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Article

Effects of Indobufen Combined with Clopidogrel on Left Ventricular Function and Inflammatory Factors in Patients after PCI

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Abstract

Background: Percutaneous intracoronary intervention (PCI) is the preferred method for treating coronary heart disease. However, the insufficient coagulation function after the procedure may lead to poor vascular reperfusion, thereby affecting cardiac function. Indobufen and clopidogrel have antiplatelet and anti-inflammatory effects, but the impact of their combined use on left ventricular function and inflammatory factors in patients after PCI remains unclear. This study aimed to explore the influence of indobufen combined with clopidogrel on left ventricular function and inflammatory factors in patients after PCI. **Methods**: Medical records of 100 patients who underwent PCI surgery were selected for retrospective analysis. Their admission time ranged from January 2022 to June 2023. All research subjects who met the inclusion criteria were assigned to two groups according to different treatment methods with 57 cases in the control and 43 cases in the observation. The left ventricular function, inflammatory factors, coagulation function levels, and occurrence of complications were compared between the two groups. **Results**: After going through treatment, the levels of left ventricular end-diastolic volume, left ventricular end-systolic diameter, and left ventricular end-diastolic diameter of the observation group were significantly lower than those of the control. The ejection fraction significantly increased in the observation group, and the difference between two groups was significant ($p < 0.05$). Furthermore, the level of high-sensitivity C-reactive protein in the observation was significantly lower than that of the control benefiting from treatment with a significant difference ($p < 0.05$). The activated partial thromboplastin time, prothrombin time, and thrombin time levels of all patients significantly increased ($p < 0.05$) with no difference between the two groups ($p > 0.05$). The complication rate in the control patients was 17.54% (10/57), and that in the observation patients was 9.30% (4/43). No significant difference existed between the two groups ($p > 0.05$). **Conclusions**: Indobufen combined with clopidogrel treatment for patients after PCI significantly improved left ventricular function, inhibited inflammatory response, enhanced coagulation function, and had high safety. These results can provide some basis for the treatment of patients after clinical PCI.

Keywords

indobufen; clopidogrel; PCI; left ventricular function; inflammatory factors

Introduction

One of the major causes of mortality around the world is coronary heart disease. Over the past few years, along with the changes in human lifestyle, the incidence of coronary heart disease has been increasing [1,2]. According to statistics in 2019, over 17 million patients died owing to coronary heart disease. By 2030, over 23 million people are expected to suffer from coronary heart disease [3]. Coronary atherosclerosis is an important cause of coronary heart disease [4]. Percutaneous intracoronary intervention (PCI) is the preferred method for treating coronary atherosclerosis. It plays an important role in unblocking blood vessels, improving blood flow, restoring myocardial perfusion, and enhancing prognosis [5–7]. A study [8] has found that the coagulation function of patients after PCI is insufficient. It may cause postoperative no reflow of blood vessels and cause transient coronary artery ischemia, thereby affecting cardiac function. In the past, clopidogrel and aspirin were commonly used clinically for anticoagulation treatment, but the combined treatment of the two drugs lasts longer and may increase the risk of bleeding [9]. Indobufen is a phenylbutyric acid derivative that can inhibit the synthesis of thromboxane. Indobufen also has good tolerance and a low incidence of adverse reactions [10]. Clopidogrel is a commonly used antiplatelet prodrug that can effectively inhibit platelet activation and aggregation. It plays some roles in inhibiting inflammatory responses [11,12]. Some studies have found that indobufen and clopidogrel can perform better in treating ischemic stroke [3,13]. Nevertheless, the effect of indobufen combined with clopidogrel on left ventricular function and inflammatory factors in patients after PCI remains unclear. An in-depth study on the influences

Table 1. Analysis and comparison of basic information between the two groups [examples (%), ($\bar{x} \pm s$)].

