Intracoronary administration of stem cells in patients with acute myocardial infarction – angiographic follow-up

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Abstract

Background: Even up-to-date reperfusion therapy using primary percutaneous intervention (PCI) in acute myocardial infarction does not result in improvement of the left ventricular (LV) function in all patients. Cellular myoblasty, a novel method using mononuclear bone marrow cells (BMC), can be applied in the infarcted myocardium area to stimulate regeneration and to limit the organ damage. However, the impact of intracoronary BMC administration on the effect of PCI is not clear.

Aim: To assess angiographic outcomes in patients with anterior myocardial infarction and LV dysfunction, undergoing intracoronary BMC administration after a successful primary PCI.

Methods: The study group consisted of 40 patients (mean age 56.2 years) with LV ejection fraction below 40%, in whom 20 ml of BMC were administered to the infarct-related artery (IRA) distally to the occlusion. The control group comprised 25 age- and sex-matched patients with similar values of LV ejection fraction undergoing bare metal stenting of IRA without BMC administration. Quantitative coronary angiography was performed 6 months later to assess IRA patency.

Results: The reference diameter of the stented artery decreased in the study group from 3.22 ± 0.28 mm to 3.16 ± 0.18 mm ($p < 0.05$) and in the control group from 3.22 ± 0.31 mm to 3.15 ± 0.28 mm ($p < 0.082$); also in the area of the implanted stent the diameter decreased from 3.57 ± 0.21 mm to 2.96 ± 0.79 mm in the study group vs. 3.48 ± 0.22 mm to 3.01 ± 0.35 mm in the control group. For lumen diameter measured 10 mm distally to the stent, the diameter loss was similar in both groups. In 6 patients from the BMC treated group and in 3 patients from the control group there was asymptomatic lumen reduction > 70% (NS).

Conclusion: The results of our study show that BMC administration into IRA is safe. The degree of lumen loss in the stent area was larger in the BMC group than in the control group. There was no significant difference in the lumen change distally to the stent; the artery diameter loss in both groups was similar, and the improvement in LV ejection fraction was greater in the BMC-treated group.

Key words: myocardial infarction, stem-cell therapy, angiography

Kardiol Pol 2009; 67: 477-484

Introduction

Up-to-date treatment of ST elevation myocardial infarction (STEMI) involves early and effective restoration of patency of the infarct-related artery (IRA), which in turn improves tissue perfusion and reduces postinfarction myocardial damage. Despite effective reperfusion therapy, not all patients experience improvement of the left ventricular (LV) systolic function. Factors that may influence prognosis in patients undergoing mechanical reperfusion therapy include infarction size and location, duration of vessel occlusion and size of revascularised vessel, as well as obtaining tissue perfusion [1]. It has been estimated that in 25% to 50% of patients, despite restoration of optimal patency of the epicardial artery and implementation of complete pharmacological treatment, inadequate tissue perfusion and even temporal no reflow phenomenon are observed [2]. Inadequate tissue perfusion is caused by damage of coronary capillaries and may be one of the causes of myocardial necrosis despite restoration of epicardial artery patency.

In the necrotic area, the injured myocardium undergoes remodelling, which leads to LV failure and adverse long-term prognosis. Medical treatment may limit this

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Received: 07 September 2008. **Accepted:** 05 February 2009.
This study was supported by grant no. 2 PO5B178 28

process, however, a large number of patients experience LV dilation and subsequently heart failure.

Administration of bone marrow cells (BMC) through an IRA in the injured myocardial zone may, in addition to routine medical therapy, stimulate regeneration and limit the damaged area [3]. Experimental studies suggest that administration of progenitor cells, despite its beneficial influence on LV systolic function and inhibition of remodelling, may promote narrowing and closure of the inserted stent lumen as well as progression of arterial atherosclerosis due to, among other things, activation of factors accelerating restenotic activity following percutaneous coronary intervention (PCI) [4, 5].

This study aimed to assess safety and effectiveness of BMC intracoronary injection in patients with anterior MI and LV dysfunction treated with primary PCI.

Methods

Study group

The study group comprised 40 patients with acute MI treated with PCI from December 2005 to September 2007. The study was approved by the Ethics Committee of the Medical University in Łódź.

