American Journal of Emergency Medicine xxx (xxxx) xxx

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Tirofiban in emergency conditions: Systematic review

To the Editor,

Rapid restoration of blood flow in the infarct-related vessel in patients with ST-elevation myocardial infarction is one of the most important factors affecting survival in these patients [1,2]. Thus, rapid patient transport to a percutaneous coronary intervention (PCI) center is essential. Unfortunately, in some cases it may be extended due to logistical problems or the need to stabilize the patient's condition. In these situations, Emergency Medical Service (EMS) teams are recommended to consider the use of antiplatelet drug in the prehospital scenario, including tirofiban [3]. Tirofiban belongs to a group of glycoprotein IIb/IIIa inhibitors. While the risk of serious bleeding or thrombocytopenia with tirofiban is low [4], it could improve the blood supply to the heart in patients with high-risk non-ST-elevation acute coronary syndrome after an emergent PCI [5].

Due to the potential benefits of tirofiban in patients with acute myocardial infarction (AMI), we aimed to assess the effectiveness and safety of tirofiban based on the time of drug administration. A systematic review of literature using PubMed, Scopus, EMBASE, Web of Science, and Cochrane Central Register and Controlled Trials (CENTRAL) database was conducted from inception through March 10th, 2021 by two reviewers (L.S. and A.G.). Studies included in this meta-analysis fulfilled the following criteria (PICOS): (1) participants, patients with AMI and 18 years old or older; (2) intervention, tirofiban in the pre-hospital setting; (3) comparison, tirofiban in the hospital setting; (4) outcomes, mortality; (5) study design, randomized controlled trials, quasi-randomized or observational studies tirofiban in the pre-hospital vs. in-hospital setting for their effects on 30-days mortality and other adverse events. All statistical analyses were performed with Review Manager Software 5.4 (The Cochrane Collaboration, Oxford, Copenhagen, Denmark). All results are presented as odds ratio (OR) with 95% confidence interval (CI). Statistical testing was two-tailed. The random-effects model was used for $I^2 > 50\%$. $P < 0.05$ was considered statistically significant.

Based on the literature search, two studies which fulfilled the inclusion criteria were included in the analysis [3,4]. Pooled analysis showed that 30-day mortality was significantly higher when the tirofiban was administrated by EMS compared to PCI laboratory (4.4% vs. 1.7%, respectively; OR = 2.58; 95%CI: 1.07, 6.26; $p = 0.04$). However, the mortality difference was not significant at 1-year follow-up (4.5% vs. 3.7%, respectively; OR = 1.23; 95%CI: 0.50, 3.02; $p = 0.66$).

Moreover, the use of tirofiban by EMS compared to PCI laboratory showed no statistically significant differences in the recurrence of myocardial infarction (1.2% vs. 0.8%), stroke (0.5% vs. 0.5%), major bleeding (4.2% vs. 2.5%) or in-stent thrombosis (0.6% vs. 1.9%). (Table 1).

In conclusion, administration of tirofiban in the pre-hospital setting was associated with higher 30-day mortality compared to PCI laboratory, with comparable rates of post-infarction complications. Although according to the Acute Cardiovascular Care Association, tirofiban in the pre-hospital setting may be considered in high risk patients presenting early (<2 h) after symptom onset and as an antiplatelet bridging therapy in patients who unable to swallow oral P2Y12 inhibitors [2], the current data does not support such a recommendation.

Table 1
Polled analysis of outcomes in included studies.

Outcome	No of studies	Event in Prehospital group	Event in Cath-lab group	OR (95%CI)	*p* value	I^2 statistic
One month follow-up						
Death	2	18/409 (4.4%)	7/403 (1.7%)	2.58 (1.07, 6.26)	0.04	3%
Recurrent MI	1	3/245 (1.2%)	2/247 (0.8%)	1.52 (0.25, 9.17)	0.65	NA
Major bleeding	2	17/409 (4.2%)	10/403 (2.5%)	1.72 (0.78, 3.80)	0.18	0%
Stroke	2	2/409 (0.5%)	2/403 (0.5%)	0.97 (0.17, 5.68)	0.08	0%
In-stent thrombosis	1	1/164 (0.6%)	3/156 (1.9%)	0.31 (0.03, 3.04)	0.32	NA
Combined (death/ re-MI / stroke or major bleeding)	1	21/245 (8.6%)	11/247 (4.5%)	2.01 (0.95, 4.27)	0.07	NA
One-year follow-up						
Death	1	11/245 (4.5%)	9/244 (3.7%)	1.23 (0.50, 3.02)	0.66	NA
Recurrent MI	1	6/245 (2.4%)	9/244 (3.7%)	0.66 (0.23, 1.87)	0.43	NA
Death of re-MI	1	17/245 (6.9%)	17/244 (7.0%)	1.00 (0.50, 2.01)	1.00	NA

https://doi.org/10.1016/j.ajem.2021.03.063

Declaration of competing interest

None.

References

[1] Hermanides RS, Kilic S, van't Hof AWJ. Optimal pharmacological therapy in ST-elevation myocardial infarction—a review. Netherlands Hear J Springer. 2018;26:296–310. https://doi.org/10.1007/s12471-018-1112-6.

[2] Franchina AG, Calderone D, D'Arrigo P, et al. Mechanisms of ST-segment elevation myocardial infarction in patients with atrial fibrillation, prior stenting and long-standing chronic coronary syndrome. Cardiol J. 2020;27(1):8–15. https://doi.org/10.5603/CJ.a2020.0002.

[3] Beygui F, Castren M, Brunetti ND, et al. Pre-hospital management of patients with chest pain and/or dyspnoea of cardiac origin. A Position Paper of the Acute Cardiovascular Care Association (ACCA) of the ESC. Eur Hear J Acute Cardiovasc. Care Oxford University Press; 2020. p. 59–81. https://doi.org/10.1701/2624.26982.

[4] Juwana YB, Suryapranata H, Ottervanger JP, van't Hof AWJ. Tirofiban for myocardial infarction. Expert Opin Pharmacother Taylor & Francis. 2010;11:861–6. https://doi.org/10.1517/14656561003690000.

[5] Wei P, Huang YJ, Zuo XH, et al. Clinical effects of treatment with Tirofiban on patients with high-risk NSTE-ACS after PCI. Eur Rev Med Pharmacol Sci. 2016;20:1356–9.

Lukasz Szarpak PhD, MBA
Institute of Outcomes Research, Maria Sklodowska-Curie Medical Academy in Warsaw, Warsaw, Poland
Maria Sklodowska-Curie Białystok Oncology Centre, Białystok, Poland
Polish Society of Disaster Medicine, Warsaw, Poland

*Corresponding author at: Institute of Outcomes Research, Maria Sklodowska-Curie Medical Academy, Solidarnosci Av. 12, 03-411 Warsaw, Poland.
E-mail address: lukasz.szarpak@gmail.com

Zubaid Rafique MD
Henry JN Taub Department of Emergency Medicine, Baylor College of Medicine, Houston, TX, USA

Aleksandra Gasecka PhD, MD
Department of Cardiology, University Medical Center Utrecht, Utrecht, the Netherlands
1st Chair and Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

Milosz J. Jaguszewski MD
1st Department of Cardiology, Medical University of Gdansk, Gdansk, Poland

Krzysztof J. Filipiak MD
1st Chair and Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

22 March 2021
Available online xxxx