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Pain management in ST-segment elevation myocardial infarction: an observational analysis

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ABSTRACT

Aim: ST-segment elevation myocardial infarction (STEMI) is one of the most severe forms of pain. However, the guidelines give quite a few places for pain control in STEMI and, do not offer strong recommendations on this issue. This study aimed to reveal which medications are given to STEMI patients for pain control until they arrive at the catheter laboratory, in which situations they are used, and the frequency of use.

Material and Method: A total of 272 consecutive STEMI patients were prospectively collected. Medications were administered to the patients until they arrived at the angiography laboratory; vital signs, comorbidities, referral status, infarction types, the time between the onset of pain and the admission to the emergency department, and the door-balloon time were also noted. The patients' pain characteristics and intensity were evaluated.

Results: It was observed that 96.3% of the patients presented with chest pain. The pain of diabetic patients was severe according to the visual analog scale (VAS) score (p=0.023). It was witnessed that 9.92% of the patients were administered drugs for analgesic purposes. The most commonly administered medication was paracetamol. It was noticed that morphine was used frequently after paracetamol. Medication administration for analgesia was more common in referred patients (p=0.040).

Conclusion: Physicians behave timidly in their clinical practice in pain control of STEMI and move away from the guideline. In terms of comfort and hemodynamic stabilization of the patients, it will be beneficial for the applications in the field to give more place to the treatments for pain control in the guidelines.

Keywords: ST-segment elevation myocardial infarction, chest pain, pain relief, morphine, paracetamol

INTRODUCTION

Acute ST-segment elevation myocardial infarction (STEMI) is a condition with mortality risk and often presents to the emergency department with chest pain (1). Apart from chest pain, patients may experience pain in the lower jaw, back, left arm, left shoulder, and abdomen (2-4). In contrast to the incidence of typical chest pain decreasing with age in acute myocardial infarction (AMI), angina equivalent symptoms, dyspnea, anxiety, palpitations, heart failure, and neurological, and abdominal symptoms increase (3,5). Apart from elderly patients, the frequency of chest pain is less common among the complaints of acute myocardial infarction in diabetic patients, and silent myocardial infarcts can be observed (1,6).

Although chest pain is still the most common symptom of acute myocardial infarction, the guidelines did not focus on pain relief as much as antiaggregant and anticoagulant treatments and did not make clear recommendations. Nevertheless, pain control provides the patient comfort and reduces the burden on the heart by preventing vasoconstriction that occurs when pain triggers sympathetic activation (2).

It is noted in the 2017 European Society of Cardiology (ESC)'s Guidelines that opioids (e.g., morphine) can be used in pain control with a class 2a recommendation. However, it is indicated that morphine may delay the effect of oral antiplatelet treatments and therefore cause early failure in treatment (2). In addition, it may cause nausea, vomiting, hypotension, and bradycardia (1,7,8).

When we look at daily practice, we observe that the administration of drugs for pain control to AMI patients in the emergency department is low due to the clinical hemodynamic status of the patients and the fear of the side effects of the drugs given for analgesia. In this study, we aimed to examine the severity of pain in STEMI patients, whether the patients were administered for pain control, and, if so, which drugs were given.

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MATERIAL AND METHOD

This study was carried out with the permission of Gaziantep İslam Science and Technology University Coordinatorship of Local Ethics Committee for Non-Interventional Clinical Researches (Date: 26.04.2022, Decision No: 111.16.14). Informed consent was obtained from all patients in this study. All procedures were carried out by the ethical rules and the principles of the Declaration of Helsinki.

Study Design

The study is an observational analysis study. Data were obtained prospectively through face-to-face interviews, emergency department and ambulance transfer documents, cardiology clinical files, and coronary angiography system.

The following data of the patients were recorded: age, gender, comorbidity, type of myocardial infarction, culprit lesion, presence of pain, the time between the onset of pain and admission to the emergency department, door-balloon time, referral status, antiaggregant, anticoagulant and drugs preferred for analgesia.

Selection of the Participants

Patients referred to our center, a state hospital where primary coronary angiography is performed 24/7, with the diagnosis of STEMI, were included in the study, either from our emergency department, the same district, the neighboring communities, or the surrounding provinces. After the ethics committee's approval, data were collected as of 27 April 2022. Data collection was performed by G.Power 3.1 (Institute of Experimental Psychology, Heinrich Heine University, Dusseldorf, Germany), selecting type I error 0.05 and power of 90% (1- β =0.90). Based on previous studies, the required sample size was determined at least 272 consecutive STEMI patients.

