

## Original Research Article

# Comparison between the effects of premedication with and placebo on the patient's anxiety, coronary angiography complications and the procedure time

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### ABSTRACT

**Background:** Cardiovascular disease is the main cause of death in the world. One of the methods for diagnosis of coronary artery diseases is angiography which may entail several complications in patients like anxiety which is one of the most common complications. Drug therapy in most of centers is often used to soothe patients and avoid complications of angiography. This study aimed at investigating the effects of two current methods of premedication for coronary angiography and placebo on the level of patients' anxiety, complication of angiography, and its duration.

**Methods:** In this clinical trial, 150 patients under coronary angiography selected through convenience sampling were randomly assigned into a control and two premedication groups, i.e., 50 patients in each group. In premedication groups, patients received drugs including diazepam+promethazin and hydrocortisone or midazolam and in the control group, the patients received only routine nursing cares. Data collection tools were a checklist about demographic information, access site, hemodynamic parameter (systolic and diastolic blood pressure, pulse rate, respiratory rate) which was completed 1 hour prior to and during angiography, and spielberger anxiety questionnaire and complications related to angiography. The data were analyzed by statistical methods in SPSS.19.

**Results:** There was no significant difference between the control and the premedication groups regarding hemodynamic parameters, the patients' anxiety level, the complications and the procedure time.

**Conclusions:** According to findings, we suggest premeditations not to be used before angiography as far as possible (except for specific cases), in order to prevent patients from undergoing inappropriate drug therapy along with an invasive diagnostic method.

**Keywords:** Angiography, Anxiety, Coronary artery, Complication, Premedication

### INTRODUCTION

Cardiovascular diseases are the main cause of mortality all around the world, though; the number of death resulting from cardiovascular diseases has declined compared to 40 years ago owing to the progress in diagnostic and surgical technologies particularly cardiovascular angiography and catheterizations.<sup>1,2</sup>

Coronary angiography is an invasive examination for the individuals diagnosed with coronary artery disease whose use has gradually increased.<sup>3</sup>

In most cases, invasive diagnostic procedures, is accompanied by stress and anxiety in patients.<sup>4</sup> Stress and anxiety raises psychological and physiological activity of the body such as heart rate, blood pressure and cardiac output and is more probably to be very harmful for

patients with myocardial infarction or other heart problem.<sup>5</sup>

Most of the factors involved in a person's stress level are having the history of angiography, pain, anxiety, unfamiliarity of environment and fear.<sup>6,7</sup> There are different ways to deal with anxiety in patients, among which consuming sedatives and antiarrhythmic drugs such as diphenhydramine and diazepam can be pointed out.<sup>8</sup>

Before coronary angiography, different drugs may be administered to the patients, such as analgesics to calm them, atropine sulfate to help prevent bradycardia and vasovagal responses or an antihistamine such as diphenhydramine-chloride.<sup>9</sup>

However, in none of the resources, the use of this medication is not definitely recommended; rather applying them has been conditioned to careful checking of the patient's history. But unfortunately without having proper knowledge of the patient's history all patients in most centers receive medication before angiography.<sup>9</sup>

Coronary angiography is a common procedure but sometimes can have major side effects, such as cardiac arrhythmia, kidney damage, blood clot formation which may lead to heart attack or brain stroke, hypotension, pericardial effusion, and death during procedures. The risk of major side-effects and serious complications is low and mostly occur in people who have serious heart disease or undergo coronary angiography in an emergency situation.

Most of the side effects are minor and include bleeding, bruising, blood vessel damage, allergic reactions to contrast agents, catheter site infection etc. In general, the angiography is almost a safe procedure and if the preparations are made, there will be less risk of complications.<sup>11,12</sup>

Therefore, identifying the complications of various premedication on patients' anxiety, as well as the complications and duration of angiography, and comparing them with each other as main objective of the present study, can provide us with insight about how to implement this diagnostic and therapeutic method.

## **METHODS**

The present study was a double-blind clinical trial that included 150 patients with age range of 35 to 75 years who were randomly chosen among the patients undergoing coronary angiography and hospitalized in Imam Khomeini Hospital in Ardabil.

Two premedication groups (each consisting 50 patients), received ordinary drugs used before angiography including diazepam + promethazine or hydrocortisone or midazolam and the placebo group received only routine

care before angiography. The information related to the patients' demographic data, history of mental illness, history of consuming sedatives and anticoagulants, the risk factors of cardiovascular disease, disease-related information, and the site of catheterization were written down, and their hemodynamic parameters (systolic and diastolic blood pressure, the number of pulse rate, respiratory rate) were recorded at intervals of an hour before angiography and during angiography.