Group	Control (n = 57)	Observation (n = 43)	χ^2/t	p
Gender (%)			0.007	0.932
Female	27 (47.37)	20 (46.51)		
Male	30 (52.63)	23 (53.49)		
Age	54.32 ± 5.73	55.63 ± 5.17	1.199	0.234
Fasting blood glucose (mmol/L)	5.69 ± 0.62	5.53 ± 0.58	1.331	0.187
Glycated hemoglobin (%)	6.20 ± 0.88	6.14 ± 0.96	0.313	0.755
Body mass index (kg/m^2)	22.71 ± 2.49	22.38 ± 3.61	0.546	0.586
Blood pressure (mmHg)				
Systolic blood pressure	136.82 ± 17.62	138.42 ± 21.23	0.399	0.691
Diastolic blood pressure	79.09 ± 9.62	79.53 ± 10.87	0.214	0.831
Blood lipids (mmol/L)				
Low-density lipoprotein	2.50 ± 0.86	2.42 ± 0.69	0.489	0.626
Total cholesterol	4.46 ± 0.79	4.51 ± 0.83	0.305	0.761
Triglycerides	1.64 ± 0.73	1.58 ± 0.66	0.400	0.690
Diabetes (%)	21 (36.84)	15 (34.88)	0.041	0.840
Hypertension (%)	24 (42.11)	17 (39.53)	0.067	0.796
Smoking history (%)	16 (28.07)	14 (32.56)	0.235	0.628
Family history (%)	8 (14.04)	4 (9.30)	0.520	0.471
Number of diseased branches (%)			1.167	0.280
Single	26 (45.61)	15 (34.88)		
Multiple branches	31 (54.39)	28 (65.12)		
Acute myocardial infarction (%)	25 (43.86)	18 (41.86)	0.040	0.842

of indobufen combined with clopidogrel on left ventricular function and inflammatory factors in patients after PCI can help further elucidate the effectiveness and safety of this treatment strategy. Such research can provide a more scientific basis for individualized treatment of patients after PCI. This has important clinical and social significance for improving patients' quality of life and reducing the occurrence of cardiac events.

Materials and Methods

Basic Information

This work was approved by the Ethics Committee of our Hospital (2024L-02-16). All procedures were conducted in accordance with the ethical standards of the 1964 Helsinki Declaration and its subsequent amendments. Our data were those of retrospective anonymous patients and did not involve patient intervention or human tissue, so informed consent was exempted. A retrospective analysis of the medical notes of 100 patients with coronary heart disease who underwent PCI surgery was included. Their admission time ranged from January 2022 to June 2023. According to different treatments, all patients who met the inclusion criteria were separated into two groups: 57 in the control and 43 in the observation. Informed-consent forms were obtained.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows. (1) The age of patients was between 20 and 65. (2) The disease type of included patients was acute myocardial infarction. (3) Patients had clear cognitive function and can cooperate with the relevant research tasks. (4) Patients had not received coronary angiography treatment in the past or antiplatelet treatment within 3 months before participating in the study.

The exclusion criteria were as follows. (1) Patients were intolerant to surgery. (2) Patients were allergic to active substances or any component of this product, had severe liver damage, or had active pathological bleeding such as intracranial hemorrhage. (3) Patients had functional abnormalities in liver, kidney, and other organs. (4) Patients had infectious diseases such as hepatitis B and Acquired Immune Deficiency Syndrome (AIDS). (5) Patients had other malignant tumors. (6) Patients had a history of digestive system diseases. (7) Patients had incomplete data.

Methods

All patients received PCI treatment. After treatment, both groups had their vital signs maintained on a routine basis, closely monitored for their clinical symptoms, and were given treatments such as warmth and oxygen inhalation. Spironolactone (Wuhan Zhonglian Group Siyao Pharmaceutical Co. Ltd., Wuhan, Hubei, China; approval number: Sinopharm Zhunzi H42020343; specification: 100 mg) was

Table 2. Analysis and comparison of left ventricular function indicators between the two groups ($\bar{x} \pm s$).

Group	Number of examples	LVESV (mL)		t	p	LVEDV (mm)		t	p
		Before treatment	After treatment			Before treatment	After treatment		
Control	57	52.09 ± 11.95	45.16 ± 10.78	3.250	0.002	112.25 ± 14.94	101.44 ± 11.89	4.272	<0.001
Observation	43	52.44 ± 10.21	39.79 ± 9.51	5.944	<0.001	107.93 ± 9.42	95.81 ± 8.85	6.147	<0.001
t		0.159	2.636			1.660	2.603		
p		0.874	0.010			0.100	0.011		

LVESV, left ventricular end systolic volume; LVEDV, left ventricular end-diastolic volume.

Table 2. Continued. Analysis and comparison of left ventricular function indicators between the two groups ($\bar{x} \pm s$).

Group	Number of examples	LVESD (mm)		t	p	LVEDD (mm)		t	p
		Before treatment	After treatment			Before treatment	After treatment		
Control	57	31.19 ± 4.80	25.65 ± 2.52	7.721	<0.001	50.96 ± 4.61	42.11 ± 5.60	9.220	<0.001
Observation	43	32.21 ± 3.83	24.02 ± 4.43	9.161	<0.001	50.70 ± 6.14	39.37 ± 5.25	9.193	<0.001
t		1.177	2.320			0.249	2.504		
p		0.242	0.022			0.804	0.014		

Table 2. Continued. Analysis and comparison of left ventricular function indicators between the two groups ($\bar{x} \pm s$).

