

Analysis of the use of nitroglycerin in pre-hospital procedure by medical rescue teams in patients with acute coronary syndrome (ACS STEMI), with particular regard to a closed right coronary artery

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ABSTRACT

Introduction: Currently, cardiological societies and associations do not recommend the use of nitroglycerin in patients with acute coronary syndrome ST-elevation myocardial infarction (ACS STEMI). However, an analysis of medical rescue practice shows that this medicine is still being used.

The aim of this study is to conduct a correlation analysis of the use of nitroglycerin by medical rescue teams (MRT) in patients with ACS STEMI and its impact on selected biochemical parameters.

Materials and methods: The study group consisted of 312 patients. Data for these patients over a period of 8 years (2009–2017) was analysed. A retrospective study of the dispatch orders for MRT, including primary transport was conducted.

Results: Coronary angiography revealed a closed right coronary artery (RCA) in 312 patients. In 210 patients, the MRT administered nitroglycerin during pre-hospital procedure, where RCA closure was confirmed in a coronary angiography. After

administering nitroglycerin and discovering an RCA occlusion, more favourable results of biochemical parameters and statistical differences between the groups in Killip class were shown ($p = 0.022$). Lower values of Troponin I and creatine kinase-myocardial band (CK-MB) max. parameters as well as higher cardiac ejection fraction (left ventricular ejection fraction – LVEF) were observed after administering nitroglycerin (no statistical significance).

Conclusions: It was not clearly demonstrated that the use or non-use of nitroglycerin at the pre-hospital stage (1–2 doses of the drug) negatively affected the patient's condition. At the same time, it was shown that the use of nitroglycerin at the pre-hospital stage, and the lack of nitroglycerin administration at hospital resulted in lower, selected biochemical parameters, and that the use of nitroglycerin had a significant impact on the Killip class.

Keywords: acute coronary syndrome; emergency medicine; nitroglycerin; right ventricular heart failure.

INTRODUCTION

Acute coronary syndrome (ACS) is a life-threatening condition and one of the most common causes of morbidity and mortality in highly developed countries. At present, the number of ACS cases is increasing, as is the development of invasive cardiology (thus leading to an increase in the survival of the 1st and the next ACS). Of all ACSs, approx. 30% are those with ST-segment elevation – ASC STEMI.

The development of emergency medical services in Poland saw the adoption of the Law on State Emergency Medical Services (PRM) in 2007. This included the provision that pharmacological treatment in ACS STEMI is the same for all emergency medical units (“S” – specialist with a doctor and “P” – basic with paramedics) [1].

Providing emergency medical units with the appropriate equipment and implementing the electrocardiogram (ECG) teltransmission system allowed most of the units in the country to have the technical possibility to carry out teletransmission and ECG consultation with a specialist physician in the invasive cardiology center. Due to the fact that ACS is a condition that directly threatens life and may lead to serious cardiac disorders

including sudden cardiac arrest (SCA), the dispatcher should send the specialist “S” unit for such interventions. In a situation where information is not clear or when the dispatcher is unable to send an “S” unit, interventions may be carried out by the basic “P” team with paramedics. It is worth noting that many countries in Europe do not have units with a physician or operate with the rendezvous system (where the doctor arrives separately after being summoned by a paramedic).

In 2012, the European Society of Cardiology (ESC) issued guidelines on how to handle a patient with ACS STEMI. These guidelines do not recommend the use of nitroglycerin in patients with ACS STEMI. This position is still upheld.

The aim of this study is to conduct a correlation analysis of the use of nitroglycerin by medical rescue teams in patients with ACS STEMI and its impact on selected biochemical parameters.

MATERIALS AND METHODS

Analysis took place on cases where ACS STEMI had occurred and been confirmed by a closed right coronary artery (RCA) in

the coronary angiography. This is due to the fact that right ventricular (RV) vascularization mainly comes from the RCA, and the use of nitroglycerin may adversely affect the right ventricle.

