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Effects of oxygen therapy on the outcome of patients with acute myocardial infarction: A randomized clinical trial

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ABSTRACT

Objective: To investigate the therapeutic effects of supplemental oxygen on patients with myocardial infarction.

Methods: This study was a randomized, double-blind clinical trial. The study population included all patients who were admitted to the emergency room of Ali-ibn-Abitaleb and Khatam-al-Anbia hospitals in Zahedan within six hours of the onset of classic symptoms of myocardial infarction. The patients (n=47) were divided into two groups: the case group (with oxygen therapy) and the control group (without oxygen therapy). The initial follow-up was evaluated after one month and the second follow-up was evaluated after three months in the target population in terms of mortality caused by acute myocardial infarction, mortality caused by any other cause, and re-hospitalization caused by acute myocardial infarction.

Results: Out of the 47 patients, 27 were male (57.4%). The average age of the patients was (60.9±8.1) years. One month after admission, 2 patients (8.7%) in the case group and 2 patients (8.3%) in the control group died due to acute myocardial infarction. A total of 7 patients (14.9%) died three months after admission. There was no significant difference between the control and case groups in terms of mortality caused by acute ischemia within one and three months. After one month, 2 patients (8.7%) in the case group and 1 patient (4.2%) in the control group died of other causes. After three months, 4 patients (8.5%) in total died for other causes. There was no significant difference between the control and case groups in terms of mortality due to other causes within one and three months. One month after admission, 5 patients (21.7%) of the case group and 4 patients (16.7%) of the control group were re-hospitalized due to acute myocardial ischemia. During the next three months, 3 patients (13.0%) of the case group and 5 patients (20.8%) of the control group were re-hospitalized. There was no significant difference between the control and case groups regarding the rate of re-hospitalization caused by acute myocardial infarction within one and three months after admission.

Conclusions: There is no significant relationship between oxygen therapy and death by acute myocardial ischemia, or any other

Significance

Oxygen therapy was regularly used in patients with acute myocardial ischemia (AMI) but new articles mentioned that patients with normal oxygen levels can increase their resistance and vasospasm of coronary arteries. In this research, we found no significant relationship between oxygen therapy and mortality rate caused by AMI and no relationship between oxygen therapy and the rate of re-hospitalization caused by AMI within one and three months after admission.

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causes. The relationship between oxygen therapy and the rate of re-hospitalization caused by acute myocardial ischemia is not found within one and three months after admission. The results show that oxygen therapy does not affect patients with acute myocardial ischemia within three months after admission.

KEYWORDS: Oxygen therapy; Myocardial infarction; Mortality; Cardiac ischemia; Hospitalization

1. Introduction

Cardiovascular disease is one of the major causes of mortality in the world[1]. Today, the mortality rate due to cardiovascular disease has decreased in most developed countries as a result of improved treatments[2]. One of the most common diseases in this category is acute myocardial infarction (AMI)[3]. Myocardial infarction is a significant complication of atherosclerosis, leading to coronary artery obstruction and interruption of blood flow to a certain heart area, followed by infarction or damage to that area. This damage can be detected immediately by the presence of increased cardiac biomarkers, changes in electrography, and changes in imaging, such as cardiac magnetic resonance imaging[4].

Oxygen therapy is a fundamental treatment method for acute coronary syndrome. When applying oxygen therapy to AMI patients, it is expected that the extra oxygen will improve the damaged or ischemic area of the heart and reduce the symptoms of ischemia, such as pain and the size of the ischemia, and ultimately reduce the mortality rate[5]. Increasing oxygen delivery to the damaged tissue of the heart using oxygen therapy is logical from the point of view of pathophysiology. This approach is acceptable only in people with reduced oxygen saturation or hypoxic. On the other hand, oxygen delivery has a paradoxical effect on the coronary arteries of people with normal oxygen levels which can increase their resistance and vasospasm of coronary arteries[6].

Oxygen therapy was regularly used in patients with AMI in the ambulance by pre-hospital emergency medical services personnel and in the emergency departments according to international treatment guidelines[7]. However, studies showed that this method might have adverse effects. The first evaluation was conducted in 2010 and suggested that more research should be done on this issue to clarify the usefulness of oxygen therapy for patients with AMI, and if there is no indication for oxygen therapy, it should not be used anymore[8]. Research had been conducted to study the effect of oxygen therapy since 2010, and several studies showed that oxygen therapy might increase ischemia[9].