The inclusion criteria were: 1) anterior STEMI and occlusion of the left anterior descending coronary artery treated with primary PCI with stent insertion, 2) no haemodynamically significant lesions in the other coronary arteries, and 3) LV ejection fraction (EF) < 40%. The exclusion criteria included haemodynamically unstable patients, cardiogenic shock on the first day of hospitalisation, and coexisting systemic disease that may influence the prognosis.

The control group consisted of 25 STEMI patients treated with primary PCI meeting similar clinical, echocardiographic and angiographic criteria, not receiving BMC.

Primary percutaneous coronary intervention (PCI)

Coronary angioplasty was performed following clopidogrel 300 mg and acetylsalicylic acid 300-500 mg administration prior to the procedure. Intraprocedural use of GPIIb/IIIa blockers was sporadic and was left to the discretion of the operator.

All patients had bare metal stents inserted. After the procedure patients continued therapy with two antiplatelet agents: clopidogrel at 75 mg/day for 12 months and acetylsalicylic acid at 75 mg/day lifelong.

The index echocardiography was performed within the first 2 days after PCI and included evaluation of LVEF, disturbances of contractility and diastolic LV function.

BMC administration

Stem cells were administered 5-11 days (mean 7th day) after primary PCI according to the methodology described previously [6]. On the procedure day, about 50 ml of bone marrow were drawn from the posterior iliac spines, which after processing aimed at isolation of precursor CD34/CD45+ and CD133+ mononuclear cells were suspended in 5% heparinised human albumin solution. Such prepared sterile material (20 ml) was administered intracoronary through an over-the-wire angiographic catheter. The balloon catheter was inserted in the previously deployed stent and dilated up to 6 atm pressure, occluding the blood flow and preventing retrograde flow of the injected suspension. The procedure was repeated at least three times with 3-5 min intervals to decrease ischaemic symptoms due to prolonged occlusion of the coronary artery.

On average, on the second day following BMC administration the patient was discharged home and followed in the outpatient cardiology clinic. Patients from the control group did not undergo another catheterisation and injection of BMC following effective primary PCI.

Follow-up tests at 6 months

After 6 months each study and control patient was readmitted for clinical evaluation, non-invasive tests and follow-up coronary angiography.

The following tests were carried out: physical examination, basic laboratory tests, resting ECG and 24-hour ECG monitoring, echocardiography with coronary reserve evaluation and an invasive procedure.

Angiographic examinations

Coronary angiography was performed using General Electric INOVA 2000 equipment. Angiographic evaluation was carried out with quantitative coronary angiography (QCA). Of the collected QCA geometric parameters, further analysis used the following: estimated reference arterial diameter proximally to the lesion, the most significant stenosis or total occlusion prior to the procedure, arterial lumen diameter immediately after deployment of stent measured in the mid part of the stent, and arterial diameter distally to the stent measured 10 mm from the end of the deployed stent (Figures 1-4). All measurements were preceded with intracoronary infusion of 0.1 mg nitroglycerine. During the final coronary angiography performed 6 months after infusion of BMC the analogous diameters were measured using the same views; based on these measurements the degree of vessel diameter reduction was assessed. Haemodynamically significant restenosis was defined as arterial lumen reduction by at least 50%.

Statistical analysis

Statistical analyses were performed using MEDCALC software. Continuous parameters of normal distribution are presented as mean ± standard deviation. Significance of differences was tested with Student's t-test, and Spearman's rank correlation. Distributions of categorical