Initially, the study group consisted of 711 patients with ACS STEMI who were transferred to the Department of Cardiology at the Independent Public Clinical Hospital No. 2 of the Pomeranian Medical University in Szczecin (SPSK No. 2 PUM) in Poland. Due to research problems, all cases of ACS STEMI where a closed coronary artery, other than the RCA, was found were excluded. Finally, 312 patients were qualified for the study. Data from all patients over a period of 8 years (2009–2017) were analyzed.

The retrospective study consisted of an analysis of exit cards from emergency medical units, including primary transport (from the place of the incident directly to the cardiology clinic), in the case of ACS STEMI (with particular reference to the use of nitroglycerin) and the results of further studies in the hospital e.g., biochemical factors.

STATISTICAL ANALYSIS

Categorical variables were expressed as numbers and percentages, whereas continuous parameters were expressed as median and interquartile ranges. The χ^2 , Student t-test, Mann–Whitney U or Wilcoxon's W test were used to compare the groups. A p-value of < 0.05 was considered statistically significant.

All statistical analyses were performed using the Statistica software package (versions 6.0 and 10.0, StatSoft Inc., Tulsa, OK, USA).

RESULTS

During the analyzed period, emergency medical services intervened in cases with ACS STEMI 711 times. In 303 cases (42.6%), basic "P" ambulances were sent for intervention, and "S" specialized ambulances were sent in 408 cases (56.4%; $p = 0.025$). In the group who underwent a coronary angiography, a RCA was responsible for the infarction in 312 patients – 43.9% of interventions. An "S" unit was deployed to 171 of these patients (24%) and the "P" unit in 141 patients (19.8%).

In the group of 711 patients, nitroglycerin was used in 483 patients (67.9%). The emergency medical units used nitroglycerin in pre-hospital procedure in 210 patients (29.5%), where coronary angiography was used to determine that the RCA was responsible for the infarction. Specialist units used nitroglycerin at the RCA responsible for infarction in 120 patients – 16.9%, while "P" units in 90 patients – 12.6% ($p = 0.032$) – Tables 1, 2 and 3.

DISCUSSION

Emergency medical services are an important part of dealing with patients at pre-hospital stage. Often, preliminary activities performed by emergency medical units have a very large

TABLE 1. Nitroglycerin usage by emergency medical teams in right coronary artery occlusion confirmed by coronarography

Variable	Total n (%)
RCA – "S" + "P"	312 (100)
RCA – "S"	171 (54.8)
RCA – "P"	141 (45.2)
RCA + nitroglycerin + "S" + "P"	210 (67.3)
RCA + nitroglycerin – "S"	120 (38.5)
RCA + nitroglycerin – "P"	90 (28.8)

RCA – right coronary artery; "S" – specialist team; "P" – basic team

TABLE 2. Nitroglycerin usage in confirmed right coronary artery occlusion and its influence on the thrombolysis in myocardial infarction scale

Cross table TIMI scale – Nitroglycerin					
		nitroglycerin		total	
		no	yes		
TIMI	0	quantity	52	126	178
		%	16.7	40.4	57.1
	1	quantity	14	25	39
		%	4.5	8.0	12.5
	2	quantity	22	40	62
		%	7.0	12.8	19.8
	3	quantity	14	19	33
		%	4.5	6.1	10.6
Total	quantity	102	210	312	
	%	32.7	67.3	100.0	

TIMI – thrombolysis in myocardial infarction grade flow

impact not only on the survival of patients but also on the effects of their subsequent treatment.

According to the medical records, 711 patients were diagnosed with ACS STEMI. The average age of the study group was 64.4 ± 11.4 years. In the observed period, a slight upward trend was noted in the number of ACS STEMI occurring at SPSK No. 2 PUM and a clear upward trend in performance of direct transport to the reference center. This situation testifies to the dynamic development of both the awareness of people working in the emergency medical teams regarding correct behavior and the intensive education of medical personnel. In the ESC guidelines, a drop in the number of ACS STEMI in the years 1997–2005 (121 to 77) was recorded in the European scale [2]. This is contrary to the upward trend of occurrences of ACS STEMI in Szczecin and requires further investigation.

