Myocardial

Synergistic cardioprotective effects of rAAV9-CyclinA2 combined with fibrin glue in rats after myocardial infarction.

Authors: Cao W., Chang Y.-F., Zhao A.-C., Chen B.-D., Liu F., Ma Y.-T., Ma X.

Publication Date: 2017

Abstract:

The present study aimed to investigate the protective effects of rAAV9-CyclinA2 combined with fibrin glue (FG) in vivo in rats after myocardial infarction (MI). Ninety male Sprague-Dawley rats were randomized into 6 groups (15 in each group): sham, MI, rAAV9-green fluorescent protein (GFP) + MI, rAAV9-CyclinA2 + MI, FG + MI, and rAAV9-CyclinA2 + FG + MI. Packed virus (5 x 10¹¹vg/ml) in 150 micro l of normal saline or FG was injected into the infarcted myocardium at five locations in rAAV9-GFP + MI, rAAV9-CyclinA2 + MI, and rAAV9-CyclinA2 + FG + MI groups. The sham, MI, and FG + MI groups were injected with an equal volume of normal saline or FG at the same sites. Five weeks after injection, echocardiography was performed to evaluate the left ventricular function. The expressions of CyclinA2, proliferating cell nuclear antigen (PCNA), and phospho-histone-H3 (H3P), vascular density, and infarct area were assessed by Western blot, immunohistochemistry, immunofluorescence, and Masson staining. As a result, the combination of rAAV9-CyclinA2 and FG increased ejection fraction and fractional shortening compared with FG or rAAV9-CyclinA2 alone. The expression level of CyclinA2 was significantly higher in the rAAV9-CyclinA2 + FG + MI group compared with the rAAV9-CyclinA2 + MI and FG + MI groups (70.1 +/- 1.86% vs. 14.74 +/- 2.02%, $P < 0.01$; or vs. 50.13 +/- 3.80%; $P < 0.01$). A higher expression level of PCNA and H3P was found in the rAAV9-CyclinA2 + FG + MI group compared with other groups. Comparing with other experiment groups, collagen deposition and the infarct size significantly decreased in rAAV9-CyclinA2 + Fibrin + MI group. The vascular density was much higher in the rAAV9-CyclinA2 + FG + MI group compared with the rAAV9-CyclinA2 + MI group. We

concluded that fibrin glue combined with rAAV9-CyclinA2 was found to be effective in cardiac remodeling and improving myocardial protection.

Myocardial revascularization after myocardial infarction using endothelial progenitor cells combined with fibrin gel. [Chinese]

Authors: Adila A., Zhao L., Zhou X.-R., Liu F., Chen B.-D., Ma Y.-T.

Publication Date: 2014

Abstract:

Background: Studies have shown that fibrin glue can promote the survival of myoblast grafts, reduce infarct size and induce neovascularization of infarct zone. Objective: To understand the condition of revascularization of infarcted heart muscle using endothelial progenitor cells combined with degradable fibrin glue materials. Methods: A total of 27 Sprague-Dawley rats were randomized into three groups, 9 rats in each group: Non-myocardial infarction group, immediate transplantation group and 1-week post-infarction transplantation group. Then, these three groups were sub-grouped into two groups, respectively: endothelial progenitor cells+fibrin glue group (experimental group) and fibrin glue group (control group). At 3 and 8 weeks after transplantation, the rats were sacrificed in each group. The revascularization and function of infracted heart muscle were observed by microscope, immunohistochemistry and echocardiography. Results And Conclusion: Under the microscope, there were some lax connective tissues between the heart and chest in the experimental groups, but no difference existed between the experimental and control groups. The heart structure was normal relatively and difficult to be distinguished between the experimental and control groups histologically and immunologically, and there was no angeioma, vascular malformation and tumor. The number of revascularization of heart muscle showed no difference between experimental and control groups as well as between different experimental groups. Additionally, there was no significant difference in cardiac function between experimental and control groups. Although there are no positive results of endothelial progenitor cells, we will modify and improve the strategy and believe that the cell delivery system is of benefit and efficacy.

Effects of scaffold-delivered SDF-1 alpha protein in chronic rat myocardial infarction model.

Authors: Yu J., Sievers R.E., Lee R.J.