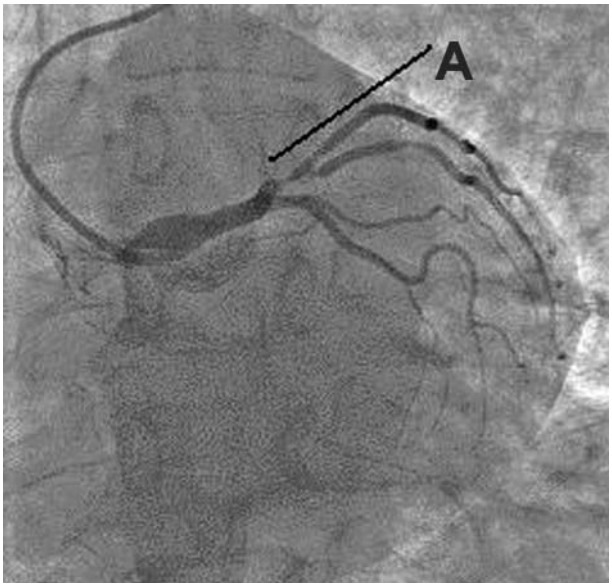

Figure 1. Coronary angiography of the left coronary artery – occlusion of the left anterior descending coronary branch
A – vessel occlusion site

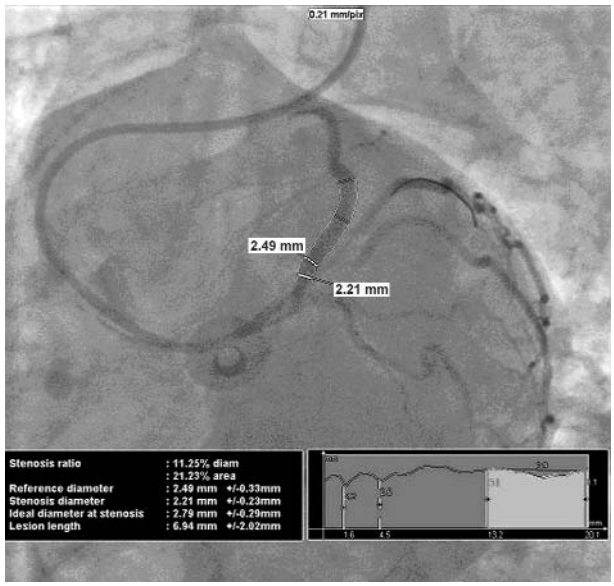

Figure 2. Coronary angiography of the left coronary artery – the left anterior descending coronary branch immediately after restoration of its patency and insertion of stent by QCA

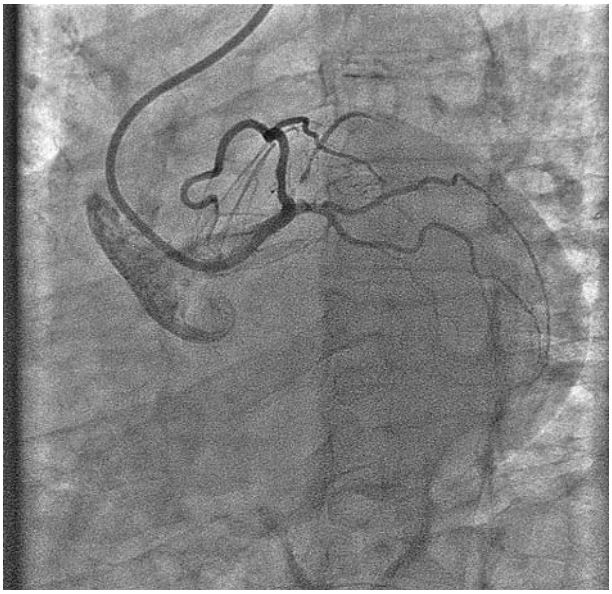

Figure 3. Coronary angiography of the left coronary artery – follow-up examination of the left anterior descending coronary branch

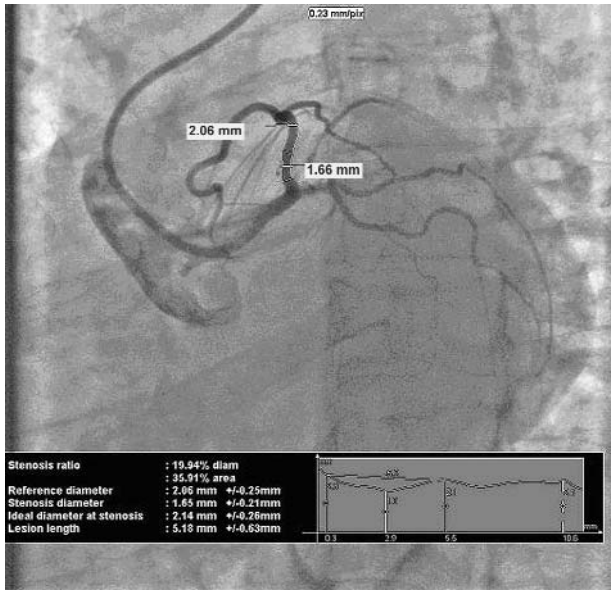

Figure 4. Coronary angiography of the left coronary artery – follow-up examination of the left anterior descending coronary branch at month 6 with QCA measurement sites marked

variables were compared using χ^2 or Fisher tests. A p value < 0.05 was considered significant.