When analyzing the frequency of the implementation of morphine, oxygen, nitroglycerin, aspirin (the MONA scheme) in the treatment of ACS, it was observed that the procedure was used to a similar degree in specialist and basic units. Not all patients used all of the drugs in the scheme. Oxygen was the most frequently provided, and nitroglycerin was the least frequent. In some years, the use of oxygen, morphine and nitroglycerin increased slightly. Ninety-two point five percent of ACS patients were given acetylsalicylic acid (ASA). It is worth mentioning that ASA is currently the only drug that does not raise controversy in its use in patients with STEMI. The frequency of use of this drug in other countries is similar, for

TABLE 3. Nitroglycerin usage by emergency medical teams in right coronary artery occlusion and its influence on selected biochemical parameters

Team	Nitroglycerin	Troponin I	CK-MB max. µg/l	LVEF when discharged	Killip	TIMI	
“S”	no	average	14.9757	301.72	45.82	1.50	0.79
		Median	10.0800	168.00	45.00	1.00	0.00
		SD	15.94175	285.576	10.417	1.022	1.122
		minimum	0.86	14	20	1	0
		maximum	81.00	1192	60	4	3
		n	51	51	51	51	51
	yes	average	13.2122	257.11	46.67	1.29	0.64
		Median	7.9800	183.50	45.00	1.00	0.00
		SD	11.26953	234.020	10.226	0.852	1.005
		minimum	0.08	16	15	1	0
		maximum	30.00	1129	70	4	3
		n	120	120	120	120	120
	total	average	13.6870	269.28	46.45	1.35	0.68
		Median	8.2800	178.00	45.00	1.00	0.00
		SD	12.65478	248.801	10.242	0.904	1.037
		minimum	0.08	14	15	1	0
		maximum	81.00	1192	70	4	3
		n	171	171	171	171	171
“P”	no	average	11.0069	257.26	48.14	1.38	0.71
		Median	6.8900	126.00	50.00	1.00	0.00
		SD	10.53087	293.351	11.120	0.922	1.001
		minimum	0.01	2	25	1	0
		maximum	30.00	1105	80	4	3
		n	51	51	51	51	51
	yes	average	11.8267	254.98	49.23	1.09	0.52
		Median	8.8000	185.00	50.00	1.00	0.00
		SD	9.67946	201.752	9.484	0.285	0.941
		minimum	0.05	19	25	1	0
		maximum	30.00	828	70	2	3
		n	90	90	90	90	90
	total	average	11.5246	255.81	48.84	1.20	0.59
		Median	7.7400	176.00	50.00	1.00	0.00
		SD	9.95375	237.713	10.061	0.619	0.963
		minimum	0.01	2	25	1	0
		maximum	30.00	1105	80	4	3
		n	141	141	141	141	141
“S” + “P”	no	average	13.4754	253.25	47.16	1.19	0.68
		Median	9.7050	202.00	50.00	1.00	0.00
		SD	10.63473	227.150	9.285	0.705	1.072
		minimum	1.02	30	30	1	0
		maximum	30.60	1337	65	4	3
		n	102	102	102	102	102
	yes	average	11.9077	243.67	49.19	1.08	0.79
		Median	8.0400	172.00	50.00	1.00	0.00
		SD	10.40896	228.946	8.543	0.340	1.073
		minimum	0.01	10	20	1	0
		maximum	76.00	1654	70	4	3
		n	210	210	210	210	210
	total	average	12.2718	245.87	48.73	1.11	0.76
		Median	8.4000	175.00	50.00	1.00	0.00
		SD	10.46764	228.249	8.746	0.450	1.072
		minimum	0.01	10	20	1	0
		maximum	76.00	1654	70	4	3
		n	312	312	312	312	312

CK-MB – creatine kinase–myocardial band; LVEF – left ventricular ejection fraction; Killip – Killip classification; TIMI – thrombolysis in myocardial infarction grade flow; “S” – specialist team; “P” – basic team; SD – standard deviation

example in the Czech Republic it was 95% [3], and 85% in the United Kingdom [4].