Publication Date: 2014

Abstract:

The delivery of stromal cell-derived factor (SDF)-1 alpha protein via a bioactive scaffold for the repair of chronically damaged myocardium was investigated using in situ tissue engineering. SDF-1 alpha protein, fibrin, or SDF-1 alpha protein in a fibrin matrix were delivered into the myocardium of a rat ischemic cardiomyopathy model five weeks after myocardial infarction (MI). Echocardiography was performed before and five weeks after treatment. The hearts were examined histologically for angiogenesis, infarct size, and stem cell migration. SDF-1 alpha protein alone and fibrin glue both retarded heart function deterioration by recruiting stem cells into the infarcted myocardium and stimulating neovascularization. SDF-1 alpha delivered with fibrin glue recruited the highest quantity of CD34+ in the infarcted area. SDF-1 alpha and fibrin influence the myocardial microenvironment in a chronic MI through the recruitment of stem cells, resulting in arteriogenesis and preservation of left ventricular function. In situ tissue engineering shown to be a viable approach for the treatment of chronic ischemic cardiomyopathy.

Autophagic changes of the endothelial progenitor cells carried with fibrin glue after transplantation into the infracted myocardium. [Chinese]

Authors: Zhang D., Wang H.-J., Tan Y.-Z., Wang Q.-L., Wu J.-H., Li Z.-H., Zhe Q.

Publication Date: 2013

Abstract:

Objective: To investigate autophagic changes endothelial progenitor cells (EPCs) carried with fibrin glue after transplantation into the infarcted myocardial and to explore effects of autophagy on maintaining the implanted cells to survive and fibrin on protecting the cells. Methods: The model of myocardial infarction was established with ligating the anterior descending branch of the left coronary artery of rats. The EPCs sorted from human umbilical cord blood were injected into the myocardium at the normal region, periphery of the infarcted region and infarcted region. After transplantation for two hours, the tissues at injection sites were removed, the semithin sections were prepared. Distribution of the EPCs carried with fibrin glue were examined. After positioning the implanted cells, the ultrathin sections were prepared. The changes of the autophagic structures in EPCs and compatibility of fibrin with EPCs and myocardium were evaluated. Results: Compared with the normal region, the autophagic EPCs in the periphery of the infarcted region increased, and the autophagic structures in the cells increased. In the infarcted region, EPC autophagy enhanced significantly, and necrosis or apoptosis occurred in some cells. Compatibility of fibrin with EPCs and myocardium was good. The implanted cells in fibrin glue extended well, some EPCs adhered to cardiaomyocytes. Conclusion: When EPCs are transplanted into the periphery of the infarcted region, mild ischemia induces autophagy of the cells, which is beneficial for maintaining survival of the transplanted cells. Carrying EPCs with fibrin glue may avoid of cell lose and promote cell survival.

Fibrin sealant in coronary artery bypass grafting surgery; reflection on risk and benefit.

Authors: Nistor R.F.

Publication Date: 2008

Abstract:

Not Available

Reply to Nistor.

Authors: Lamm P., Reichart B.

Publication Date: 2008

Abstract:

Not Available

Transplantation of neonatal cardiomyocytes plus fibrin sealant restores myocardial function in a rat model of myocardial infarction.

Authors: Li Y.-S., Gao B.-R.

Publication Date: 2007

Abstract:

Background: Most cardiac regenerative approaches can restore injured heart muscles. In this study, we investigated if fibrin sealant could help neonatal cardiomyocytes restore myocardial function in a rat model of myocardial infarction. Methods: The left anterior descending artery in adult female Sprague-Dawley (SD) rats was ligated to make a myocardial infarction model. Neonatal ventricular cardiomyocytes from one-day male SD rats were isolated, labeled and cultured. The cells were injected into the infarcted area three weeks later. The animals were randomized into four recipient groups: (1) cardiomyocytes plus fibrin sealant (group CF, n=10); (2) cardiomyocytes alone (group C, n=10); (3) fibrin sealant recipients alone (group F, n=10); (4) control group (n=10). Four weeks after transplantation, echocardiography and Langerdoff model were used to assess heart function. Immunohistochemical staining and polymerase chain reaction (PCR) were performed to track the implanted cardiomyocytes and detect the sex-determining region Y gene on Y chromosome. Results: Echocardiography showed the fraction shortening (FS) in groups CF, C, F and control group was (27.80+/-6.32)%, (22.29+/-4.54)%, (19.24+/-6.29)% and (20.36+/-3.29)% respectively with statistically significant differences in group CF compared with the other groups (P<0.05). The Langendoff model revealed that the left ventricular development of peak pressure (LVDPmax, mmHg) in groups CF, C, F and control group was 104.81+/-17.05, 80.97+/-21.60, 72.07+/-26.17 and 71.42+/-17.55 respectively with statistically significant differences in group CF compared with the other groups (P<0.05). Pathological examination and PCR indicated that transplanted cardiomyocytes in group CF survived better than those in the other groups. Conclusion:

Transplanted neonatal cardiomyocytes plus fibrin sealant can survive in myocardial infarctioned area and improve heart function greatly in rat models.

