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Original Article

ANALYZE THE TREATMENT REGIMENS AND THROMBOSIS PROPHYLAXIS USED IN CORONARY ARTERY INTERVENTION AT INTERVENTIONAL CARDIOLOGY UNIT IN CAN THO CENTRAL GENERAL HOSPITAL

V. U. TRI-THANH[a*], NGUYEN-HUYNH DUNG-TAM[b]

[a]University of Medicine and Pharmacy at Ho Chi Minh city, Vietnam
[b]University of Medicine and Pharmacy at Can Tho city, Vietnam
Email: drthanhtrinh2000@yahoo.com

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ABSTRACT

Objective: The study was conducted to analyze the rationality of treatment regimens and thrombosis prophylaxis used in coronary artery intervention to compare to guidelines for treatment according to VNHA and recommendation of ACC/AHA at Interventional cardiology in Can Tho Central General Hospital.

Methods: The cross-sectional study was based on the data collected from entire medical records of patients at Interventional cardiology in Can Tho Central General Hospital from August 2017 to February 2018. The rationality of the antithrombotic regimen used at the Hospital is assessed through criteria such as medical combination, dosage, time to take medicine, clinical trials during the treatment.

Results: The study found that 95.6% and 90.7% were suitable for medical combination before and after PCI; 100% fit for the use of medicine; and 100% was suitable for antithrombotic agents and clinical trials during treatment time; in terms of dosage, the result showed that entrance and maintenance were 84.9% and 100% for aspirin respectively; 71.7% and 100% for clopidogrel; 100% and 94.7% for ticagrelor; 90.2-92.8% and 98.1% for enoxaparin; especially, heparin-100% anticoagulant was appropriate to recommend.

Conclusion: The study showed that treatment regimens and thrombosis prophylaxis in percutaneous coronary intervention at Interventional cardiology in Can Tho Central General Hospital were quite suitable compared to the recommendations of the Heart Association. The results from the study are a scientific basis for the Hospital to maintain or consider adjustments to improve the quality of treatment, ensure the effectiveness and safety of patients.

Keywords: Antithrombotic agents, Acute coronary syndrome, Coronary artery intervention

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INTRODUCTION

Currently, coronary artery disease tends to increase, in which myocardial infarction is serious, dangerous and fatal. In the United States, about 1,000,000 people are hospitalized every year for acute myocardial infarction and about 200,000 to 300,000 people die before hospitalization by acute myocardial infarction and the overall mortality rate is about 40 percent [1]. According to statistics of the Vietnam National Heart Institute, the rate of hospitalization for acute myocardial infarction in 2003 was 4.2%, but in 2007 it increased to 9.1% [2].

In coronary artery intervention, the use of antithrombotic agents plays an important role in preventing platelet activation process and activating clotting factors that may lead to the risk of thrombus. However, the use of this medicine can cause blood clotting disorders, increasing the risk of bleeding; sometimes, it can be life-threatening. In the age of evidence-based medicine and the "era of antiplatelet drug", in general with many new study applications in the treatment of coronary artery disease and coronary artery intervention in particular, Worldwide Heart Association, such as ACC/AHA, ESC, and Vietnam National Heart Institute, have also issued and continuously updated recommendations on using antithrombotic agents. Following to evidence-based recommendations will help people use medicine effectively and safely.

As a first-class hospital under the Ministry of Health, Can Tho Central General Hospital is also one of the pioneering units in the Mekong Delta region to implement the percutaneous coronary intervention technique (PCI-Percutaneous Coronary Intervention) from over 5 y. However, there have been no studies comparing the current treatment regimen supported by anticoagulant in the Hospital with current recommendations. Therefore, the study was conducted to analyze the rationality of treatment regimen and thrombosis prophylaxis used in coronary artery intervention compared with the guidelines of treatment according to Vietnam National Heart Institute and recommendations of ACC/AHA.

MATERIALS AND METHODS

Research design

The cross-sectional study was based on the data collected from entire medical records of patients at Interventional cardiology in Can Tho Central General Hospital from August 2017 to February 2018. Information regarding antithrombotic agents was synthesized, including the active ingredient, medical combination, dosage, time to take medicine, clinical trials during the treatment. Based on the recommendations of Vietnam Heart Association and American Heart Association ACC/AHA [2-8], the study conducted to build a set of evaluation criteria to analyze the rationality of regimens used in the treatment and thrombosis prophylaxis.

Synthesize and process data

The characteristics related to the treatment regimen and thrombosis prophylaxis were analyzed "suitable" or "unsuitable" according to the recommendations, expressed through frequency and percentage. Data was aggregated, processed and analyzed by Microsoft Excel.

