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Effect of the therapy of amiodarone combined with atorvastatin on cardiac function of patients with acute myocardial infarction after percutaneous coronary intervention (PCI)

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Abstract: This study aimed to investigate the effect of the therapy of amiodarone combined with atorvastatin on cardiac function of patients with acute myocardial infarction after percutaneous coronary intervention (PCI). A total of 90 patients with acute myocardial infarction who underwent PCI in the tertiary care hospital from January 2019 to January 2020 were selected as the subjects and randomly assigned into the control group and the study group, with 45 cases in each group. All the subjects had undergone PCI. The control group received amiodarone while those the study group received atorvastatin additionally. Comparison was done on the clinical efficacy, cardiac function, myocardial injury indicator and inflammatory factor between the two groups. The overall response rate (ORR) in the study group was significantly higher than that in the control group ($P<0.05$); patients in the study group had markedly better cardiac function compared with those in the control group ($P<0.001$); patients in the study group had considerably lower creatine kinase (CK) index, creatine kinase-MB (CK-MB) index, tumor necrosis factor (TNF-α) and interleukin-6 (IL-6) as opposed to those in the control group ($P<0.001$). It was observed that the therapy of amiodarone combined with atorvastatin could effectively improve the clinical indicators and cardiac function of patients with acute myocardial infarction after PCI. It is effective and worthy of wide promotion and application.

Keywords: Amiodarone, atorvastatin, acute myocardial infarction, cardiac function.

INTRODUCTION

As one of the commonly-seen diseases related to cardiovascular system, acute myocardial infarction occurs frequently in middle-aged and elderly population with a shift in the age distribution to lower age groups (Lakusic *et al.*, 2019; Sattler *et al.*, 2019). Its cause is the atherosclerosis which is associated with smoking, hypertension, obesity, diabetes and genetic factors. The clinical manifestations of acute myocardial infarction include chest pain, arrhythmia, shock and heart failure. Patients may suffer a variety of complications such as cardioschisis, post-myocardial infarction syndrome and embolism if they are not treated in time, seriously endangering their life safety and lowering their quality of life (Benak *et al.*, 2019; Sharma *et al.*, 2019; Weng *et al.*, 2019). Currently, drug therapy and surgical treatment are the main clinical measures to treat acute myocardial infarction, aiming to restore myocardial blood perfusion, maintain cardiac function and help patients survive. Although amiodarone has been found to feature high relative bioavailability and rapid onset with effective inhibition to myocardial signal transduction, low negative conversion rate coexists with high recurrence rate (Martinez-Sotillo *et al.*, 2019; Robinson *et al.*, 2019; Schupp *et al.*, 2019). Meanwhile, atorvastatin can reduce the cholesterol level of patients and improve the clinical symptoms. The combination treatment of the two medicine has a significant clinical effect. To further investigate the effect of amiodarone combined with atorvastatin on cardiac function of patients with acute myocardial infarction after PCI, the study selected 90 patients with acute myocardial infarction who had undergone PCI in a tertiary hospital from January 2019 to January 2020 as the subjects, and the results are reported as follows.

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MATERIALS AND METHODS

General data

In this study, 90 patients with acute myocardial infarction who received PCI in the tertiary care hospital from January 2019 to January 2020 were selected as the subjects and randomly assigned into a control group and a study group, with 45 cases in each group.

Ethical consideration

All subjects and their families knew the purpose and process of the study, and had signed the informed consent form. The protocol was ethically approved by the ethic committee of the tertiary care hospital (Approved No. of ethic committee: CLH-2019-045).

Inclusion criteria

(1) Aged from 18 to 75 years; (2) Met the diagnostic criteria of acute myocardial infarction; (3) Those undergoing coronary angiography had one or more arterial occlusion or subarterial occlusion; (4) Successfully treated with PCI.

Exclusion criteria
(1) Those with other cardiovascular diseases; (2) Those had a history of trauma or received surgery recently; (3) Those allergic to the tested drugs.