Group	Number of examples	LVEF (%)		t	p
		Before treatment	After treatment		
Control	57	54.56 ± 4.36	59.70 ± 2.86	7.439	<0.001
Observation	43	54.09 ± 2.29	61.53 ± 4.88	9.061	<0.001
t		0.640	2.354		
p		0.524	0.021		

LVEF, left ventricular ejection fraction.

given in batches every day for at least 2 weeks, and then the dosage was adjusted as appropriate to promote the discharge of electrolyte and water (Shakubaqu/Valsartan; Beijing Novartis Pharmaceutical Co. Ltd., Beijing, China; approval number: Sinopharm Zhunzi J 22). Based on the patient's tolerance, it was doubled every 2–4 weeks until the target maintenance dose of 200 mg twice a day was reached. Ventricular remodeling and propranolol (Northeast Pharmaceutical Group Shenyang No.1 Pharmaceutical Co. Ltd., Shenyang, Liaoning, China; approval number: National Medicine Zhunzi H21021826; specification: 10 mg) were improved by administering 10–30 mg per day taken two to three times a day to control the ventricular rate. Dapagliflozin (AstraZeneca Pharmaceutical Co. Ltd., London, UK; National Medicine Standard Word HJ20170119; specification: 10 mg) was given to control blood sugar and other basic treatments. The control group was given aspirin (Shenyang Kangzhi Pharmaceutical Co. Ltd., Shenyang, Liaoning, China; National Drug Approval No. H10960331; specification: 50 mg × 100 tablets). The initial dose was 300 mg, and the maintenance dose was 50–100 mg + clopidogrel daily (Henan Xinshuaike Pharmaceutical Co. Ltd., Xiangcheng, Henan, China; National Drug Approval No. H20123115; specification: 25 mg). The recommended dose for adults or the elderly was 75 mg once a day, taken with or without food and 75 mg orally, q.d. The observation group was given clopidogrel combined with indobufen (Hangzhou Zhongmei Huadong, Hangzhou, Zhejiang, China; approval number: National Medicine Zhunzi H20163311; specification: 200 mg × 7 tablets) twice a day, 100 mg each time, and taken orally after meals. It was forbidden to patients with congenital or acquired bleeding and pregnant or lactating women. Patients in both groups were treated with drugs continuously for 3 months.

Observation Indicators

(1) Left ventricular function: The left ventricular end systolic volume (LVESV), left ventricular end diastolic volume, left ventricular end systolic diameter, left ventricular end diastolic diameter (LVEDD), and left ventricular ejection fraction (LVEF) of patients were detected using color Doppler ultrasonic diagnostic instrument (Zhejiang Jiesheng Medical Equipment Co. Ltd., Hangzhou, Zhejiang, China, model: Vivid E95) before and after PCI.

(2) Inflammatory factors: Median elbow venous blood (4.5 mL) with fasting for more than 8 h was collected before and after treatment. The supernatant was centrifuged for 15 min with a centrifugal force of 4500 r/min and a centrifugal radius of 13.5 cm by using a low-temperature high-speed centrifuge (Shanghai Shujie Biotechnology Co. Ltd., Shanghai, China, model: BC-6800). Serum high-sensitivity C-reactive protein (Hs-CRP) was detected by enzyme-linked immunosorbent assay.

Table 3. Analysis and comparison of inflammatory factor indicators between the two groups ($\bar{x} \pm s$/M [P25, P75]).

Group	Number of examples	Hs-CRP (mg/L)		*t*/Z	*p*
		Before treatment	After treatment		
Control	57	6.00 (2.00, 10.00)	2.60 (2.00, 3.20)	–4.465	<0.001*
Observation	43	6.45 ± 3.12	1.30 ± 0.40	10.744	<0.001
t		0.218	10.492		
p		0.828	<0.001		

Notes: * showed the results of Mann-Whitney U test. Hs-CRP, high-sensitivity C-reactive protein.

Table 4. Comparison of coagulation function analysis between the two groups ($\bar{x} \pm s$).

Group	Number of examples	APTT (s)		*t*	*p*	PT (s)		*t*	*p*
		Before treatment	After treatment			Before treatment	After treatment		
Control	57	27.19 ± 3.50	33.58 ± 4.06	8.988	<0.001	12.18 ± 2.36	15.89 ± 2.77	7.711	<0.001
Observation	43	27.60 ± 2.31	32.20 ± 3.73	6.886	<0.001	12.58 ± 1.80	14.79 ± 3.63	3.531	0.001
t		0.659	1.752			0.967	1.708		
p		0.511	0.083			0.336	0.092		

APTT, activated partial thromboplastin time; PT, prothrombin time.