Additionally, spielberger anxiety questionnaire and the complications of angiography were completed. In this study, subjects were randomly assigned to three groups. In order to control the intervening factors and prevent patients from communicating with each other, the protocols of premedication were at nurses' disposal. Then, they along with providing patients with ordinary cares before angiography, randomly injected diazepam (5 mg) + promethazine (25 mg) + intravenous hydrocortisone (100 mg) to 50 patients, 0.02 mg/kg of intravenous midazolam to other 50 patients, and 2 mL of normal saline without pre-medication to remaining 50 patients.

The level of anxiety was evaluated in patients based on spielberger anxiety inventory and clinical symptoms. The implemented technique for all patients was femoral-artery-access; and the used contrast media were omnipaque and visipaque. The duration of angiography, the access time, the volume of used contrast media and the complications of angiography were recorded until a week after angiography in the questionnaires.

Arterial bleeding requiring haemostasis or techniques other than compression, hematoma larger than 3 cm, vasovagal reflexes requiring blood pressure and heart rate control were taken as complications of angiography. In the cases which having pain in the site of angiography, swelling, bruits in the route of the femoral artery, etc. colour Doppler ultrasound was taken to confirm the diagnosis of pseudo aneurysm. Three days after angiography serum creatinine and urea were checked to rule out kidney damage. In patients doubt to vascular complications at the catheterization site, arterial colour Doppler ultrasound was requested at the site of angiography.

Collected data were analysed, using SPSS.19, by descriptive and analytical statistical methods. The significance level for all the above mentioned tests was set at 0.05. This study was conducted after receiving approval from the research ethics committee and being registered on IRCT with number IRCT20131020115096N1.

## **RESULTS**

The patients in all three groups were similar to each other regarding gender, age and BMI, diagnosis of the disease, history of heart disease, taking sedative, consuming

anticoagulant, smoking and other risk factors for cardiovascular disease, as well, all patients underwent elective angiography. Therefore, there was no statistically significant difference among the three groups in these respects (Table 1). The comparison of hemodynamic

variables showed statistically significant difference only in diastolic blood pressure ( $P = 0.032$ ). No significant difference was detected among three groups of patients concerning access time, volume of angiography contrast agent, and the duration of angiography (Table 2).

**Table 1: Demographic variables by groups.**

Group variables	Diazepam N = 50	Placebo N = 50	Midazolam N = 50	p-value
Male	26 (52%)	24 (48%)	22 (44%)	0.8
Female	24 (48)	26 (52)	28 (56)	
Age	57.6	56.4	57.1	0.8
BMI	27.2	28.2	27.6	0.8
Elective angiography	50 (100%)	50 (100%)	50 (100%)	0.6
Hypertension history	34 (68%)	40 (80%)	35 (70%)	1
Diabetes history	9 (18%)	13 (26%)	14 (28%)	0.4
Smoking	12 (24%)	15 (30%)	12 (24%)	0.6
Sedation uses	3 (6%)	4 (8%)	3 (6%)	0.7
Taking anticoagulant	4 (8%)	3 (6%)	3 (6%)	0.6

**Table 2: Hemodynamic variables in three groups before angiography and during angiography.**

Group variables	Diazepam N = 50	Placebo N = 50	Midazolam N = 50	p-value
SBP	6.7±3.4	7.8±3.1	4.1±4.4	0.25
DBP	9.4±1.9	13.9±3.3	13.2±3.4	0.03
PR	2.6±1.5	3±1.5	0.6±0.1	0.35
RR	7.6±1.2	3.1±1.3	3.7±2.1	0.1
Access time (second)	22.8±5	22.7±4	24±4	0.4
The volume of contrast agent (cc)	54.5±7.5	52.5±5.4	51.3±5.5	0.06
Angiography duration time (min)	5.1±22	4.1±18	4.2±16	0.06

**Table 3: Anxiety levels in three groups.**

Group variables	Diazepam N = 50	Placebo N = 50	Midazolam N = 50	p-value	
Anxiety level	Mild	40 (33%)	42 (35.1%)	39 (32%)	0.9
	Moderate and low	10 (34.8%)	8 (26.1%)	11 (39.1%)	0.7

**Table 4: Side effects due to angiography in three groups.**

Group variables	Diazepam N = 50	Placebo N = 50	Midazolam N = 50	p-value
Allergic reactions	1 (2%)	1 (2%)	1 (2%)	1
Bleeding	1 (2%)	1 (2%)	1 (2%)	1
Vasovagal reactions	4 (8%)	3 (6%)	3 (6%)	0.9
Hematoma	5 (10%)	5 (10%)	6 (12%)	0.9
Pseudo-aneurysm	1 (2%)	1 (2%)	0	0.4

The comparison of anxiety level among three groups of patients showed statistically significant differences between the three groups in terms of level of anxiety. It should be mentioned that anxiety level in none of the patients was higher than average (Table 3).