Methods
All subjects underwent PCI and received the therapy for controlling the heart rate, conventional antiplatelet drugs and ARB drugs.

Additionally, patients in control group were required to take 100-200mg amiodarone [Manufacturer: Sanofi (Hangzhou) Pharmaceutical Co., Ltd.; SFDA Approval No.: H199993254; Specification: 0.2g* 10 tablets], 3 times per day.

Besides the above-mentioned treatment, patients in study group were also treated with 10mg atorvastatin [Manufacturer: Sandoz (China) Pharmaceutical Co., Ltd.; SFDA Approval No.: J20140002; Specification: 20 mg * 10 tablets] once a day. The dosage could be increased according to the actual condition of patients, and the dose of atorvastatin must be under 80 mg. Treatment in both groups lasted for 21 days.

Observation of indicators
The two groups were compared on clinical efficacy. It was markedly effective if the clinical symptoms disappeared and the dynamic electrocardiogram suggested that the degree of premature contraction reduction was above 90%; it was effective if the clinical symptoms were improved and the dynamic electrocardiogram suggested that the degree of premature contraction reduction was 50%-90%; otherwise, it was ineffective. The overall response rate was equal to the markedly effective rate plus the effective rate.

Echocardiography (Manufacturer: Shanghai Photoelectric Medical Electronic Instrument Co., Ltd.; Specification: ECG-2350) was used to measure the cardiac function of patients in the two groups respectively before and after treatment, including: cardiac output (CO), left ventricular end-diastolic dimension (LVEDD) and left ventricular ejection fraction (LVEF).

Totally 3mL of fasting cubital venous blood was collected before breakfast. After centrifugation, the CK and CK-MB in myocardial injury indicators were measured by enzyme-linked immunosorbent assay respectively before and after treatment in both groups. The test was performed strictly in accordance with the instructions and operating procedures of the kits all of which were from Merck Biological Co., Ltd.

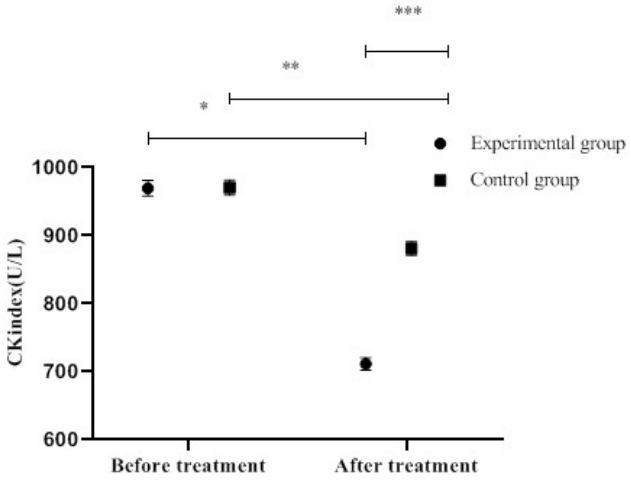
Then 3ml of fasting venous blood was collected from all subjects, and serum was separated by centrifugation. TNF-α and IL-6 were measured by enzyme-linked immunosorbent assay respectively before and after treatment in both groups. The kits were purchased from Quanzhou Jiubang Biotechnology Co., Ltd. and the test was performed strictly in accordance with the instructions of the kits.

STATISTICAL ANALYSIS

The statistical analysis was conducted with SPSS 20.0 software and Graphics drawing was carried out with GraphPad Prism 7 (GraphPad Software, San Diego, USA). The study had measurement data and enumeration data which were analyzed by t-test, $\chi 2$ test and normality Test. It indicated a statistically significant difference when $P<0.05$.

RESULTS

Comparison of general data
There was no significant difference in age, gender, BMI, location of myocardial infarction, smoking and alcohol consumption between the two groups ($P>0.05$), as shown in table 1.