Long-term usefulness of percutaneous intrapericardial fibrin-glue fixation therapy for oozing type of left ventricular free wall rupture: A case report.

Authors: Shuji J., Hidetsugu A., Masao S., Keiko N., Tomoki K., Tadakazu H., Takashi N., Keiju K., Takuro M., Masaki J., Hiroshi I.

Publication Date: 2002

Abstract:

This report describes a long-term survival case of left ventricular free wall rupture treated with percutaneous intrapericardial fibrin-glue fixation therapy. A 82-year-old woman was admitted to the emergency room because of vomiting and syncope diagnosed as acute posterolateral myocardial infarction complicated by cardiac tamponade. After her hemodynamic condition was stabilized by drawing off the bloody pericardial effusion, fibrin-glue was injected into pericardial space with the expectation that the glue would cover the oozing site of the left ventricular epicardium. After this therapy, the patient recovered and did not have any no recurrent cardiac events for 1 year. Serial echocardiographic studies revealed a preserved left ventricular function and no development of left ventricular restriction. This case suggests that percutaneous intrapericardial fibrin-glue fixation therapy is an effective treatment for the oozing type of left ventricular free wall rupture and that there is no risk of left ventricular restriction during long-term follow-up.

Oozing type cardiac rupture repaired with percutaneous injection of fibrin-glue into the pericardial space - Case report.

Authors: Murata H., Masuo M., Yoshimoto H., Toyama J., Shimada M., Shimamura Y., Hojo H., Kondo K., Kitamura S., Miura Y.

Publication Date: 2000

Abstract:

Two patients, a 56-year-old man and an 81-year-old woman who were admitted to hospital because of anteroseptal acute myocardial infarction, were initially treated successfully with direct percutaneous transluminal coronary angioplasty. However, both patients later developed sudden cardiogenic shock due to cardiac tamponade caused by left ventricular free wall rupture (LVFWR). Prompt, life-saving pericardiocentesis was performed, then fibrin-glue was percutaneously injected into the pericardial space. After the procedure, there was no detectable pericardial effusion on echocardiography and the hemodynamic state became stable. The surgical treatment was the standard procedure for LVFWR, but percutaneous fibrin-glue therapy can also be considered for oozing type LVFWR.

Subacute left ventricular free wall rupture complicating acute myocardial infarction. Successful surgical repair with a sutureless technique.

Authors: Lijoi A., Scarano F., Parodi E., Dottori V., Secchi G.L., Delfino R., Tallone M., Venere G.

Publication Date: 1996

Abstract:

The high mortality index related to surgical therapy with direct suture of rupture of left ventricular free wall following acute myocardial infarction, suggested we analyze and use alternative techniques. So we applied the sutureless technique described by Padro to two patients. We used a Teflon patch fixed to the ventricular wall with a biocompatible synthetic glue, an ethyl-2-cyanoacrylate monomer, without any direct suturing of the infarcted myocardium. The two patients survived the operation and were discharged from the hospital 12 and 14 days after surgery. The sutureless technique allows, in our opinion, a more confident and safe aggressive attitude to subacute left ventricular free wall rupture.

Surgical management of left ventricular free wall rupture after acute myocardial infarction.

Authors: Coletti G., Torracca L., Zogno M., La Canna G., Lorusso R., Pardini A., Alfieri O.