Analysis of pharmacological procedures with particular reference to nitroglycerin in acute coronary syndrome ST-elevation myocardial infarction

The use of oxygen in patients with ACS seems reasonable in all cases as, during infarction, the heart is hypoxic. The 2009 guidelines of the ESC include recommendations that the implementation of oxygen therapy should be carried out in patients with respiratory depression or shock [5]. In cases where dyspnea is reported by patients, oxygen must be used with a "nasal cannula" and the decision on the implementation of oxygen therapy should be based on the result of a non-invasive measurement of oxygen saturation. There are no specific guidelines in the 2009 recommendations of when treatment should be implemented. In the 2012 guidelines, however, these are defined at SpO₂ level <95% [2].

A very important aspect of treating myocardial infarction is the treatment of pain. The occurrence of pain is closely related to sympathetic activation, which causes vasoconstriction and increased heart load [2, 5]. The drug of choice during emergency medicine is morphine and this drug is included in all guidelines for dealing with heart attack – ESC, American Heart Association and Polish Cardiac Society. The use of morphine in in-house studies is difficult to consider satisfactory, as it was 77.2% in the entire study group.

Another highly discussed issue is the use of nitroglycerin in patients with ACS. This medicine has several contraindications that preclude its use. These contraindications may occur in patients with ACS. This includes hypotonia which was found in nearly 12% of patients in the study group. A separate and significant problem is the occurrence of inferior myocardial infarction (classic changes in ECG leads – II, III and aVF) which account for nearly 50% of all ACS STEMI. Due to the fact that this infarction may also be accompanied by a RV infarction, administration of nitroglycerin in such a situation may lead to an increased chance of failure in the left ventricle. To avoid RV infarction, a 12-lead right-handed ECG should be performed (recommendation class I B). Changes in V_{3R} and V_{4R} are indicative of the occurrence of this infarction. In addition, it should be remembered that changes in the ECG do not last very long (12–48 h). In the case of ACS STEMI, nitroglycerin is not recommended by cardiologic associations or where tests carried out in hospitals show a right heart ventricular infarction [2, 5, 6]. In 2010, the provincial consultant of cardiology for the West Pomeranian Voivodeship recommended that nitroglycerin should not be provided in ASC STEMI infarction in the event of an inferior myocardial infarction.

In the Kumar et al. study, a RV infarction was diagnosed in 59% of patients with inferior myocardial infarction [7]. In our research, inferior myocardial infarction constituted 43.9% of all cases [8], similar to a study conducted in Serbia, where the percentage was 46.5% [9].

Analysis of the data showed that, in every third patient (210 cases), both emergency medical units used nitroglycerin in the inferior infarction where a coronary angiography revealed

a closed RCA. The occlusion of the RCA is not synonymous with the occurrence of an acute myocardial infarction; however, studies indicate that nearly 80% of RV infarctions occur at the time of its closure [10]. This may have been due to the lack of teletransmission and/or the correct interpretation of the ECG. Nowadays, all emergency medical units in Poland and in the majority of European countries have the technical possibility of carrying out ECG teletransmission. Therefore, the recommended procedure would be to abstain from prescribing nitroglycerin until the location of the infarction has been discovered by the doctor, e.g., in the clinic. According to the current guidelines of cardiologic associations, nitroglycerin is not recommended in cases of ACS STEMI. Considering that emergency medical units may have problems with the location of ECG changes, consideration should be given to the need for teletransmission as a mandatory procedure in pre-hospital proceedings regardless of the type of unit performing the intervention (this solution is used in some ambulance stations in Poland as an internal order of the medical directors). It is intriguing, however, that there is little in the literature describing the impact of the use of nitroglycerin at the pre-hospital stage and its impact on the patient's biochemical parameters. The vast majority of research concerns situations where the patient is already in the hospital.