Note: the abscissa represents two time points of before treatment and after treatment; and the ordinate indicates CK index, U/L;
The CK indexes in the study group before and after treatment were (969.23±11.23) U/L and (711.12±8.95) U/L, respectively;
The CK indexes in the control group before and after treatment were respectively (970.12±11.35) U/L and (876.35±10.23) U/L;
* indicated that there was a significant difference in CK index of the study group before and after treatment (t=120.573, P=0.000);
** suggested that there was a significant difference in CK index of the control group before and after treatment (t= 41.167, P=0.000);
*** stated that there was a significant difference in CK index between the two groups of patients after treatment (t=81.545, P=0.000).

Fig. 1: Comparison of CK index (X ± S)

Comparison of clinical efficacy
The overall response rate of the study group was significantly higher than that of the control group ($P<0.05$), as shown in table 2.

Table 1: Comparison of general data [n (%)]

	Study group (n = 45)	Control group (n = 45)	χ2 or t	P
Sex			0.045	0.832
Male	26 (57.78)	25 (55.56)		
Female	19 (42.22)	20 (44.44)		
Age (years)			0.085	0.933
	56.23 ± 3.6	56.29 ± 3.1		
BMI (kg/m2)			0.501	0.618
	24.89 ± 1.64	25.06 ± 1.58		
Myocardial infarction site				
Myocardial infarction site				
Left ventricular posterior wall	11 (24.44)	9 (20.00)	0.257	0.612
Posterior wall of right ventricle	9 (20.00)	9 (20.00)	0.000	1.000
Anterior wall of left ventricle	10 (22.22)	11 (24.44)	0.062	0.803
Anterior wall of right ventricle	10 (22.22)	11 (24.44)	0.062	0.803
Smoking			0.194	0.660
Yes	30 (66.67)	28 (62.22)		
No	15 (33.33)	17 (37.78)		
Alcohol consumption			0.421	0.517
Yes	29 (64.44)	26 (57.78)		
No	16 (35.56)	19 (42.22)		
Residence			0.051	0.822
Town	31 (68.89)	30 (66.67)		
Rural	14 (31.11)	15 (33.33)		

Table 2: Comparison of clinical efficacy [n (%)]

Group	N	Markedly effective	Effective	Ineffective	Overall response rate
Study group	45	66.67% (30/45)	28.89% (13/45)	4.44% (2/45)	95.56% (43/45)
Control group	45	48.89% (22/45)	26.67% (12/45)	24.44% (11/45)	75.56% (34/45)
x^2					7.283
P					0.007

Table 3: Comparison of cardiac function ($\bar{x}$ ± s)

Group	N	CO (L/min)	LVEDD (min)	LVEF (%)
Study group	45	4.62 ± 0.67	39.99 ± 3.52	55.22 ± 8.98
Control group	45	3.11 ± 0.55	52.37 ± 4.69	41.21 ± 8.36
		11.686	14.162	7.660
		0.000	0.000	0.000

Comparison of cardiac function

It was detected that patients in the study group had significantly better cardiac function compared with those in the control group (P<0.05), as shown in table 3.

Comparison of CK index

The CK index of the study group was considerably lower than that of the control group after treatment (P<0.05), as shown in fig. 1.

Comparison of CK-MB index

The CK-MB index of the study group was significantly lower than that of the control group after treatment (P<0.05), as shown in fig. 2.

Comparison of TNF-α index

The study found that the TNF-α index of the study group was significantly lower than that of the control group after treatment (P<0.05), as shown in fig. 3.

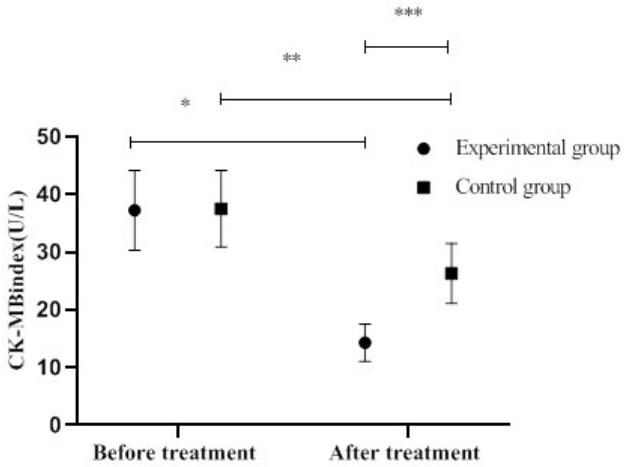
Comparison of IL-6 index

The study group presented significantly lower IL-6 index compared with the control group after treatment (P<0.05), as shown in fig. 4.