(3) Coagulation function: The changes in coagulation function indices including activated partial thromboplastin time (APTT), prothrombin time (PT), and thrombin time (TT) were detected with an automatic coagulation analyzer (Hersch Biomedical Co. Ltd., Ningbo, Zhejiang, China, model: ACL TOP 750).

(4) Complications: We observed the occurrence of complications such as angina pectoris, stent thrombosis, bleeding, and allergy during the treatment and follow-up period.

Statistical Methods

All data analyses in the study were conducted using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Digital data such as gender and incidence of complications were represented by [n (%)]. The two comparisons passed independent samples, and the χ^2 test was used. When $1 \leq$ theoretical frequency < 5, we used the chi-square test correction formula. To determine whether the data follow a normal distribution, the Kolmogorov-Smirnov test was employed. For data that conform to a normal distribution, results were expressed as means ± standard deviations ($\bar{x} \pm s$), and a *t*-test was conducted. For data that do not follow a normal distribution, results were presented using M [P25, P75], and the Wilcoxon rank-sum test was performed. According to the analysis of covariance adjusted by baseline value, we considered the statistical result $p < 0.05$ to be statistically significant.

Results

Analysis of Two Groups of Basic Data

No significant existed between the control and observation group in terms of gender, diabetes, hypertension, smoking history, family medical history, number of lesions, proportion of lesion types, age, fasting blood glucose, glycated hemoglobin, body mass index, blood pressure, and blood lipid levels ($p > 0.05$; Table 1).

Analysis of Left VentricularFunction Indicators in the Two Groups

Compared with no treatment, the levels of LVESV, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic diameter (LVESD), and LVEDD in the control and observation groups were slumped after treatment. The level of LVEF greatly increased. An obvious difference existed between the two groups ($p < 0.05$). Compared with the control group, the levels of LVESV, LVEDV, LVESD, and LVEDD in the observation group significantly decreased. Conversely, the level of LVEF significantly increased. An obvious difference also existed between the two groups ($p < 0.05$; Table 2).

Analysis of Inflammatory Factor Indicators between the Two Groups

Compared with no treatment, the levels of Hs-CRP in all patients significantly decreased after undergoing treatment. A significant difference existed between the two groups ($p < 0.05$). Compared with the control, the level of Hs-CRP in the observation group was lower with a significant difference ($p < 0.05$; Table 3).

Table 4. Continued. Comparison of coagulation function analysis between the two groups ($\bar{x} \pm s$).

Group	Number of examples	TT (s)		t	p
		Before treatment	After treatment		
Control	57	5.29 ± 1.27	12.79 ± 5.35	10.303	<0.001
Observation	43	5.07 ± 2.24	13.59 ± 4.35	11.429	<0.001
t		0.604	0.826		
p		0.547	0.411		

TT, thrombin time.

Table 5. Analysis and comparison of patient complications [n (%)].

Group	Number of examples	Angina pectoris	Stent thrombosis	Bleeding	Allergy	Total
Control	57	2 (3.51)	3 (5.26)	4 (7.02)	1 (1.75)	10 (17.54)
Observation	43	1 (2.33)	0 (0.00)	1 (2.33)	2 (4.65)	4 (9.30)
χ^2						1.383
p						0.240

Analysis of Coagulation Function in Two Groups

After treatment, the levels of APTT, PT, and TT were significantly higher in both groups than they were before treatment. A significant difference existed between the two groups ($p < 0.05$). However, no significant difference existed between the observation and control groups ($p > 0.05$; Table 4).

Analysis of Patient Complications

The morbidity of complications in the control group was 17.54% (10/57), and that in the observation group was 9.30% (4/43). The difference was not significant ($p > 0.05$; Table 5).

Discussion

The stability of plaque plays a crucial role in the occurrence and expansion of coronary atherosclerotic diseases, and inflammatory response are inseparably related to the stability of plaque [14,15]. PCI is the basis of treatment of coronary heart disease patients. It can improve left ventricular function and improve lifespan, but not all patients recover left ventricular function after PCI [16,17]. Studies have found [18] that giving patients drugs to regulate platelet aggregation, vascular endothelial function, and inflammatory response after PCI can effectively reduce myocardial damage and inhibit thrombosis. Adjuvant medical therapy may play an irreplaceable role in optimizing patient outcomes after PCI.