Publication Date: 1995

Abstract:

Left ventricular rupture after acute myocardial infarction occurs more often than suspected and diagnosis is rarely made before death. Left ventricular rupture has been reported to contribute to the overall in-hospital mortality after acute myocardial infarction in up to 24% of cases and to be present in 40% of patients dying within the first week after infarction. Only prompt diagnosis and aggressive surgical treatment can be lifesaving under these circumstances. Between February 1991 and August 1993 five patients underwent emergency operation for left ventricular rupture after acute myocardial infarction using exclusively transoesophageal echocardiography as a diagnostic tool. All patients had evidence of cardiac tamponade and electrocardiography showed signs of anterolateral acute myocardial infarction in one, inferolateral acute myocardial infarction in three and lateral acute myocardial infarction in one. In two cases the infarcted area was debrided and an interrupted pledgetted 2/0 polypropylene suture was placed from inside of the ventricle outward to the epicardial surface and then through the pericardial patch. In the other three cases an original technique was used: an autologous glutaraldehyde-stiffened pericardial patch was sealed over the infarcted area using fibrin glue and fixed with running suture on the surrounding healthy myocardium. One patient died in the operating room because of low cardiac output syndrome which was possibly the result of an excessively extended area of infarction. Left ventricular rupture is a catastrophic complication of acute myocardial infarction and prompt diagnosis with transoesophageal echocardiography followed by emergency operation can be lifesaving. The surgical technique with pericardial patch and fibrin glue, without infarct excision, used in three patients, can be a useful and simple surgical option in

this pathology when no active bleeding is observed from the tear.

Preservation of the cardiac function in infarcted rat hearts by the transplantation of adipose-derived stem cells with injectable fibrin scaffolds.

Authors: Zhang X, Wang H, Ma X, Adila A, Wang B, Liu F, Chen B, Wang C, Ma Y

Publication Date: 2010

Abstract:

Cell-based therapy can improve cardiac function but is limited by the low cell retention and survival within ischemic tissues. Injectable cardiac tissue engineering aims to support cell-based therapies and enhance their efficacy for cardiac diseases. So far, no research has been devoted to studying the usefulness of the combination of fibrin glue (as scaffold) and adipose-derived stem cells (ADSCs) to treat myocardial infarction. In our study, the rat ADSCs were isolated from subcutaneous adipose tissues. The surface phenotype of these cells was analyzed by flow cytometry. The fibrin glue was then co-injected with ADSCs into the left ventricular wall of rat infarction models. The structure and functional consequences of transplantation were determined by detailed histological analysis and echocardiography. Most cultured ADSCs expressed CD105 and CD90, and were negative for CD34 and CD45. After injection, both the 24-h cell retention and four-week graft size were significantly higher and larger in the Fibrin + ADSCs group than those of the ADSCs group alone ($P < 0.01$). The heart function improved significantly in the Fibrin + ADSCs group compared with that of the ADSCs group four weeks after transplantation ($P < 0.01$). In addition, the arteriole densities within the infarcted area improved significantly in the Fibrin + ADSCs group compared with those in the ADSCs group four weeks after transplantation ($P < 0.01$). In conclusion, the ADSCs with the fibrin glue has the therapeutic potential to improve the function of infarcted hearts. The method of in situ injectable tissue engineering combining fibrin glue with ADSCs is promising clinically.

Restoration of left ventricular geometry and improvement of left ventricular function in a rodent model of chronic ischemic cardiomyopathy.

Authors: Yu J, Christman KL, Chin E, Sievers RE, Saeed M, Lee RJ

Publication Date: 2009

Abstract:

OBJECTIVES: Various approaches to myocardial reconstruction have been developed for the treatment of congestive heart failure resulting from ischemic cardiomyopathy.

METHODS: In this study we determined whether in situ application of polymers could reshape left ventricular geometry in a chronic rodent model of ischemic cardiomyopathy.

RESULTS: We demonstrate that alginate and fibrin can augment left ventricular wall thickness, resulting in reconstruction of left ventricular geometry and improvement of cardiac function. Echocardiographic results at 5 weeks after injection of alginate demonstrated persistent improvement of left ventricular fractional shortening and prevention of a continued enlargement of left ventricular dimensions, whereas fibrin glue demonstrated no progression of left ventricular negative remodeling. There was increased arteriogenesis in both the alginate and fibrin glue groups compared with that seen in the phosphate-buffered saline control group. Infarct size was significantly reduced in the fibrin group ($P < .05$), and there was a trend toward a smaller myocardial infarction in the alginate group.

CONCLUSION: Intramyocardially injected polymers can be used to reshape the aneurysmal left ventricle and might therefore be an approach for myocardial reconstruction and a potential option in

treating chronic heart failure in human subjects.

Cell transplantation and fibrin matrix.