DISCUSSION

Acute myocardial infarction featured high mortality and disability rate, while the inducement is related to notably emotional fluctuations overeating and external

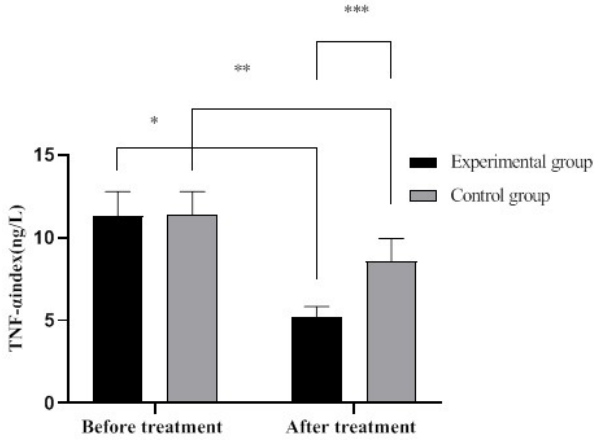
environmental factors (Deng *et al.*, 2019; Kim *et al.*, 2019).



Note: the abscissa represents two time points of before treatment and after treatment; and the ordinate indicates CK-MB index, U/L;
The CK-MB indexes of the study group were respectively (37.25±6.88) U/L before treatment and (14.32±3.25) U/L after treatment;
The CK-MB indexes of the control group were respectively (37.54±6.62) U/L before treatment and (26.32±5.21) U/L after treatment;
*indicated that there was a significant difference in CK-MB indexes of the study group before and after treatment (t=20.215, P=0.000);
**indicated that there was a significant difference in CK-MB index of the control group before and after treatment (t=8.934, P=0.000);
***suggested that there was a significant difference in CK-MB index between the two groups after treatment (t=13.109, P=0.000).

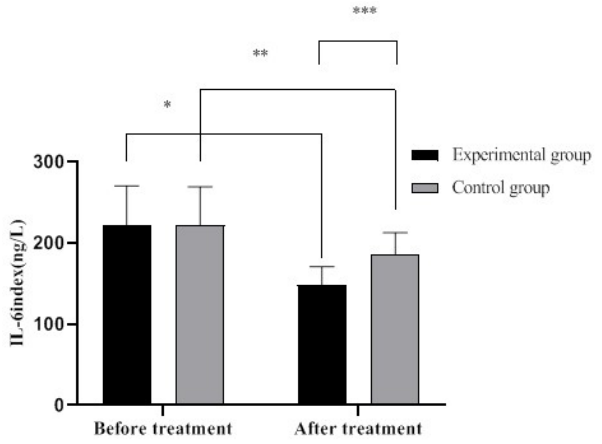
Fig. 2: Comparison of CK-MB index ($\bar{x}$ ± s)

Studies have found that more than 50% of such patients experience prodromal symptoms 1 week to 2 weeks before its onset, with ventricular premature contraction as its main manifestation, so it is important to take effective clinical treatment measures (Ghasemi *et al.*, 2019; Wang *et al.*, 2019; Wildes *et al.*, 2019). As a widely used cardiac catheterization technique in clinical practice, PCI can effectively dredge the stenotic or even occluded coronary artery to improve myocardial blood perfusion. However, some patients present vascular stenosis and thrombosis after PCI treatment (Ahmed *et al.*, 2019; Ma *et al.*, 2019; Snela *et al.*, 2019). Amiodarone has a long half-life, which can prolong the action potential and effective refractory period of myocardial tissues and eliminate reentrant activation, thereby further inhibiting the sodium influx in atrial and myocardial conduction fibers and slowing the conduction velocity. Taking amiodarone does not achieve the desired effect though it can improve cardiac function and reduce peripheral vascular resistance in patients (Guo *et al.*, 2019; Hosseinzadeh *et al.*, 2019; Varghese and Kochupappy Ravi, 2019). Atorvastatin, as an HMG-coA reductase inhibitor, is a common lipid-lowering drug which can reduce the cholesterol level of patients, promote reductase synthesis, increase low-density lipoprotein receptor synthesis and effectively improve the angiocutaneous function and clinical symptoms such as the inflammatory response, having great significance for the treatment of acute myocardial infarction (Qin *et al.*, 2020; Schamroth Pravda *et al.*, 2020; Zakeri *et al.*, 2020).