The patient age group was chosen as 18-99 years. Patients presenting with cardiac arrest were not included in the study. Patients (n=3) who were unclear about which drugs were administered until they were admitted to the coronary angiography unit were excluded from the study.

Measurements and Outcomes

The definition of STEMI is based on the electrocardiogram (ECG) changes in the ESC fourth universal myocardial infarction guideline (9).

Although it is used in the chronic pain scoring system, the Visual Analogue Scale (VAS) scoring system, which is also reliable in acute pain, was used in grading pain (10). Patients were scores between 0-10. 0 was recorded as no pain, and ten as very severe pain. Less than three is classified as mild, 3-6 as moderate, and seven or more as severe pain. Since there was no patient with a score below 3 in our study, the evaluations were made 3-6, and 7 and above.

Statistical Analysis

Statistical Package for the Social Sciences version 25.0 software program (SPSS, IBM, Corp.; Armonk, NY, USA) was used for data analysis in this study. Descriptive data on the sociodemographic information of the patients are given as n (%) or Mean± SD tables. The Chi-Square test or Fisher's Exact test was used to compare the groups according to VAS score groups and diabetes mellitus, drugs used for analgesic, acetylsalicylic acid use, and referral status and analgesic drug use. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 272 consecutive patients with STEMI were included in the study. The mean age of the patients was 58.20±12.94 years, and 75.4% (n=205) were male.

When the patients were divided according to VAS, it was observed that there were no patients in the mild pain group with a score of 3 or less. While 12.9% (n=35) of the patients had moderate pain, 87.1% (n=237) reported severe pain. 96.3% (n=262) of the patients suffered chest pain at admission. Demographic information, VAS score, and admission symptoms of the patients are presented in **Table 1**.

Table 1. Demographic data, comorbidity, symptoms, and VAS score of STEMI patients

		N	%
Age, Mean ±SD		58.20±12.94	
Gender	Male	205	75.4
	Female	67	33.3
DM	No	192	70.6
	Yes	80	29.4
HT	No	177	65.1
	Yes	95	34.9
CAD	No	206	75.7
	Yes	66	24.3
CVD	No	268	98.5
	Yes	4	1.5
VAS	3-6	35	12.9
	7≤	237	87.1
Chest pain	No	10	3.7
	Yes	262	96.3
Back pain	No	240	88.2
	Yes	32	11.8
Abdominal pain	No	223	82.0
	Yes	49	18.0
Arm pain	No	216	79.4
	Yes	56	20.6
Referral status	No	88	32.4
	Yes	184	67.6

DM: Diabetes Mellitus; HT: Hypertension; CAD: Coronary Artery Disease; CVD: Cerebrovascular Disease; SD: standard deviation, VAS: visual analogue scale

It was observed that 67.6% (n=184) of the patients were referred from other hospitals (**Table 1**). The most

common type of myocardial infarction was 57.7% (n=157), the inferior myocardial infarction. It was determined that the mean time between the onset of pain and admission to the emergency department was 517.37±1611.34 minutes, and the mean door-balloon time was 71.41±94.96 minutes (**Table 2**).

Table 2. Clinical characteristics of the patients in the emergency department and the catheter laboratory

		N	%
MI type			
Anterior & anterolateral		98	36.0
Lateral		16	5.9
Inferior & inferolateral		157	57.7
Posterior & posterolateral		1	0.4
	Min	**Max**	**Mean±SD**
ER- SBP (mm Hg)	70.00	160.00	126.48±30.53
ER-DBP (mm Hg)	15.00	134.00	74.59±15.63
ER-HR (bpm)	35.00	140.00	77.16±18.27
CL-SBP (mm Hg)	52.00	180.00	121.70±22.48
CL-DBP (mm Hg)	40.00	110.00	71.65±13.98
CL-HR (bpm)	40.00	142.00	77.73±17.38
Onset of pain-ER (minute)	10.00	20160.00	517.37±1611.34
Door-Balloon (minute)	5.00	780.00	71.41±94.96

ED- SBP: Emergency department- systolic blood pressure, ED-DBP: Emergency department- diastolic blood pressure, ED-HR: Emergency department- heart rate, CL-SBP: Catheter laboratory- systolic blood pressure, CL-DBP: Catheter laboratory- diastolic blood pressure, CL-HR: Catheter laboratory- heart rate

It was observed that 7%(n=19) of the patients were not given acetylsalicylic acid until they arrived at the catheter laboratory. It was determined that 10.3%(n=28) of the patients were given clopidogrel loading as the second antiplatelet, and 8.5%(n=23) were given ticagrelor loading. It was found that 8.8%(n=24) of the patients were given Heparin iv, 50.7%(n=138) enoxaparin sc, and 0.4%(n=1) enoxaparin iv as anticoagulant treatment. It was also marked that 40.07%(n=109) of the patients were not given any anticoagulant treatment (**Table 3**).

