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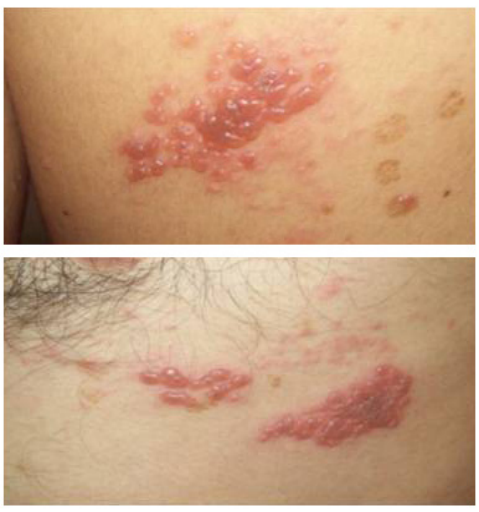

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A comparision of left ventricular functions after acute myocardial infarction receiving different reperfusion therapy

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ABSTRACT

It is demonstrated that primary angioplasty is more effective than thrombolytic therapy on the clinical outcomes in ST- segment elevation acute myocardial infarction (STEMI). The aim of this study was to compare the effects of reperfusion therapies on left ventricular systolic and diastolic functions.
We assigned 114 patients (19 female, mean age 60.2 ± 10.7 years, and 95 male, mean age 53.6 ± 11.0 years) with first STEMI treated with primary angioplasty (n=54) or thrombolytic drug therapy (n=60) in accordance with selection criteria. Assesment of LV systolic function was done by wall motion score index (WMSI) and left ventricular ejection fraction (LVEF). Left ventricular diastolic function was evaluated by the pulsed Doppler technique. WMSI was significantly lower in angioplasty group (1.31 ± 0.30) compared to thrombolysis group (1.45 ± 0.40) ($p<0.01$). LVEF did not differ between treatment groups (50 ± 9 % vs 47 ± 8 %, $p>0.05$). The frequency of diastolic dysfunction tended to lower in angioplasty group but the difference was not significant (50% vs 62%, $p>0.05$). Nevertheless, rates of restrictive filling pattern cases was significantly higher in thrombolysis group (7% vs 22%, $p<0.05$). There was a significant difference for E/A ratio between two groups (0.99± 0.38 versus 1.20± 0.60, $p<0.05$).
The results showed that the left ventricular systolic and diastolic functions were preserved with STEMI treated by primary angioplasty. This may contribute to better clinical outcomes in patients with STEMI treated with primary angioplasty.

1. Introduction

Modern management of acute myocardial infarction is estabish on clinical evidence from randomised controlled trials. Reperfusion therapy using either intravenous thrombolytic agents or primary angioplasty is established therapy for acute myocardial infarction (AMI) (Milavetz et al., 1998). Meta-analyses of clinical trials which compared primary angioplasty with thrombolytic therapy have been shown significant reduction in rates of mortality, reinfarction, total stroke and hemorhagic stroke with angioplasty (PCAT Collaborators, 2003; Keeley and Grines, 2004). Early and effective flow through the infarct-related artery has a paramount importance for limitation of infarct size and preservation of left ventricular function in patients with AMI (de Boer et al., 1994).

Left ventricular systolic and diastolic functions were predictors of the clinical outcomes in patients with AMI (Keeley and Grines, 2004; Azevedo et al., 2004). Reducing myocardial ischemia by revascularization in early period of AMI, improves left ventricular systolic functions, but its effect is unclear on diastolic functions (de Boer et al., 1994). However, the link between left ventricular function and clinical outcome has not been satisfaying demonstrated in the nowadays. The aim of this study was to compare the effects of reperfusion therapies on left ventricular systolic and diastolic functions by echocardiogarpic indexes.

2. Experimental procedure

Study population

This study consisted of 116 consecutive patients (99 male, 55+ 11 years) admitted to the coronary care unit with a first acute ST-segment elevation myocardial infarction. The STEMI patients were prospectively enrolled in our clinic. STEMI was defined according to the WHO criteria with a typical chest pain, ST segment elevation> 1 mm in contiguous leads and elevation of creatine kinase isoenzyme MB (CKMB) at least two times. The exclusion criteria were as follows; previous AMI, previous coronary artery bypass grefting or coronary intervention, atrial fibrillation, inadequate view of echocardiography, chronic renal insufficiency, presence of mechanical complications. Written informed consent was optained from all patients

Clinical characteristics

All of the patients were treated by either primary angioplasty or thrombolytic therapy and patients were assigned into two groups: angioplasty group (n=54); and thrombolysis group (n=60). Reperfusion strategies in each patient were determined by recommendation of ACC/AHA guidelines for the management of patients with STEMI (Antman et al., 2004). Initial fibrinolytic therapy were chosen in patient with low bleeding risk who present very early after symptom onset (<2 to 3 hours) and who have longer delay to PCI (>120 minute). Of these patients, 54 were treated with primary angioplasty and 60 had thrombolytic agents. Low-flow nasal oxygen, oral aspirin (300 mg), intravenous nitroglycerin, beta-blocker, angiotensin converting enzyme inhibitors were administered to patients without contrandications in each group. Heparin was given according to treatment group to which the patients was assigned. CKMB levels were measured in blood samples to enzymatic estimation of infarct size.