RESULTS

Combination of antithrombotic agents

Prior to intervention, 4.4% of cases of medicine combination were not consistent with the recommendations, including 2 cases of clopidogrel (1.0%), 3 cases of clopidogrel+aspirin+ticagrelor+ enoxaparin (1.5%) and 4 cases of clopidogrel+enoxaparin (2.0%).

After the intervention, 9.3% of cases were not suitable for recommendations, including 2 (1.0%) cases using ticagrelor+enoxaparin and 17 (8.3%) cases using clopidogrel only+aspirin. In 19 cases of ticagrelor using after the intervention, 17 cases (8.3%) were combined with aspirin+enoxaparin, and mainly for STEMI bodies (11 cases) (table 1)

Table 1: Characteristics of combined medicine use according to clinical characteristics of disease before and after PCI

Medicine combination*	Before intervention				After intervention			
	UA	NSTEMI	STEMI	Total	UA	NSTEMI	STEMI	Total
	n=57 (%)	n=37 (%)	n=111 (%)	n=205 (%)	n=57 (%)	n=37 (%)	n=111 (%)	n=205 (%)
C	1 (1.8)	1 (2.7)	–	2 (1.0)	–	–	–	0 (0.0)
CA	20 (35.1)	8 (21.3)	8 (7.2)	36 (17.6)	6 (10.5)	7 (18.9)	4 (3.6)	17 (8.3)
CE	–	–	4 (3.6)	4 (2.0)	–	–	–	0 (0.0)
TE	–	–	–	0 (0.0)	–	–	2 (1.8)	2 (1.0)
CAE	36 (63.2)	27 (73.0)	97 (87.4)	160 (78.1)	47 (82.5)	28 (75.7)	94 (84.7)	169 (82.4)
ATE	–	–	–	0 (0.0)	4 (7.0)	2 (5.4)	11 (9.9)	17 (8.3)
CATE	–	1 (2.7)	2 (1.8)	3 (1.5)	–	–	–	0 (0.0)

*C: Clopidogrel; A: Aspirin; E: enoxaparin; T: ticagrelor.

How to take medicine and dosage

How to take antithrombotic agents in the study was consistent with the recommendations in which antiplatelet drug was taken orally and anticoagulant was used by injection.

In the group of antiplatelet drugs, the appropriate dose rates differed between active ingredients. For aspirin, cases of non-use or doses outside the recommended dose range were inappropriate. The ratio of using aspirin with the starting and maintenance doses in accordance with the recommendations was 84.9% and 100%, respectively. Cases of indicated doses of clopidogrel outside the recommended dose range or using in combination with ticagrelor were inappropriate. The appropriate rate of clopidogrel was 71.7% for the starting dose and 100% for the maintenance dose. Regarding to ticagrelor, cases that doses used outside the recommended dose range were inappropriate. The recommended starting and maintenance doses of ticagrelor were 100% and 94.7%, respectively (table 2).

Table 2: Dosage appropriateness of antiplatelet drug before and after using PCI

Active	Disease	Starting			Maintenance		
		Suitable use	Unsuitable use	Non-use	Suitable use	Unsuitable use	Non-use
Aspirin	UA n=57 (%)	51 (89.5)	–	6 (10.5)	57 (100.0)	–	–
	NSTEMI n=37 (%)	33 (89.2)	4 (10.8)	–	37 (100.0)	–	–
	STEMI n=111(%)	90 (81.1)	21 (18.9)	–	109 (98.2)	–	2 (1.8)
	Total n=205 (%)	174 (84.9)	25 (12.2)	6 (2.9)	203 (99.0)	0 (0.0)	2 (1.0)
Clopidogrel	UA n=57 (%)	40 (70.2)	17 (29.8)	–	53 (93.0)	–	4 (7.0)
	NSTEMI n=37 (%)	29 (78.4)	8 (21.6)	–	35 (94.6)	–	2 (5.4)
	STEMI n=111(%)	78 (70.3)	33 (29.7)	–	98 (88.3)	–	13 (11.7)
	Total n=205 (%)	147 (71.7)	58 (28.3)	0 (0.0)	186 (90.7)	0 (0.0)	19 (9.3)
Ticargrelor	UA n=57 (%)	–	–	57 (100.0)	4 (7.0)	–	53 (93.0)
	NSTEMI n=37 (%)	1 (2.7)	–	36 (97.3)	2 (5.4)	–	35 (94.6)
	STEMI n=111(%)	2 (1.8)	–	109 (98.2)	12 (10.8)	1 (0.9)	98 (88.3)
	Total n=205 (%)	3 (1.5)	0 (0.0)	202 (98.5)	18 (8.8)	1 (0.5)	186 (90.7)

For the anticoagulant group, the research was also noted differences in dose suitability between enoxaparin and heparin. Enoxaparin-prescribed cases included intravenous injections of 30 mg for those under 75 y of age, with a 90.2% recommended compliance rate, and subcutaneous injection, including STEMI and maintenance doses for all three clinical forms of coronary artery disease, with appropriate rates as recommended, were 92.8% and 98.1%, respectively (table 3). In the meantime, all cases in the research sample conducted PCI were assigned appropriate recommended heparin dose in the range of 70-100 UI/kg and were conducted aPPT test.