Table 3. Data on antiaggregant and anticoagulant administered

Medications		**N**	**%**
Acetylsalicylic acid	No	19	7.0
	Yes	253	93.0
Clopidogrel	No	244	89.7
	Yes	28	10.3
Ticagrelor	No	249	91.5
	Yes	23	8.5
Prasugrel	No	272	100.0
	Yes	0	0.0
Heparin iv	No	248	91.2
	Yes	24	8.8
Heparin sc	No	272	100.0
	Yes	0	0.0
Enoxaparin sc	No	134	49.3
	Yes	138	50.7
Enoxaparin iv	No	271	99.6
	Yes	1	0.4

In terms of pain control, it was observed that 9.92%(n=27) of the patients were administered drugs for analgesia. The most commonly administered drug for this purpose was paracetamol (4.4%, n=12), followed by morphine (2.6%, n=7) as the second most frequently administered (**Table 4**).

Table 4. Data on analgesics administered to patients

Analgesics		**N**	**%**
Paracetamol	No	260	95.6
	Yes	12	4.4
Dextroprofen	No	270	99.3
	Yes	2	0.7
Metamizole	No	271	99.6
	Yes	1	0.4
Tenoxicam	No	270	99.3
	Yes	2	0.7
Tramadol	No	271	99.6
	Yes	1	0.4
Morphine	No	265	97.4
	Yes	7	2.6
Diclofenac	No	271	99.6
	Yes	1	0.4
Fentanyl	No	272	100.0
	Yes	0	0.0
Pethidine	No	271	99.6
	Yes	1	0.4

When the referral status of patients who received analgesic medication was examined, a statistically significant relationship was observed between medication administration and referral (p=0.040). It was found that 85.25%(n=23) of the patients who were administered analgesic drugs were referred to (**Table 5**).

Table 5. Comparison of the referral status and analgesic use

	Referral Status		**p**
	No N(%)	**Yes N(%)**	
Administration of analgesics			0.040
No	84 (34.3)	161 (65.7)	
Yes	4 (14.8)	23 (85.2)	

Chi-Square test, p<0.05 statistically significant.

In addition, our study revealed a statistically significant relationship between VAS score and diabetes mellitus. It was determined that 80%(n=64) of the patients with diabetes mellitus had a VAS score of ≥ 7, while 20%(n=16) had a VAS score between 3-6 (p=0.023). No statistically significant relationship was observed when the VAS score was compared with the patients treated with analgesic drugs, (p=0.222). Moreover, no statistically significant relationship was observed when the VAS score was compared with the patients given acetylsalicylic acid (p=0.752) (**Table 6**).

Table 6. Comparison of VAS score groups and diabetes mellitus, analgesic drugs, and acetylsalicylic acid use

	VAS Score		p
	3-6 N(%)	7≥ N(%)	
DM			0.023[a]
No	19 (9.9)	173 (90.1)	
Yes	16 (20.0)	64 (80.0)	
Administration of analgesics			0.222[b]
No	34 (13.9)	211 (86.1)	
Yes	1 (3.7)	26 (96.3)	
Acetylsalicylic acid			0.752[b]
No	2 (10.5)	17 (89.5)	
Yes	33 (13.0)	220 (87.0)	

DM: Diabetes Mellitus, VAS: visual analogue scale, a: Chi-Square test, b: Fisher's Exact test, p<0.05 statistically significant.

DISCUSSION

In our study, 96.3% of the patients presented with chest pain, and no patient was in the mild pain group according to the VAS score. We determined that the pain severity of diabetic patients was in the severe pain group according to their VAS scores. We witnessed that only 9.92% of the patients were given drugs for analgesia. We have seen that paracetamol is used most frequently in drug administrations for analgesia. It was determined that most patients administered drugs were transferred from another hospital for primary percutaneous intervention.

In the study, chest pain was the most common pain region in acute myocardial infarction, consistent with the literature (1). In addition, severe chest pain was observed more frequently, consistent with previous research (11). Diabetic patients may not have typical chest pain in acute coronary syndromes and acute myocardial infarction due to autonomic neuropathy (12,13). In the literature, it has been that diabetics patients are less likely to present with chest pain due to acute myocardial infarction (1,6). However, in our study, unlike in the literature, severe pain was observed in diabetic patients presenting with STEMI. This issue may be because the mean age of our patients was younger than in other studies, and the neuropathy associated with diabetes was less developed.