Left ventricular function is one of the important factors determining the prognosis of patients with coronary heart disease [19]. Indobufen is an antiplatelet drug. A previous study has found that it can play a good role in the treatment of atherosclerotic ischemic heart disease and peripheral vascular diseases with less adverse reactions [20]. According to a previous report [21], the combined action of indobufen and Tigrello can obviously reduce LVEDD and LVESD, increase LVEF, effectively improve patients' new function, and improve myocardial blood-flow reperfusion. In this study, after treatment, the levels of LVEV, LVEV, LVESD, and LVEDD in the observation group significantly decreased compared with those of the control group. Conversely, LVEF significantly increased ($p < 0.05$). This finding showed that indobufen combined with clopidogrel can better improve the left ventricular function of patients. By analyzing the reasons, indobufen may inhibit thromboxane synthesis by reversibly inhibiting platelet cyclooxygenase and selectively inhibiting platelet aggregation, thereby preventing thrombosis quickly and effectively. It can also promote the proliferation of myocardial cells and restore myocardial function while restoring blood flow.

Inflammation plays an important role in myocardial cell apoptosis and necrosis [22,23]. Hs-CRP is a marker of inflammatory reaction, and its metabolism can be regulated by antioxidants [24]. One study [25] has found that when coronary heart disease occurs, the Hs-CRP level becomes significantly higher than that of healthy people. Inflammation may play a central role in atherosclerosis, which runs through the whole atherosclerotic disease. With intensified inflammatory reaction, plaques rupture and thrombosis ensues. These phenomena easily cause clinical acute cardiovascular events. In this study, the Hs-CRP level in the observation group became significantly lower than that in the control group after treatment ($p < 0.05$). This finding suggested that indobufen combined with clopidogrel may improve the cardiac function of patients after PCI by inhibiting inflammatory reaction. The reason may be that indobufen takes effect quickly. Thus, it can regulate platelet activity, reduce platelet adhesion, inhibit neutrophil activation, reduce the secretion of inflammatory cells, reduce its promotion on platelet aggregation, prevent inflammatory factors and platelets from blocking microvessels, and further reduce the occurrence of myocardial "no reflow".

In the pathogenesis of cardiovascular diseases, the damage or dysfunction of vascular endothelium may activate platelet activation, thereby causing platelet aggregation and pathological thrombosis [26,27]. Bleeding events after PCI can reportedly [28] increase the risk of poor prognosis of patients. A certain relationship may also exist between bleeding events after PCI and patients' death. Hemorrhage can serve as an important prognostic indicator to assess patients with coronary heart disease, and reducing bleeding events has become the main goal to improve the treatment outcome. Therefore, reasonable antiplatelet therapy after PCI is very important. APTT, PT, and TT are indicators related to coagulation [29]. Our findings demonstrated that the levels of APTT, PT, and TT in the control and observation groups increased significantly after treatment, but no significant difference existed between the two groups. Results further showed that indobufen combined with clopidogrel can effectively prevent platelet aggregation and prolong coagulation time and bleeding time. Conversely, indobufen and aspirin had similar effects of reducing platelet aggregation efficiency and hindering platelet adhesion and activation. Moreover, no significant difference existed in the incidence of angina pectoris, cardiac death, gastrointestinal reaction, and allergy between the two groups ($p > 0.05$). This finding further showed the safety of indobufen combined with clopidogrel.

Despite the meaningful conclusions drawn from this work, it had several limitations. First, as a retrospective analysis, the study may have had selection bias. Second, we did not conduct long-term follow-up and observed only short-term treatment effects, so our data cannot be used to evaluate long-term efficacy and safety. Lastly, we did not exclude the impact of other potential confounding factors such as patients' lifestyle and dietary habits. Therefore, future large-scale prospective studies are needed to validate our conclusions and further explore the related mechanisms.

Conclusions

Indobufen combined with clopidogrel treatment for patients after PCI has high safety and can significantly improve a patient's left ventricular function, inhibit inflammatory response, and enhance coagulation function. These features are beneficial to clinical PCI surgery. However, this study also had limitations. First, to avoid the influence of confounding factors on both groups, only typical cases were included, so the sample size was relatively small. Second, owing to the single-center analysis and the lack of regional representativeness, further validation is needed in the future, such as increasing the sample size, conducting multiregional sample collection, and designing prospective studies.

Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Author Contributions

RW designed the study; both authors conducted the study. KW collected and analyzed the data. RW and KW participated in drafting the manuscript, and both authors contributed to critical revision of the manuscript for important intellectual content. Both authors gave final approval of the version to be published. Both authors participated fully in the work, take public responsibility for appropriate portions of the content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study has been approved by the Medical Ethics Committee of Taizhou Central Hospital (Approval No.:2024L-02-16). Informed-consent forms were obtained.

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Conflict of Interest

The authors declare no conflict of interest.

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