Note: the abscissa represents two time points of before treatment and after treatment; and the ordinate indicates TNF-α index, ng/L;
The study group had the level of TNF-α (11.33±1.45) ng/L before treatment and (5.21±0.62) ng/L after treatment.
The control group had the level of TNF-α (11.37±1.41) ng/L before treatment and (8.57±1.39) ng/L after treatment.
*indicated that there was a significant difference in TNF-α index of the study group before and after treatment (t=26.033, P=0.000);
**stated that there was a significant difference in TNF-α index of the control group before and after treatment (t=9.487, P=0.004);
***suggested that there was a significant difference in TNF-α index between the two groups after treatment (t=14.809, P=0.000).

Fig. 3: Comparison of TNF-α index (X ± s)



Note: the abscissa represents two time points of before treatment and after treatment and the ordinate indicates IL-6 index, ng/L;
The study group obtained the level of IL-6 (221.32±49.27) ng/L before treatment and (148.23±22.62) ng/L after treatment.
The control group obtained the level of IL-6 (222.13±47.26) ng/L before treatment and (185.32±27.41) ng/L after treatment.
*indicated a significant difference in IL-6 index of the study group before and after treatment (t=9.044, P=0.000);
**stated a significant difference in IL-6 index of the control group before and after treatment (t=4.519, P=0.000);
**suggested a significant difference in IL-6 index between the two groups of patients after treatment (t=7.001, P=0.000).

Fig. 4: Comparison of IL-6 index ($\bar{x}$ ± s)

The treatment of amiodarone combined with atorvastatin can not only reduce the level of inflammatory factors and oxygen consumption, increase blood flow, and relieve the clinical symptoms of patients, but also improve the cardiac function and avoid the occurrence of adverse events. This study found that the TNF-α index and the IL-6 index in the study group were significantly lower than those in the control group after treatment ($P<0.05$), suggesting that the inflammatory factor level index was related to atherosclerosis of patients. The increase of inflammatory factor level could reconstruct myocardial cells, promote the adhesion and aggregation of inflammatory cells in body, and further aggravate the TNF-α index and the IL-6 index. In contrast, patients in the study group obtained significantly lower inflammatory factor level compared with those in the control group, further demonstrating better effect of the combined drugs than a single drug.

It has been clinically observed that the treatment of amiodarone combined with atorvastatin can reduce the mortality and morbidity, effectively improve clinical indicators, and promote the rapid recovery of physical function of patients (Chen *et al.*, 2020; Gasecka *et al.*, 2020). The results of this study showed that the overall response rate after treatment in the study group was significantly higher than that in the control group ($P<0.05$), consistent with the findings of scholars Kalyan *et al.* (Kurapati *et al.*, 2019). Their article pointed that "the effective rate of the study group was 98% higher than that of the control group, with a significant difference ($P<0.05$)", suggesting that the tested therapy had a significant effect in the treatment of acute myocardial infarction and could effectively improve the cardiac function of patients.

CONCLUSION

Amiodarone plus atorvastatin could effectively reduce the level of inflammatory factors, reduce myocardial injury and improve cardiac function, which is worthy of promotion and application.

REFERENCES

Ahmed EA, Abd-Eldayem AM and Aboulhagag NA (2019). The possible protective effects of vitamin D and l-carnitine against used atorvastatin-induced myopathy and hepatotoxicity. *Comp. Clin. Path*, **28**(28): 1751-1759.