The opioid group, especially morphine, is recommended for pain control in patients with acute STEMI (2). It is known that morphine decreases gastric motility, increases nausea and vomiting, delays the effect of oral antiplatelets in absorption, and may cause respiratory depression, cause bradycardia, and hypotension at high doses (1,14,15). In addition, the TREAT trial, published recently, showed that morphine use was associated with early reinfarction and less bleeding in STEMI patients administered fibrinolytic therapy and dual antiplatelet therapy (16). Apart from morphine, another opioid that can be preferred in acute myocardial infarction is pethidine. Nielsen et al. (17) showed that pethidine has similar efficacy and safety as morphine in ischemic chest pain in acute myocardial infarction. Pethidine, like morphine, has side effects such as nausea, vomiting, and respiratory depression (14). Studies have revealed that fentanyl, another opioid, can be an alternative to morphine in ischemic chest pain (18). It has been demonstrated that fentanyl has fewer gastric side effects than morphine. Like morphine, fentanyl has been observed to delay the absorption of oral antiplatelets, but no study compares the two (14).

Apart from the opioid recommendation, another essential point we know is that nonsteroidal anti-inflammatory drugs are contraindicated because of increased major adverse cardiovascular events (MACE) in acute myocardial infarction (14). Physicians are encountering STEMI experience fear and confusion in choosing analgesic therapy due to limited data, the lack of hemodynamic stability of patients, and the side effects of drugs. In the study of Rahul et al. (19), it was stated that morphine should be chosen in acute myocardial infarction in evaluating the questionnaire made to medical practitioners and the administrations made in practice. However, it was observed that the most administered drug was pentazocine. We detected that only 9.92% of the patients were administered drugs for analgesic purposes. In our study, opioids recommended as the first choice were not the most commonly used drug. The most commonly used was paracetamol. The second most frequently used drug was morphine. This may be due to fear of possible side effects of morphine such as hemodynamic or reinfarction, or because it is a narcotic group drug, paperwork procedures are required during its use, and the patient loses time for primary percutaneous intervention during the supply of analgesic drugs. This is supported by the fact that administering analgesic drugs to referral patients is significantly higher than in non-referral patients.

One of the remarkable results of our study is the onset of pain, the time of arrival to the emergency department, and the time of the door-balloon. The prolonged time between the onset of pain and arrival to the emergency department may be why patients do not want to come to the hospital because of Coronavirus disease 2019 (COVID-19). Soylu et al. (20), in their study comparing STEMI patients during the pandemic and pre-pandemic period, showed that the prehospital period was longer during the pandemic period.

The door-balloon time of our patients is close to the median of the door-balloon time in the literature (21). However, it was observed that there were strikingly high times in our door-balloon times. When the patient files were examined, it was observed that ECG could not make the diagnosis of STEMI in the emergency department. However some patients were diagnosed with STEMI after being noticed after cardiac enzyme follow-up.

Our study showed that patients with acute STEMI were also deficient in antiplatelet and anticoagulant treatments. While acetylsalicylic acid was not given to 7% of the patients, 40.07% did not receive anticoagulants. In addition, it was observed that no patient with a door-balloon time longer than 120 minutes was given fibrinolytic therapy. This shows problems in diagnosing STEMI in the emergency department and administering treatment algorithms.

Our study has several limitations. It is unknown whether the emergency medicine specialist or the general practitioner evaluated the patient in the hospitals that referred them. For the diabetic patient group, it is unknown how many years the patients have had diabetes and whether their diabetes is under control. Another limitation is that it is unknown whether the glyceryl trinitrate administered to the patients was given for blood pressure control or analgesic purposes, so these patients could not be included in the study.

CONCLUSION

We concluded that using medications for analgesic purposes in STEMI patients is insufficient and ignored. Although opioid use is mentioned in the guidelines, we found that paracetamol, which is not more effective, is preferred in STEMI pain control. In addition to the delays in the diagnosis of STEMI, there is a problem of not completing oral antiplatelet and anticoagulant therapy before the catheterization laboratory. It would be beneficial for best medical practices in the field to include more about pain management in the guidelines for STEMI, which is among the severe pain types.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was carried out with the permission of Gaziantep İslam Science and Technology University Coordinatorship of Local Ethics Committee for Non-Interventional Clinical Researches (Date: 26.04.2022, Decision No: 111.16.14).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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