limitations

The number of the patients may be the major limitations of the study, especially the ones with hemorrhagic stroke. The second limitation of the study is measuring the cerebral oxygen only with INVOS™. As we know that cerebral blood flow and oxygen distribution as altered in CVDs, it is hard to explain the reason why no difference was found between patients and healthy population according to cerebral oxygen saturations. Our sample size may be inadequate to find out a statistical difference between groups. Confirmation of the cerebral oxygen saturations either with another non-invasive infrared oximeter or any other method measuring cerebral blood flow, with a bigger sample size, the results of the study would have been much trustable and we would be able to discuss the study results.

6. Conclusion

Results of this study revealed that there was no difference in cerebral oxygen saturations measured by near-infrared cerebral oximetry system between the patients with cerebrovascular disease and healthy population. Furthermore, our results did not support that the cerebral oxygen saturations may be used for determining the prognosis of the patients with cerebrovascular disease.

Author contribution statement

Serkan Emre EROĞLU and Gökhan AKSEL conceived and designed the study; 2) Hayrullah YÖNAK and Merve Osoydan SATICI performed the patient management and collection of the data 3) Gökhan AKSEL analyzed and interpreted the data; 4) Serkan Emre EROĞLU contributed reagents, materials, analysis tools or data; 5) Serkan Emre EROĞLU and Gökhan AKSEL wrote the paper.

Conflicts of interest

The authors declare no conflict of interest.

Funding

No funding was needed for this original article.

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