Results

Baseline analysis showed no significant differences between the study and control groups (Table I). Both groups comprised predominantly males, and had comparable mean age and incidence of risk factors. Left ventricular EF in the study group was similar to the one in controls. Also TIMI blood flow in the IRA and QCA parameters were similar in both groups (Table II).

None of the patients experienced arrhythmias or other side effects during intracoronary administration of BMCs and the periprocedural period.

During 6-month follow-up patients were treated consistently with current guidelines. All subjects were on

Table I. Demographic data and risk factors

Parameter	Study group	Control group	p
Number of patients	40	25	
Age [years]	56 (34-69)	55 (38-67)	NS
Males, n (%)	28 (70)	18 (72)	NS
Hypertension, n (%)	16 (40)	9 (364)	NS
Hypercholesterolemia, n (%)	14 (35)	8 (32)	NS
Smoking, n (%)	22 (55)	11 (44)	NS
Diabetes mellitus type 2, n (%)	8 (20)	4 (16)	NS

Table II. Baseline and post-primary PCI angiographic data

	Study group	Control group	p
Ejection fraction [%]	36 (28-39)	34 (22-40)	NS
TIMI blood flow prior to PCI in IRA [n (%)]			
0	35 (87.5)	20 (80)	0.063
I	4 (10)	4 (16)	0.12
II	1 (2.5)	1 (4)	0.072
III	0	0	NS
Pre-PCI artery reference diameter [mm]	3.32 ± 0.28	3.22 ± 0.31	0.838
Stenosis [%]	87 ± 13	84 ±16	NS
Post-PCI arterial diameter – in-stent [mm]	3.57 ± 0.21	3.48 ± 0.22	0.612
Arterial diameter distally to stent [mm]	3.17 ± 0.34	3.09 ± 0.12	0.357
TIMI blood flow after the procedure [n (%)]			
0	0	0	NS
I	1 (2.5)	1 (4)	NS
II	4 (10)	2 (8)	NS
III	35 (87.5)	22 (88)	NS

Table III. Treatment administered during 6-month follow-up

	Study group n (%)	Control group n (%)	p
Acetylosalicylic acid	40 (100)	25 (100)	NS
Clopidogrel	40 (100)	25 (100)	NS
ACE inhibitors	36 (90)	24 (96)	NS
Sartans	4 (10)	2 (8)	NS
Beta-blockers	35 (87.5)	23 (92)	NS
Statins	40 (100)	25 (100)	NS

dual antiplatelet therapy and statins, and the majority were given ACE inhibitors and beta-blockers (Table III). One patient died in the study group. It was a sudden cardiac death most likely due to coronary causes; all patients survived in the control group.

At six-month coronary angiography, a decrease in reference lumen diameter was observed in both groups. A significant reduction of in-stent lumen diameter was also found (Tables IV and V). Larger in-stent re-stenosis was observed in the study group, and the differences were higher than in the reference segment. The vessel diameter distally to the inserted stent decreased in both groups. Luminal narrowing defined as haemodynamically significant instent restenosis, requiring reintervention, was found in 6 patients in the study group and in 3 patients in the control group. In the study group, 4 subjects received drug-eluting stents, and in 2 patients balloon angioplasty was performed. In the control group, re-stenosis required insertion of 2 drug-eluting stents and 1 patient was referred for surgical treatment.

Patients who received BMC, had significantly higher LVEF (Table V) than controls. One patient from the study group had progression of lesions in the other than IRA coronary artery; effective coronary angioplasty with insertion of stent was performed.