An interesting result is that in our research, specialist units administered nitroglycerin in the inferior wall infarction slightly more frequently (a difference of 4 percentage points) than in the basic units – thus, they followed the guidelines of scientific associations less frequently. This element, i.e., which unit performs ECG teletransmission from the place of the incident more often, requires a deeper and more extensive analysis. It should be emphasized that the execution of teletransmission does not significantly affect the time it takes to perform medical rescue operations, and the time devoted to its implementation in terms of technology varies in the range of 2–3 min. This can also be conducted during medical transport with the internal memory of the device. It is therefore difficult to explain why emergency medical units do not use this diagnostic tool more often and why specialist units administered nitroglycerin despite changes in ECGs showing inferior myocardial infarction. It is worth noting that myocardial infarction of the right ventricle occurs in 30–50% of cases of infarctions of the inferior wall of the left ventricle with ST elevation occurring most often in the course of the RCA closure. The extent of RV vascularization depends on the domination of coronary arteries. When the RCA dominates (in about 70–80% of cases) the RCA supplies the bigger part of the free RV wall [9]. It should be noted that research on ECG teletransmission in different countries showed a significant reduction in medical intervention times both at pre-hospital and specialist stages. [11, 12]. Also noteworthy is a new regulation implemented by the Minister of Health in Poland regarding the use of medicines by paramedics. It dictates that administering clopidogrel by paramedics can only take place after teletransmission and consultation with a cardiologist.

Based on our results and in spite of the diagnosed ACS STEMI (inferior wall and closed RCA confirmed by coronary

angiography), it was observed that the administration of nitroglycerin in pre-hospital care by emergency medical units, does not adversely affect selected biochemical parameters. Despite the lack of statistical significance, studies showed that the administration of nitroglycerin had an impact on the lower (better) values of selected biochemical parameters. In contrast, administration of nitroglycerin had a significant impact on lower results in patients in the Killip scale. The assessment was made by the cardiologist at the clinic when the patient was admitted. In light of our research, there is no conclusive evidence to indicate whether contraindication of the drug in the case of ACS STEMI regardless of the location of ECG changes at the pre-hospital stage. The lack of clear evidence indicates that both the non-use of nitroglycerin at the pre-hospital stage and the use of the drug does not adversely affect the patient's condition. However, it should be emphasized that in the 2012–2015 guidelines of the ESC, nitroglycerin is not recommended for use in patients with ACS STEMI. [2, 13]. Nevertheless, an upward trend in the frequency of drug administration was observed in our study [8].

Analysis of the data showed that emergency multidisciplinary units do not act in accordance with the guidelines of scientific associations in nearly 30% of cases in patients with ACS STEMI (as they are administering nitroglycerin in cases of inferior myocardial infarction and closure of RCA). A positive aspect of this is the fact that basic units are becoming increasingly effective [8]. In many countries, it is the paramedics that are not only the 1st ones at the scene, but also the only unit that provides assistance to the victim at the pre-hospital stage. As well as this, due to the heavy load on the system in Poland, basic units are often the only units available despite the theoretical assumption that for such cases a unit with a doctor should be dispatched. Such a situation may also indicate that medical dispatchers increasingly trust basic units with paramedics. Another problem is the lack of medical staff in "S" units, and hence the liquidation of these units for the creation of "P" units. Good education and professional improvement of paramedics allows to fully satisfy the needs of emergency operations despite the absence of a doctor in the unit.

CONCLUSIONS

The use of nitroglycerin occurred in nearly every third patient with ACS STEMI, despite criticism for the use of the drug by cardiologic associations. On the basis of the study, it has not

been clearly demonstrated that the use or non-use of nitroglycerin at the pre-hospital stage has a negative impact on the patient's condition. At the same time, it was shown that the use of nitroglycerin at the pre-hospital stage had an impact on lower values of selected biochemical parameters in patients with ACS STEMI, and that the use of nitroglycerin in patients with ACS STEMI had a significant impact on lower Killip scores.

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