Authors: Chekanov V, Kipshidze N, Nikolaychik V

Publication Date: 2005

Abstract:

Not Available

Enhanced neovasculature formation in ischemic myocardium following delivery of pleiotrophin plasmid in a biopolymer.

Authors: Christman KL, Fang Q, Yee MS, Johnson KR, Sievers RE, Lee RJ

Publication Date: 2005

Abstract:

Coronary heart disease is currently the leading killer in the western world. Therapeutic angiogenic agents are currently being examined for treatment of this disease. We have recently demonstrated the effective use of Pleiotrophin (PTN) as a therapeutic agent for treatment of ischemic myocardium. We have also shown that injection of the biopolymer fibrin glue preserves left ventricular geometry and prevents a deterioration of cardiac function following myocardial infarction. Due to the low transfection efficiency of naked plasmid injections, we examined the use of PTN plasmid and the biopolymer as a gene-activated matrix in the myocardium. In this study, we demonstrate that delivery of PTN plasmid in fibrin glue increases neovasculature formation compared to injection of the naked plasmid in saline.

Injectable fibrin scaffold improves cell transplant survival, reduces infarct expansion, and induces neovasculature formation in ischemic myocardium.

Authors: Christman KL, Vardanian AJ, Fang Q, Sievers RE, Fok HH, Lee RJ

Publication Date: 2004

Abstract:

OBJECTIVES: In this study, we determined whether fibrin glue improves cell transplant retention and survival, reduces infarct expansion, and induces neovasculature formation.

BACKGROUND: Current efforts in restoring the myocardium after myocardial infarction (MI) include the delivery of viable cells to replace necrotic cardiomyocytes. Cellular transplantation techniques are, however, limited by transplanted cell retention and survival within the ischemic tissue.

METHODS: The left coronary artery of rats was occluded for 17 min followed by reperfusion. One week later, bovine serum albumin (BSA), fibrin glue, skeletal myoblasts in BSA, or skeletal myoblasts in fibrin glue were injected into the infarcted area of the left ventricle. The animals were euthanized five weeks after injection, and their hearts were excised, fresh frozen, and sectioned for histology and immunohistochemistry.

RESULTS: After five weeks, the mean area covered by skeletal myoblasts in fibrin glue was significantly greater than the area covered by myoblasts injected in BSA. Myoblasts within the infarct were often concentrated around arterioles. The infarct scar size and myoblasts in the fibrin group were significantly smaller than those in the control and BSA groups. Fibrin glue also significantly increased the arteriole density in the infarct scar as compared with the control group.

CONCLUSIONS: This study indicates that fibrin glue increases cell transplant survival, decreases infarct size, and increases blood flow to ischemic myocardium. Therefore, fibrin glue may have potential as a biomaterial scaffold to improve cellular cardiomyoplasty treat and MIs.

Successful management of a postinfarction left ventricular rupture using a sutureless technique with concomitant myocardial revascularization.

Authors: Kalangos A, Panos A, Chatelain P, Vala D, Fromage P, Faidutti B

Publication Date: 1997

Abstract:

We present a case of left ventricular (LV) rupture that occurred on the second day after inferolateral myocardial infarction (MI). An aggressive diagnostic approach with rapid coronary angiography prior to surgical repair provides a benefit characterized postoperatively by complete recovery of myocardial contractility in the akinetic infarcted area. We believe that coronary artery disease associated with subacute ventricular rupture may, in fact, be better investigated and simultaneously treated under a protocol of early surgical repair.

[Repair of post-infarction left ventricular wall ruptures by biological glue and a flap from the pericardium. Results from 2 to 10 years]. [French]

Authors: Hvass U, Chatel D, Assayag P, Juliard JM, Caliani J, Oroudji M, Pansard Y

Publication Date: 1996

Abstract:

The authors report their experience with a simple and efficient technique for repair of left ventricular free wall rupture complicating myocardial infarction. The technique consists, with the aid of cardiopulmonary bypass, in suturing a plaque of the patients own pericardium (6 to 8 cm in diameter) to the more normal tissue encircling the pathologic myocardium, and by injecting five ml of human fibrin glue as a cement under the pericardium to reinforce the remair and prevent leaking throughout the suture line. With a 10 year follow-up, we are able to be confident with the long term results. The five patients, at the time of operation were aged 46 to 74 years. The post-operative results and the annual echocardiographic controls have proved the technique to be sound without recurrences and without late complications such as pseudo aneurysms at the site of the repair.