Discussion

The use of BMC for regeneration of damaged myocardium due to MI is of growing interest [7-9]. This method seems to be safe, and its use as an adjuvant therapy to medical or invasive treatment in patients with significant LV dysfunction is supported by an increase of LVEF, and improved viability and contractility observed in the vast majority of studies [10, 11].

During and immediately after administration of BMC in our patients no complications were observed, including life-threatening arrhythmias and side effects, while significant improvement of LVEF was documented. The beneficial effects of BMC on the myocardium reported in the literature may depend on a number of factors, including, but not limited to, direct differentiation of bone marrow cells into cardiomyocytes, stimulation by released cytokines of repair processes of damaged myocytes in the peri-infarction zone [12, 13], and stimulation of mobilisation of endogenous stem cells [14, 15].

Published studies focused mainly on the evaluation of implanted cells on systolic function and myocardial viability. However, a relatively small number of publications address reactions of the target vessel [16]. It seems that more detailed analysis of this problem is necessary, taking into account the variability of opinions on this issue [5, 13].

A number of experimental studies have shown that stem cells have the ability to regenerate tissues and induce angiogenesis. There are ongoing trials on the use of epithelial precursors for therapy of diseases caused by

Table IV. Post primary PCI 6-month follow-up data in the study and control groups

	Study group			Control group		
	baseline	at month 6	p	baseline	at month 6	p
TIMI III flow [%]	87.5	95	< 0,05	88	96	< 0.05
Reference diameter [mm]	3.32 ± 0.28	3.16 ± 0.18	< 0.05	3.22 ± 0.31	3.15 ± 0.28	0.082
Stent diameter [mm]	3.57 ± 0.21	2.96 ± 0.79	< 0.05	3.48 ± 0.22	3.01 ± 0.35	< 0.05
Post-stent diameter [mm]	3.17 ± 0.36	2.78 ± 0.51	< 0.05	3.09 ± 0.17	3.01 ± 0.09	0.26

their disturbed function. The use of BMC in the treatment of lower limb obliterative atherosclerosis has been shown to cause clinical improvement and development of collateral circulation. According to the authors, such a therapeutic effect is highly dependent on mobilisation of pro-angiogenic growth factors [17].

Stem cells also have diverse proliferative potential which is useful in angiogenesis, but may also add to unfavourable remodelling of the injured vessel, by promoting neointimal growth, hypertrophy of the media, and collagen deposition, resulting in restenosis [4, 18]. Some of the investigators have found higher incidence of restenosis and decrease of arterial lumen diameter in patients treated with BMC [4, 5, 9, 19].

In our study restenosis was observed in both groups, being slightly more enhanced in the study group. However, significant restenosis above 70% requiring reintervention was seen in a small percentage of patients in both the study and control groups (15.4 vs. 12%). It should be mentioned that none of those patients had clinical signs of restenosis. In the remaining patients evaluation for in-stent restenosis showed a significantly greater in-stent diameter reduction in the BMC than the control group.

A similar trend was noted when evaluating arterial diameter distally to the inserted stent, so in the area potentially penetrating the suspended stem cells. The established 10 mm distance from the end of the stent does not include the adjacent vessel zone, which may be affected during implantation, being more prone to the reparation processes. There were small and insignificant differences regarding this measurement between the study and control groups (0.34 vs. 0.28 mm, respectively) and reduction of luminal diameter in both groups was minor. It should also be highlighted that greater reduction of the lumen in patients undergoing BMC injection was not associated with clinical worsening and had no unfavourable implications for LVEF, of which the increase was significantly higher in the study group than in controls.