Benak A, Kohari M, Herczeg A, Makai A, Bencsik G, Saghy L and Pap R (2019). Selecting persistent atrial fibrillation patients for pulmonary vein isolation based on the response to amiodarone: Efficacy of the one step back strategy. *J. Interv. Card Electrophysiol.*, **56**(56): 291-297.

Chen G, Huang S, Song F, Zhou Y and He X (2020). Lnc-Ang362 is a pro-fibrotic long non-coding RNA promoting cardiac fibrosis after myocardial infarction by suppressing Smad7. *Arch Biochem Biophys*, **685**(685): 108354.

Deng Y, Zou W, Chen G, Shangguan S, Zhou F, Jiang W and Li X (2019). Comparative studies on the effects of different doses of atorvastatin combined with aspirin on inflammatory cytokines and carotid plaques in patients with ischemic cerebrovascular disease. *Int. J. Neurosci.*, **129**(129): 1133-1138.

Gasecka A, Nieuwland R, Budnik M, Dignat-George F, Eyileten C, Harrison P, Huczek Z, Kaplon-Cieslicka A, Lacroix R, Opolski G, Pluta K, van der Pol E, Postula M, Leroyer A, Siljander P, Sturk A and Filipiak KJ (2020). Randomized controlled trial protocol to investigate the antiplatelet therapy effect on extracellular vesicles (AFFECT EV) in acute myocardial infarction. *Platelets*, **31**(31): 26-32.

Ghasemi A, Ghashghai Z, Akbari J, Yazdani-Charati J, Salehifar E and Hosseinimehr SJ (2019). Topical atorvastatin 1% for prevention of skin toxicity in patients receiving radiation therapy for breast cancer: A randomized, double-blind, placebo-controlled trial. *Eur J. Clin. Pharmacol.*, **75**(75): 171-178.

Guo X, Wang L, Xia X, Wang P and Li X (2019). Effects of atorvastatin and/or probucol on recovery of atherosclerosis in high-fat-diet-fed apolipoprotein E-deficient mice. *Biomed Pharmacother*, **109**(109): 1445-1453.

Hosseinzadeh A, Bahrampour Juybari K, Kamarul T and Sharifi AM (2019). Protective effects of atorvastatin on high glucose-induced oxidative stress and mitochondrial apoptotic signaling pathways in cultured chondrocytes. *J. Physiol. Biochem.*, **75**(75): 153-162.

Kim IS, Kim HJ, Yu HT, Kim TH, Uhm JS, Kim JY, Joung B, Lee MH and Pak HN (2019). Non-vitamin K antagonist oral anticoagulants with amiodarone, P-glycoprotein inhibitors, or polypharmacy in patients with atrial fibrillation: Systematic review and meta-analysis. *J. Cardiol*, **73**(73): 515-521.

Kurapati K, Parvathareddy KMKR, Srinivas R and Nagula P (2019). Study of efficacy of tissue Doppler imaging in diagnosing systolic and diastolic dysfunction and comparison to the conventional methods of left ventricular function assessment in heart failure patients. *Heart India*, **7**(7): 165.

Lakusic N, Slivnjak V, Ciglenecki N and Cerovec D (2019). Torsades de pointes in elderly patient with paroxysmal atrial fibrillation treated by short-term parenteral amiodarone therapy. *Acta Clin Croat*, **58**(58): 751-756.

Ma YB, Chan P, Zhang Y, Tomlinson B and Liu Z (2019). Evaluating the efficacy and safety of atorvastatin + ezetimibe in a fixed-dose combination for the treatment of hypercholesterolemia. *Expert Opin Pharmacother*, **20**(20): 917-928.

Martinez-Sotillo N, Pinto-Martinez A, Hejchman E and Benaim G (2019). Antiproliferative effect of a benzofuran derivate based on the structure of amiodarone on *Leishmania donovani* affecting mitochondria, acidocalcisomes and intracellular Ca^{2+} homeostasis. *Parasitol Int.*, **70**(70): 112-117.