Table 3: Dosage appropriateness of enoxaparin before and after using PCI

How to take medicine and dosage	Time	Disease	Recommended		Unrecommended		Suitability*	
			Use	Non-use	Use	Non-use	Have	Do not have
Slow I. V 30 mg	Staring	UA n=57 (%)	49 (86.0)	8 (14.0)	–	–	49 (86.0)	8 (14.0)
		NSTEMI n=37 (%)	32 (86.5)	5 (13.5)	–	–	32 (86.5)	5 (13.5)
		STEMI n=111(%)	86 (77.5)	7 (6.3)	–	18 (16.2)	104 (93.7)	7 (6.3)
		Total n=205 (%)	167 (81.5)	20 (9.8)	–	18 (8.7)	185 (90.2)	20 (9.8)
Subcutaneous	Starting	STEMI n=111(%)	103 (92.8)	8 (7.2)	–	–	103 (92.8)	8 (7.2)
1 mg/kg	Maintenance	UA n=57 (%)	51 (89.5)	–	–	6 (10.5)	57 (100.0)	0 (0.0)
(<75 y old)		NSTEMI n=37 (%)	30 (81.1)	–	–	7 (18.9)	37 (100.0)	0 (0.0)
0,75 mg/kg		STEMI n=111 (%)	107 (96.4)	4 (3.6)	–	–	107 (96.4)	4 (3.6)
(≥ 75 y old)		Total n=205 (%)	188 (91.7)	4 (1.9)	–	13 (6.4)	201 (98.1)	4 (1.9)

*Suitability was considered by each clinical form and the total number of patients in the sample

Time to take medicine and treatment monitor

The time for patients used prescribed anticoagulant ranged from 2 to 8 d from the time of intervention when enoxaparin was discontinued. All cases were monitored for drug use, weight determination, AP measurement, liver function test, kidney function, hematological test, platelet test, following bleeding complications during treatment, and undesirable effects on the stomach (risk of inflammation, peptic ulcer, gastrointestinal bleeding).

DISCUSSION

The study analyzed the rationality of some key characteristics related to the treatment regimen and thrombosis prophylaxis in coronary artery intervention compared with the current recommendations at the Interventional Cardiovascular Disease Unit in Can Tho Central General Hospital in the period of 08/2017-02/2018.

The types of medicine combination in the study sample were consistent with the recommendations of the AHA/ACC and guidelines of the Vietnam Cardiology Association that included the combination of 2 antiplatelet drugs (aspirin+clopidogrel/ticagrelor) and combination of 2 antiplatelet drugs with an anticoagulant (enoxaparin) and indications for additional heparin for intervention. There were 2 cases of clopidogrel or 3 cases of combination of clopidogrel+aspirin+ticagrelor+enoxaparin that had not been mentioned in recommendations and treatment guidelines [2-8]. The combination of clopidogrel+aspirin+enoxaparin (CAE) was indicated mainly for all three clinical forms-UA, NSTEMI, STEMI, with the rates of 63.2%, 73.0%, 87.4% respectively before the intervention and 82.5%, 75.7%, 84.7% after PCI intervention. This result was relatively consistent with many other related studies conducted in Vietnam [9-11]. Many studies had demonstrated the benefits of combining aspirin with a P2Y12 receptor inhibitor for the treatment of coronary artery disease, paving the way for a new era in the treatment of acute coronary syndrome. This oral dual antiplatelet therapy enhanced the antiplatelet effect, played an important role in reducing ischemic events, improving prognosis, and reducing mortality in patients with coronary artery pathology [12]. The study recorded that 17 cases (8.3%) after using dual antiplatelet therapy between aspirin+ticagrelor and 186 cases (90.7%) combined with aspirin+clopidogrel, mainly for STEMI and PCI cases.