A number of investigators have reported results similar to our findings. Kang et al. showed that 4 months after administration of granulocyte-colony stimulating factor (G-CSF) 7 of 19 subjects experienced restenosis in the target

Table V. Results for the study and control groups at month 6

	Study group (n = 39)	Control group (n = 25)	p
Ejection fraction [%]	49 ± 12	43.2 ± 9	0.04
Reference diameter [mm]	3.16 ± 0.18	3.15 ± 0.28	0.27
In-stent diameter [mm]	2.96 ± 0.79	3.01 ± 0.35	0.012
Over 70% in-stent restenosis [%]	6 (15.4)	3 (12)	0.32
Arterial diameter distally to stent [mm]	2.78 ± 0.51	3.01 ± 0.7	0.051
Mean post-stent vessel diameter reduction [mm]	0.34	0.28	0.08
Mean in-stent diameter reduction [mm] (%)	0.63 ± 0.39 (17.6)	0. 22 ± 0.23 (6.3)	0.008

vessels, which was significantly more often present in thae study group compared to the controls [5]. In later papers of those authors, being part of the MAGIC Cell-3-DES clinical trial, implantation of drug-eluting stents in patients undergoing G-CSF therapy did not cause reduction of in-stent luminal diameter but in the distal segment – as in our study – it was higher than in the control group [20]. Similar conclusions were reported by Mansour et al., who found higher incidence of restenosis in the BMC treated patients [9]. In the REPAIR AMI trial pre- and post-stem cell implantation angiographic data were analysed for in-stent restenosis. There were no significant changes regarding the percentage of early restenoses and occlusions in the group receiving stem cells and the control group; however, during 12-month follow-up only echocardiographic assessment was performed without coronary angiography [21].

As opposed to the above-mentioned authors, Schachinger et al. and Engelman et al. reported no differences regarding stenoses in patients receiving BMC compared to the placebo group [12, 15]. Also, Valgimitli

et al. observed in a group of 20 subjects receiving G-CSF a trend towards lower restenosis rate than in controls [14].

The mechanism of restenosis in patients treated with stem cells is complex and not fully clear. It most likely depends on a variety of factors. Only the influence of the cellular implantation procedure and related additional mechanical damage of the endothelium may encourage the vascular reparative reaction. The effect of cells and their mediators may have some effect as well.

It seems that most likely it is a consequence of mechanical injury due to in-stent dilation of a balloon catheter. This interpretation is also supported by less severe stenosis distally to the stent than in-stent restenosis found in our study. The mode of administration of stem cells used in our patients – prolonged balloon inflation at low pressure with its in-stent placement –prevented retrograde flow of the injected material; however, it was a mechanical factor irritating and injuring the arterial wall itself. It is known that in the first 2 weeks after the primary PCI the vascular wall undergoes reparative procedures, and several, although low pressure, inflations may additionally promote more potent and long-lasting neointimal proliferation [22]. In addition, influence of other factors related to re-catheterisation of IRA is possible – injury caused by a guide wire, contrast agent effect and influence of the medium for stem cells and stem cells themselves. The *in vitro* experimental studies confirmed superficial expression of VEGFR 2 responsible for reparative processes and stimulation of angiogenesis [17]. The deployed stent is inserted into the injured vessel at the unstable atherosclerotic plaque and covers the arterial segment with pathology responsible for its initial occlusion. The stabilising stent due to its openwork structure does not cover continuously the entire wall, and areas between stent components may be susceptible to mediators stimulating the extensive proliferation of neointima. This confirms the stent ingrowth process, which in 10-12% of patients leads to haemodynamically significant restenosis within the first month [19].

Also it cannot be excluded that the procedure of injection of stem cells itself performed only in the study group may contribute to development of restenosis. The control subjects have not been treated with inactivated stem cells due to ethical reasons; therefore it makes the differentiation of cellular and non-cellular effects of regenerative therapy impossible.

Study limitations

The relatively small size of the study group is some limitation; however, the study protocol assumed enrolment of 40 subjects and rigorous inclusion criteria were established in order to make a group as homogeneous as possible. It should be noted that the sample size did not differ from the majority of previous publications from a single site.

Another limitation is selection of the control group, and predominantly lack of simulated injection of deactivated cells ('sham procedure'), which was not justified by ethical reasons. It should be stressed that the standards of control group selection have not been established yet and similar criteria are used in most studies comparable to ours.

Conclusion

Administration of BMC in patients with anterior STEMI, LV dysfunction and stenosis of the left anterior descending coronary artery treated with primary PCI is safe, however, it may increase the severity of in-stent restenosis.