Qin X, Luo J, Qin L, Liu B, Li H, Li Z, Yang W, Xue R, Yang X, Gong M, Shi B, Wei Y and Ge J (2020). Long-term impact of thrombus aspiration in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Am. J. Cardiol.*, **125**(125): 1471-1478.

Robinson D, Hand G, Ausman J and Hackett A (2019). Brugada pattern exposed with administration of amiodarone during emergent treatment of ventricular tachycardia. *Am. J. Emerg. Med.*, **37**(37): 376 e373-376 e377.

Sattler SM, Lubberding AF, Skibsbye L, Jabbari R, Wakili R, Jespersen T and Tfelt-Hansen J (2019). Amiodarone treatment in the early phase of acute myocardial infarction protects against ventricular fibrillation in a porcine model. *J. Cardiovasc Transl Res.*, **12**(12): 321-330.

Schamroth Pravda N, Witberg G, Zusman O, Landes U, Bental T, Assali A, Vaknin Assa H, Greenberg G, Codner P, Perl L and Kornowski R (2020). A risk score based on simple angiographic characteristics to aid in choosing the optimal revascularization strategy for patients with multivessel disease presenting with ST-elevation myocardial infarction. *Coron Artery Dis*, **31**(31): 597-605.

Schupp T, Behnes M, Reiser L, Bollow A, Taton G, Reichelt T, Ellguth D, Engelke N, Ansari U, El-Battrawy I, Bertsch T, Weiss C, Nienaber C, Lang S, Akin M, Mashayekhi K, Borggrefe M and Akin I (2019). Prognostic impact of beta-blocker compared to combined amiodarone therapy secondary to ventricular tachyarrhythmias. *Int. J. Cardiol.*, **277**(277): 118-124.

Sharma SP, Turagam M, Atkins D, Bommana S, Jeffrey C, Newton D, Nydegger C, Carroll H, Gopinathannair R, Natale A and Lakkireddy D (2019). Safety of rapid switching from amiodarone to dofetilide in atrial fibrillation patients with an implantable cardioverter-defibrillator. *Heart Rhythm.*, **16**(16): 990-995.

Snela A, Jadach B, Froelich A, Skotnicki M, Milczewska K, Rojewska M, Voelkel A, Prochaska K and Lulek J (2019). Self-emulsifying drug delivery systems with atorvastatin adsorbed on solid carriers: Formulation and in vitro drug release studies. *Colloids Surf*, **577**(577): 281-290.

Varghese SJ and Kochupappy Ravi T (2019). Liquid chromatography/mass spectrometry method for the simultaneous determination of atorvastatin and telmisartan in human plasma. *Anal. Chem.*, **9**(9): 552-563.

Wang J, Cheng X, Zhang X, Liu G, Wang Y, Zhou W and Zhang Y (2019). A combination of indomethacin and atorvastatin ameliorates cognitive and pathological deterioration in PrP-hAbetaPPswe/PS1(DeltaE9) transgenic mice. *J. Neuroimmunol.*, **330**(330): 108-115.

Weng J, Tu M, Wang P, Zhou X, Wang C, Wan X, Zhou Z, Wang L, Zheng X, Li J, Wang Z, Wang Z and Chen C (2019). Amiodarone induces cell proliferation and myofibroblast differentiation via ERK1/2 and p38 MAPK signaling in fibroblasts. *Biomed. Pharmacother.*, **115**(115): 108889.

Wildes TJ, Grippin A, Fasanya H, Dyson KA and Brantly M (2019). Effect of atorvastatin on humoral immune response to 23-valent pneumococcal polysaccharide vaccination in healthy volunteers: The StatVax randomized clinical trial. *Vaccine*, **37**(37): 1313-1324.

Zakeri MA, Khoshnood Z, Dehghan M and Abazari F (2020). The effect of the continuous care model on treatment adherence in patients with myocardial infarction: A randomised controlled trial. *J. Res. Nurs.*, **25**(25): 54-65.