The evaluation of the complications from the procedure in all patients revealed that hematoma complications and vasovagal responses with 16 and 10 cases had the highest frequency compared to other complications in three groups, but the difference among the three groups of patients was not statistically significant. It is necessary to

be noted that none of the patients had complications related to kidneys, brain or lung (Table 4).

## DISCUSSION

Drug therapy with benzodiazepines is used in most cardiac catheterization centers during angiography and angioplasty, but the studies done on their efficacy and benefits is limited. The study showed that the hemodynamic parameters except for the difference between diastolic blood pressure before receiving the drug and during angiography didn't vary significantly in patients undergoing coronary angiography and those taking premedication before angiography. And the diastolic blood pressure difference in the group receiving diazepam + promethazine + hydrocortisone was lower than the other two groups, which was not consistent with the result of Kazemi et al.'s study indicating a significant reduction in diastolic blood pressure for patients in the midazolam group.<sup>9</sup>

Most patients undergoing cardiac catheterization have a history of heart disease and receive several medications such as beta-blockers and blood pressure lowering drugs. Therefore, physiological responses are mostly affected by these drugs.

In this study, patients in all three groups had higher blood pressure and heart rate during angiography than before angiography, which indicates that people experience greater amount of anxiety during angiography.

Bally et al. showed that anxiety by activating the sympathetic nervous system causes increased heart rate, blood pressure and cardiac output. And when patients are anxious or experience more discomfort, it is possible that physiological response along with increased heart rate and blood pressure to be observed.<sup>7</sup>

In this study, the patients experienced maximum anxiety during angiography. The study by Papolo and Kurdesko has found that when patients are faced with a stressful situation they experience heart palpitations.<sup>13</sup> Therefore, in this study it appears that angiography as a stress factor raises the degree of sympathetic activity and thus results in increased heart rate in patients.

Overall, in this study, the comparison of two stages of hemodynamic parameters' measurements (one hour before the injection of pre-medication and during angiography) revealed no significant difference among three groups.

Accordingly, the hypothesis, that the hemodynamic parameters change in the patients undergoing coronary angiography who receive drug is identical to the control group, which supports the Haneafy et al finding.<sup>10</sup>

In this study, vascular complications were observed in 14% of patients. The complications were mostly common

among females, the patients with short stature, and those with a history of HTN.

In the midazolam group one of the patient showed agitations during the procedure which was considered as a midazolam side effect. Although Midazolam is taken as a sedative into account, in some patients, it can cause restlessness and agitation. However, there was no statistically significant difference in respect of side effects among the three groups.

Currently, in most of Cardiac catheterization centers, intravenous Midazolam is injected to the patients, and if a patient complains about severe anxiety and asks for a drug, 5-10 mg of diazepam is administered orally.

In a study by Bergeron et al., oral midazolam had been administered instead of intramuscular injection due to its faster and better absorption. However, based on the results of this study, oral diazepam also had little effect on anxiety and pain. In addition, the number of angiographic complications didn't decrease.<sup>11</sup>

Alamri et al in their study explored that diazepam and chlorpheniramine didn't reduce the complications of angiography and anxiety.<sup>12</sup> In Kazemi et al.'s study, as well, intramuscular diazepam and intravenous midazolam had no effect on anxiety of the patients.<sup>9</sup>

High levels of anxiety can make the patient not cooperate with the operator during the procedure and in turn increase the access time or raise the number of puncture and thus prolong the time of angiography, and due to higher risk of complications in patients. This study showed that medication with benzodiazepines compared with the placebo has no effect on patients' anxiety, angiography complications and time.

In this study, the level of anxiety in patients was measured with Spielberger scale, which is one of the reliable scales for evaluation the patient's anxiety. We obtained that in this study, all patients had mild or moderate anxiety and so the need to use premedications to reduce patients' anxiety before angiography becomes pale.

Moreover, unnecessary injection of these drugs may be associated with complications in some cases and increase hospital costs for patients.

So this study does not support the routine use of these drugs except for emergencies.

The improvement of angiographic and cardiac catheterization techniques, using more advanced equipment and smaller arterial sheaths, and mechanical closure devices (vascular closure devise), the increased level of awareness among people and educating them about cardiovascular disease and the heart disease diagnostic methods have been reduced the complications

of cardiac catheterization and angiography, as well as the patients' anxiety.

On the other hand, the angiography procedure lasts only for a short while (a few minutes) which also decreases the complications and the necessity of premedication before angiography.

## CONCLUSION

The results showed that routine injection of premedication doesn't have any effect on anxiety of patients who undergo coronary angiography and doesn't reduce the duration and complications of angiography. Thus, it is recommended that before such aggressive methods, the premedication in the emergency cases be administered. This need for a careful examination of the patients which by doing this, the patients wouldn't receive undue drug therapy.

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