References

1. Bolognese L, Neskovic AN, Parodi G, et al. Left ventricular remodeling after primary coronary angioplasty: patterns of left ventricular dilatation and long-term prognostic implication. *Circulation* 2002; 106: 2351-7.
2. Moens AL, Claevs MJ, Timmermans JP, et al. Myocardial ischemia/reperfusion-injury, a clinical view on a complex pathophysiological process. *Int J Cardiol* 2005; 100: 179-90.
3. Siminiak T, Grajek S. Przeszczepianie komórek w regeneracji serca. Obecny stan wiedzy i polskie doświadczenia kliniczne. *Kardiologia po Dyplomie* 2007; 6: 13-21.
4. Sata M, Saiura A, Kunisato A, et al. Hematopoietic stem cells differentiate into vascular cells that participate in the pathogenesis of atherosclerosis. *Nat Med* 2002; 8: 403-9.
5. Kang HJ, Kim HS, Zhang SY, et al. Effects of intracoronary infusion of peripheral blood stem cells mobilized with granulocyte colony stimulating factor on left ventricular systolic function and restenosis after coronary stenting in myocardial infarction: the MAGIC cell randomized clinical trial. *Lancet* 2004; 363: 751-6.
6. Korycka A, Plewka M, Jeżewski T, et al. Ocena efektywności izolacji komórek CD34+ i CD 133+ uzyskanych ze szpiku kostnego chorych ze świeżym zawałem mięśnia sercowego serca. *Acta Haematol Pol* 2008; 39: 73-86.
7. Wieczorek P, Tendera M. Application of bone marrow cells in myocardial infarction. *Kardiol Pol* 2008; 66: 328-34.
8. Lunde K, Solheim S, Aakhus S, et al. Intracoronary iniection of mononuclear bone marrow cells in acute myocardial infarction. *N Engl J Med* 2006; 355: 1199-209.
9. Mansour S, Vanderheyden M, De Bruyene B, et al. Intracoronary delivery of hematopoietic bone marrow stem cells and luminal losse of the infarct-related artery in patients with recent myocardial infraction. *J Am Coll Cardiol* 2006; 47: 1727-30.
10. Strauer BE, Brehn M, Zeus T, et al. Intracoronary human autologous stem cells transplantation for myocardial infarction. *Dtsch Med Vochenschr* 2001; 126: 932-8.
11. Tse HF, Kwong YL, Chan JK. Angiogenesis in ischaemic myocardium by intramyocardial autologous bone marrow mononuclear cell implantation. *Lancet* 2003; 361: 47-9.
12. Schachinger V, Erbs S, Elsasser A, et al. Intracoronary bone-marrow-derived progenitor cells in acute myocardial infarction. *N Engl J Med* 2006; 355: 1210-20.
13. Assmus B, Walter D, Lehmann R, et al. Intracoronary infusion of progenitor cells is not associated with aggravated restenosis development or atherosclerotic disease progression in patients with acute myocardial infarction. *Eur Heart J* 2006; 27: 2989-95.

14. Valgimigli M, Rigolin G, Cittanti C, et al. Used of granulocyte-colony stimulating factor during acute myocardial infarction to enhance bone marrow stem cell mobilization in humans: clinical and angiographic safety profile. *Eur Heart J* 2005; 26: 1838-945.
15. Engelmann MG, Theiss HD, Hennig-Theiss C, et al. Autologous bone marrow stem cell mobilization induced by granulocyte colony-stimulating factor after subacute ST segment elevation myocardial infarction undergoing late revascularization. *J Am Coll Cardiol* 2006; 48: 1712-21.
16. Penicka M, Horak J, Kobylka P, et al. Intracoronary injection of autologous bone marrow-derived mononuclear calls in patients with large anterior acute myocardial infarction: a prematurely terminated randomized study. *J Am Coll Cardiol* 2007; 49: 2373-4.
17. Tateishi-Yuyama E, Matsubara H, Murohara T, et al. Therapeutic angiogenesis for patients with limbischemia by autologous transplantation of bone marrow cells. *Lancet 2002*; 360: 427-35.
18. Whittaker A, Moore JS, Vasa-Nicotera M, et al. Evidence for genetic regulation of endothelial progenitor cells and their role as biological markers of atherosclerosis susceptibility. *Eur Heart J* 2008; 29: 332-8.
19. Mansour S, Vanderheyden M, Vandekerckhove B, et al. Effects of intracoronary administration of enriched hematopoietic bone marrow cells on in-stent restenosis and progression of coronary atherosclerosis in patients with recent myocardial infarction. *Eur Heart J* 2005; 26: (Suppl. 122).
20. Kang HJ, Lee HY, Na SH, et al. Differential effect of intracoronary infusion of mobilized peripheral blood stem cells by granulocyte colony-stimulating factor on left ventricular function and remodeling in patients with acute myocardial infarction versus old myocardial infarction: the MAGIC Cell-3-DES randomized, controlled trial. *Circulation* 2006; 114: 145-51.
21. Schachinger V, Erbs S, Elsasser A, et al. Improved clinical outcome after intracoronary administration of bone-marrow-derived progenitor cells in acute myocardial infarction: final 1-year results of the REPAIR-AMI trial. *Eur Heart J* 2006; 27: 2775-83.
22. Farb A, Sangiorgi G, Carter A, et al. Pathology of acute and chronic coronary stenting in humans. *Circulation* 1999; 99: 44-52.