In 2015, a randomized clinical trial was conducted on patients with AMI. The results showed that oxygen therapy in patients without hypoxia might increase heart failure[10]. A study conducted Sweden in 2018 investigated the effect of oxygen on myocardial infarct area size in patients with AMI who were referred to the hospital and were ready for percutaneous coronary intervention (PCI). The results showed that there was no significant difference between people who received oxygen and those who did not[11].

However, oxygen therapy is still recommended in the guidelines. Guidelines published since 2010 took a cautious approach and recommended it to patients with hypoxia. For example, the American Heart Association announced that emergency medical services personnel should perform oxygen therapy in patients with acute coronary syndrome and hypoxia with oxygen saturation below 94%[12]. Therefore, pulse oximetry should be used to detect the clinical need for additional oxygen[13].

Today, there are still some treatments based on past habits and experiences, which are not logical from the point of view of evidence-based medicine. Although there is still insufficient evidence about the advantages of oxygen therapy for all patients with ischemia, it is still used to treat patients with cardiac ischemia. Therefore, the present study aimed to investigate the effects of oxygen therapy on patients with such conditions.

2. Patients and methods

2.1. Study setting and desgin

This study was a randomized, double-blind clinical trial conducted at Ali-ibn-Abitaleb and Khatam-al-Anbia hospitals of Zahedan between March 2019 to September 2020.

2.2. Ethical approval

The ethics code IR.ZAUMS.REC.1397.430 was obtained from the ethics committee of Zahedan University of Medical Sciences and the study was registered on the Iranian registry of clinical trials with No.IRCT20200901048576N1 (https://www.irct.ir/trial/50628). Participation by all subjects was voluntary. Consent (first orally and then in writing) was obtained from all participants, and a commitment was given that their personal information would not be disclosed in anyway.

2.3. Inclusion criteria

The statistical population of the present study included the patients referred to the emergency departments of Ali-ibn-Abitaleb and Khatam-al-Anbia hospitals in Zahedan (by ambulance or by foot). The inclusion criteria were age over 30 years, having a normal oxygen concentration (normoxic) (SpO_2 ≥90%), having classic symptoms of myocardial infarction in the last six hours, having changes in the electrocardiogram (ST-segment elevation of >2 mm in lead V1-V4 or >1 mm in other leads, ST segment depression >1

mm in each lead, the presence of inverted T waves in leads V2-V6, the presence of pathological Q waves in at least two adjacent leads, and new left bundle branch block), and having an increased cardiac biomarkers (troponin) level.

2.4. Sampling and randomization

Patients entering the emergency room with chest pain who met the inclusion criteria were recruited after using a random sampling method based on a computer program for 50 participants. Random sequences were prepared online through a website, the sequences were then written on 50 cards, and the cards were placed in envelopes. Next, envelopes were allocated by a triage nurse who did not know their contents to the patients who were referred to the emergency room with chest pain, met the inclusion criteria, and consented to participate in the study. After the patient was admitted to the emergency room, the nurse opened the envelopes.

The 50 patients were divided into two groups: control (25 patients without oxygen therapy) and case (25 patients with oxygen therapy). If the patient was placed in the oxygen therapy group, oxygen therapy was administered at the rate of 6 L/min. The oxygen saturation level was recorded at the beginning and end of the treatment. During the study, oxygen was administered (outside the treatment protocol) to the patients in the control group who had hypoxia (SpO_2 <90) caused by circulatory disorders or respiratory failure, and it was reported separately.

2.5. Follow–up methods and intervals

The initial follow-up was evaluated after one month and the second follow-up was evaluated after three months in the target population in terms of mortality caused by AMI, mortality caused by any other cause, and re-hospitalization caused by AMI. All these cases were evaluated in all studied patients, patients with ST-elevation myocardial infarction who underwent PCI, and patients with confirmed infarction during one month (30 days) and three months (90 days).

2.6. Primary and secondary outcomes

The primary outcomes was evaluated mortality rate caused by AMI, mortality rate caused by any other cause, and re-hospitalization caused by AMI after one month and secondry outcomes was evaluated mortality rate caused by AMI, mortality rate caused by any other cause, and re-hospitalization caused by AMI after three month.

2.7. Statistical analysis

Based to the research by Khoshnood *et al*.[11], the sample size was set at 50, for this sample size would enable the detection of 15% points between groups with a power of more than 90% (actual power 96%) at a 5% risk of an α error.