Regarding the dose of aspirin, there were 31 cases (15.1%) of not complying with the recommendations, in which 12 patients were prescribed with a dose of 400 mg to 648 mg. Specifically, cases used Duoplavin (clopidogrel 75 mg+aspirin 100 mg) before the intervention, if they used 4 Duoplavin tablets, they would ensure to be suitable for the recommended dose of clopidogrel (300 mg). However, the dose of aspirin (400 mg) was higher than recommended. Using aspirin at doses higher than 400 mg was recorded in 4 cases with 486 mg (324 mg+162 mg or 162 mg+324 mg) and 1 case with 648 mg (324 mg+324 mg). These cases had been recorded using aspirin at doses of 162 mg or 324 mg in the previous glands when they moved to the hospital and were assigned additional doses of aspirin 162 mg or 324 mg. In addition, the results showed that 100% of the maintenance dose of aspirin was suitable for the recommendations, which was equivalent to or higher than in relevant studies in Vietnam [10, 11]. For clopidogrel, the dosage designation that was appropriate for the defect before and after intervention was 71.7% and 100%, respectively. Compared with the related studies, the study noted a difference in using clopidogrel at different hospitals [9-11]. With important limitations of clopidogrel such as individualized response and irreversible platelet suppression [12], ticagrelor was considered an alternative method to optimize antiplatelet therapy in acute coronary syndrome, especially in the moderate and high-risk cases [12]. However, at the hospital, the number of patients prescribed ticagrelor was low, the level of the suitable recommendation was 100% (3/3 cases) for the starting dose and 94.7% (18/19 cases) for maintenance dose. This is also consistent with the research results of Nurâ€™aminH. W. *et al.*: Clopidogrel had a higher risk of MACE compared to clopidogrel in patients with CHD after PCI, but there were no significant differences in the risk of repeat revascularization, myocardial infarction [13].

The cases of using enoxaparin in the sample had a high proportion of recommended doses according to the similar studies [10], with 90.2% and 92.8%, respectively, with 30 mg intravenous injection doses for patients under 75 y old and subcutaneous dose for STEMI cases; and 98.1% for maintenance doses administering subcutaneously. Alam, S. *et al.* said that: In patients with unstable angina (UA)/non-ST-elevation myocardial infarction (NSTEMI), enoxaparin was found to be most widely prescribed low molecular weight heparin (LMWH) among other available alternatives. However, economic assessment considered fondaparinux as cost-saving therapeutic agent for initial conservative management of 2-8 d, added financial benefits over current therapies in the treatment of UA/NSTEMI. In fact, at the Can Tho Central General Hospital, the form of enoxaparin was available as an injection solution of 4000 UI/0.4 ml and 6000 UI/0.6 ml, so it was difficult to clinically withdraw the exact amount of enoxaparin at the recommended dose of 1 mg/kg or 0.75 mg/kg. The dose of enoxaparin ranged from 30 mg-90 mg corresponding to the injection volume of 0.3 ml-0.9 ml, in which the dose of 30 mg corresponding to a volume of 0.3 ml was the previous intravenous bolus dose before intervention without weight; the remaining cases ranged from 40 mg-90 mg depending on the weight of the patient. Based on the peak concentration of Xa-factor resistance of 0.2 IU/ml and 0.4 IU/ml after subcutaneous enoxaparin injection of 20 mg and 40 mg respectively, the dose of enoxaparin used for patients was assessed through Xa, to ensure Xa>0.5 IU/ml in blood during PCI [14]. It was recommended that heparin was administered intravenously during coronary artery intervention, was transfer anticoagulant veins in acute coronary syndrome and appoint a heparin dose of 60 to 100 UI/kg, in case of coronary artery intervention according to the program, the dose of 60 UI/kg can be used [1, 14]. Through surveys, all cases in the sample conducted PCI was indicated by intravenous heparin doses in the range of 70-100 UI/kg and were available for testing aPPT. Regarding to time to take medicine, the study noted the compliance with the recommendations of the anticoagulant group [2-8], specifically enoxaparin was indicated from 2 to 5 d after the intervention; heparin only injected intravenously dose 60-100 UI/kg, if the intervention time was over 1 hour that would be considered to inject another dose of heparin during the intervention depending on treatment experience and patient, no heparin was indicated after intervention. The antiplatelet drug group was indicated for longer treatment [15], the study was only conducted during the time the patient was hospitalized, so there is no basis to evaluate the appropriateness of time using as recommended.

CONCLUSION

This is one of the first studies conducted at Interventional Cardiology in Can Tho Central General Hospital in relation to evaluate the rationality of antithrombotic regimen being used with recommendations of Cardiovascular Associations. The research showed that the use of antithrombotic agents at the Hospital is quite appropriate, from which the Hospital can maintain or consider adjusting to continue improving the quality of treatment, ensuring effectiveness and safety for patients.

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AUTHORS CONTRIBUTIONS

Vu Tri-Thanh directed the study process, evaluated the research results and revised manuscript. Nguyen-Huynh Dung-Tam analyzed data, performed data interpretation and drafting of the manuscript. All authors have read and approved the final manuscript.

CONFLICTS OF INTERESTS

The data and research results are honest and the author reports no conflicts of interest in this work.

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