Dowieńcowe podanie komórek macierzystych chorym z zawałem serca – obserwacja angiograficzna

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Streszczenie

Wstęp: Nowoczesne i skuteczne leczenie reperfuzyjne ostrego zawału serca nie u wszystkich chorych pozwala uzyskać poprawę funkcji skurczowej. Wydaje się, że podanie szpikowych komórek macierzystych (BMC) w strefę uszkodzonego miokardium wraz z rutynową farmakoterapią może stymulować procesy regeneracji i ograniczać uszkodzenie.

Cel: Ocena angiograficzna i kliniczna chorych z zawałem serca ściany przedniej i dysfunkcją lewej komory, którym po skutecznym zabiegu pierwotnej przezskórnej interwencji wieńcowej (PCI) podano bezpośrednio dowieńcowo BMC.

Metody: Grupę badaną stanowiło 40 chorych (średnia wieku 56,2 roku) z wyjściową frakcją wyrzutową lewej komory poniżej 40%, którym dowieńcowo podano zawiesinę 20 ml BMC. Grupę kontrolną stanowiło 25 chorych z podobnymi wartościami frakcji wyrzutowej. Po 6 miesiącach wszystkich chorych z obydwu grup ponownie hospitalizowano w celu oceny klinicznej. Wykonywano badania nieinwazyjne oraz kontrolną koronarografię, w której badano naczynie dozawałowe, wyliczając średnicę referencyjną naczynia, średnice w implantowanym stencie oraz w odcinku za stentem.

Wyniki: Stwierdzono zmniejszenie średnicy referencyjnej naczynia w grupie badanej z 3,32 ± 0,28 do 3,16 ± 0,18 mm ($p < 0,05$), a w grupie kontrolnej z 3,22 ± 0,31 do 3,15 ± 0,28 mm ($p = 0,082$). W implantowanych stentach odnotowano zmniejszenie średnicy z 3,57 ± 0,21 do 2,96 ± 0,79 mm w grupie badanej *vs* 3,48 ± 0,22 do 3,01 ± 0,35 mm w kontrolnej, natomiast w odległości 10 mm za stentem stopień utraty światła był podobny w obydwu grupach. Bezobjawowy nawrót zwężenia powyżej 70% wymagający ponownego zabiegu rewaskularyzacji rozpoznano u 6 chorych w grupie badanej *vs* 3 w kontrolnej.

Wnioski: Wyniki naszych badań wskazują, że podanie BMC jest procedurą bezpieczną. Utrata światła w stencie była istotnie większa w grupie badanej niż w kontrolnej, a w odcinku za stentem utrata światła w obydwu grupach po 6 miesiącach była podobna. Należy podkreślić, że w obydwu grupach utrata światła naczynia była niewielka i nie miała niekorzystnego wpływu na wielkość frakcji wyrzutowej.

Słowa kluczowe: zawał serca, komórki macierzyste, angiografia

Kardiol Pol 2009; 67: 477-484

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Praca wpłynęła: 07.09.2008. **Zaakceptowana do druku:** 05.02.2009.