SPSS version 25 was used to analyze the data. The data were analyzed by descriptive statistics (frequency, frequency percentage, mean, and standard deviation). Inferential statistics (chi-square and independent *t*-test) were used to determine significance. The oxygen therapy results in patients with myocardial infarction were compared using the chi-square test. The average length of hospitalization in the two groups was compared using an independent *t*-test. *P*-value <0.05 was considered statistically significant.

3. Results

The present study aimed to evaluate the effect of oxygen on patients with AMI. Out of the 50 patients, 2 patients from the case group and 1 patient from the control group were excluded from the study due to the critical conditions of the illness. Finally, 47 patients were evaluated (Figure 1). Out of the 47 patients, 27 were male (57.4%). The average age of the patients was (60.9±8.1) years. Table 1 shows the demographic and baseline characteristics of the study patients.

The case and control groups both had 2 patients who died due to AMI after one month of the start of the study and 4 and 3 patients died for the same cause in the case and control groups after three months, respectively. There was no statistically significant difference between the two groups in terms of mortality caused by AMI one month (*P*=0.965) and three months after admission (*P*=0.638) (Table 2).

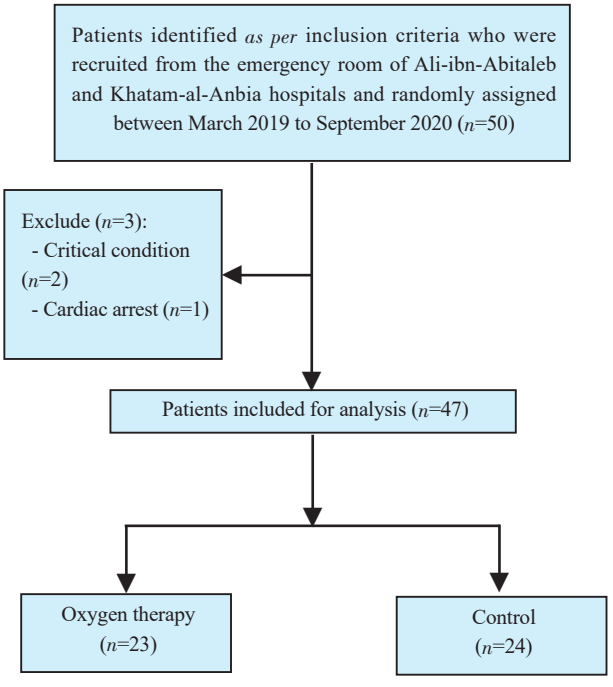

Figure 1. The study flowchart.

Table 1. Demographic and baseline characteristics of the study patients.

Variables	Total (*n*=47)	Case (*n*=23)	Control (*n*=24)	t/χ^2	*P*
BMI, kg/m^2, mean±SD	26.0±3.0	25.0±4.0	26.0±2.0	0.847[t]	0.402
Sex, *n*, %					
Male	26 (55.3%)	14 (60.9%)	12 (50.0%)	0.561[C]	0.454
Female	21 (44.7%)	9 (39.1%)	12 (50.0%)	-	-
Hypertension, *n*, %					
Yes	38 (80.9%)	18 (78.3%)	20 (83.3%)	0.195[C]	0.659
No	9 (19.1%)	5 (21.7%)	4 (16.7%)	-	-
Diabetes mellitus, *n*, %					
Yes	9 (19.1%)	5 (21.7%)	4 (16.7%)	0.195[C]	0.659
No	38 (80.9%)	18 (87.3%)	20 (83.3%)	-	-
Dyslipidemia, *n*, %					
Yes	27 (57.4%)	12 (52.2%)	15 (62.5%)	0.512[C]	0.474
No	20 (42.6%)	11 (47.8%)	9 (37.5%)	-	-
Stroke, *n*, %					
Yes	3 (6.4%)	1 (4.3%)	2 (8.3%)	0.312[C]	0.576
No	44 (93.6%)	22 (95.7%)	22 (91.7%)	-	-
Smoking, *n*, %					
Yes	12 (25.5%)	7 (30.4%)	5 (20.8%)	0.569[C]	0.450
No	35 (74.5%)	16 (69.6%)	19 (79.2%)	-	-

[t] *t*-test; [C] chi-square test; Smoking: smoking at least one cigarette per day.

Table 2. Mortality due to acute myocardial infarction or other causes.

Mortality	Total (*n*=47)	Case (*n*=23)	Control (*n*=24)	χ^2	*P*
Due to acute myocardial infarction					
One month after admission	4 (8.5%)	2 (8.7%)	2 (8.3%)	0.002	0.965
Three months after admission	7 (14.9%)	4 (17.4%)	3 (12.5%)	0.222	0.638
Due to other causes					
One month after admission	3 (6.4%)	2 (8.7%)	1 (4.2%)	0.403	0.525
Three months after admission	4 (8.5%)	2 (8.7%)	2 (8.3%)	0.002	0.965

Table 3. Re-hospitalization rate at one month and three months after admission.

Re-hospitalization caused by acute myocardial infarction	Total (*n*=47)	Case (*n*=23)	Control (*n*=24)	χ^2	*P*
One month after admission					
Re-hospitalization	9 (19.1%)	5 (21.7%)	4 (16.7%)	0.195	0.659
No re-hospitalization	38 (80.9%)	18 (78.3%)	20 (83.3%)	-	-
Three months after admission					
Re-hospitalization	8 (17.0%)	3 (13.0%)	5 (20.8%)	0.505	0.477
No re-hospitalization	39 (83.0%)	20 (87.0%)	19 (79.2%)	-	-

There were 2 patients in the case group and 1 patient in the control group who died from any other cause after one month, and both the case and control groups had 2 patients die from any other cause after three months. There was no statistically significant difference between the two groups in terms of mortality caused by any cause other than AMI one month (*P*=0.525) and three months after admission (*P*=0.965) (Table 2).

Based on Table 3, there was no statistically significant difference between the two groups in terms of re-hospitalization after one month and three months (*P*=0.659, *P*=0.477, respectively). The results showed that after one month, 5 and 4 patients in the case and control groups were re-hospitalized, respectively, and after three months, 3 and 5 patients in the case and control groups were re-hospitalized, respectively.

4. Discussion

The present study aimed to evaluate the effect of oxygen on patients with AMI. The results showed no statistically significant difference between the case and control groups in terms of mortality caused by AMI, caused by any other cause, and re-hospitalization one month and three months after admission.

Stub *et al*. conducted a study on 490 patients with AMI and evaluated the effect of oxygen therapy on patients with myocardial infarction. They reported that the size of the ischemic area in patients who received oxygen therapy was larger than that in patients without oxygen therapy. It can be concluded that the size of the ischemic area has led to an increase in mortality in the group receiving oxygen therapy[14]. Hofmann *et al*. evaluated the effect of oxygen therapy

on 6629 patients with AMI. The results showed that the routine use of supplemental oxygen in treating suspected myocardial infarction patients without hypoxemia decreased mortality[15]. The results from the two studies are not consistent with the results of the present study in which there was no significant difference between the two groups in terms of mortality rate caused by AMI after one month of admission (P=0.965).

Khoshnoud *et al*. evaluated the effect of oxygen therapy on patients with myocardial salvage in ST elevation myocardial infarction who were accepted for acute PCI. The results showed no significant difference between patients who received oxygen and those who did not[11]. This result is consistent with the results of the present study in which there was no significant difference between the two groups in terms of re-hospitalization after one month and three months of admission (P=0.659, P=0.477, respectively).

Jerenberg *et al*. evaluated the effect of oxygen therapy on patients with acute cardiac ischemia and normoxic condition. This study investigated the rate of mortality, re-hospitalization, and heart failure for one year. The results showed no significant difference between these two groups in terms of the rate of mortality and re-hospitalization caused by cardiac ischemia and heart failure in the long term[16]. This result is consistent with the findings of the present study.

Alfredson *et al*. investigated the effect of oxygen therapy (6 L/min) on 6629 patients with acute cardiac ischemia and normoxic condition. They compared the rate of mortality, hospitalization, and heart failure between two groups (control and case) in the long term. No difference was observed between these two groups in terms of the rate of mortality and re-hospitalization caused by cardiac ischemia and heart failure in the long term[17]. This result is consistent with the present study's results.

The result of this study reflects that oxygen therapy did not affect the rate of mortality and re-hospitalization of patients with AMI within three months after admission. However, having a small sample size being one limitation of this study, it is suggested to conduct more extensive studies with larger sample sizes and extended treatment periods for more definitive results.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

MZ: study design, preparing document for publication. AB: study design, case enrollment, preparing document for publication. HRN: study design, data analysis. MG: case enrollment. MK: case enrollment. AA: case enrollment.

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