Coronary angioplasty procedure

Coronary angiography (Siemens Artist, Acompc ver. 1.1) was performed in angioplasty group patients before and after the procedure without ventriculography. Coronary angiography was not performed in patients treated with thrombolytic agents in the acute phase of myocardial infarction unless recurrent ischemia. Angioplasty procedures were performed using the Judkins technique with a 6-7 French (Fr) guiding catheter via the femoral artery approach. A bolus of 75–100 IU/kg of heparin was administered after securing arterial access achieving an activated clotting time of at least 300 seconds. Oral 300-600 mg loading dose of clopidogrel was administered to these patients. Platelet glycoprotein IIb/IIIa-receptor blockers (tirofiban) were administered (70%) at the discretion of the physician.

The infarct-related artery was treated if it was totally occluded, if there was a culprit lesion with stenosis of more than 50 percent of the luminal diameter, or if it had a flow grade of less than 3 according to the Thrombolizis in Myocardial Infarction (TIMI) classification. Stenting of the culprit lesion was attempted in all patients, unless the vessel had a diameter of less than 2 mm and stent-like results (two patients) after balloon angioplasty. Also direct stenting was performed in 8 patients. The duration of each inflation was at least 30 s (30–60 s) and mean inflation pressure 12 atm (8–15 atm). Angioplasty for non-infarct-related arteries did not performed.

Thrombolytic therapy protocol

Thrombolytic agents were administered to patients in whom primary angioplasty not recommended by ACC/AHA guidelines (Antman et al., 2004). The patients received either streptokinase (86%) or tissue-type plasminogen activator [tPA] (14%). Streptokinase was given intravenously 1.5 Million Units within a period of 60 minutes. Accelerated t-PA an intravenous bolus of 15 mg, followed by an infusion of 0.75 mg per kilogram of body weight [not to exceed 50 mg] over a 30-minute period and then 0.50 mg per kilogram [not to exceed 35 mg] over the next 60 minutes, for a maximal total dose of 100 mg was given.

Echocardiographic examination and Doppler measurement

Two dimensional and Doppler echocardiographic examination were performed with a Vingmed cardiac ultrasound unit using a 2.5 MHz transducer. Echocardiographic examination was performed 3 (2–4) days after AMI and the results were assessed by two cardiologist. Assesment of LV systolic function was done by Wall motion score index (WMSI) and left ventricular ejection fraction (LVEF). WMSI and LVEF were measured in all patients by two-dimensional echocardiography to assess the left ventricular systolic function. Left ventricular wall motion was analyzed

according to the 16-segment model and global wall motion score index was calculated. LVEF was estimated using Simpson's method (Schiller et al., 1989).

Left ventricular diastolic function was evaluated by the pulsed Doppler technique. The mitral inflow velocity pattern was recorded from the apical four chamber view by placing the sample volume between the tips of the mitral leaflets during diastole. Three consecutive beats were measured and averaged for each measurement. Diastolic filling indexes, including the peak transmitral velocity of early rapid filling wave (E), peak velocity of late filling wave (A), the E/A ratio and mitral deceleration time (DT) were analysed. Echocardiographic measurements were applicable in 114 patients. One patient was excluded as the mitral flow did not measurable due to fusion of the Doppler waves. Other patient was died 12 h after AMI.

Diastolic dysfunction was diagnosed in the presence of one of the following diastolic pattern; 0.75<E/A<1.5 and DT >150 was defined normal filling pattern, E/A less than 0.75 was defined as impaired relaxation pattern, 0.75<E/A<1.5 and DT <150 ms was defined as pseudonormal pattern and E/A>1.5 was defined as restrictive filling pattern (van Kraaijn et al., 2002; Khouri et al., 2004). These diastolic patterns were considered as from low to high level of the severity of diastolic dysfunctions respectively.

Statistical analysis

All data are expressed as mean ± SD. The statistical analysis were performed using the Statistical Package for Social Sciences software (SPSS Inc. Chicago, Illinois, USA). Differences between mean values in the two groups were compared using by Student's t-test and Mann-Whitney nonparametric test. The frequencies between the two groups were compared by the chi-square test. The association of WMSI with mean CKMB levels was analysed with the use of Pearson correlation. P value of less than 0.05 was considered as statistically significant.

3. Results

Clinical characteristics

The clinical characteristics of subjects are summarized in Table 1. Baseline clinical characteristics were similar in both groups. A total of 114 patients who had STEMI were screened for inclusion. Two patients were excluded (see above). The time from the onset of symptoms to initiation of reperfusion treatment did not differ in two groups (4.12± 3.04 h vs 4.40± 2.43h, p>0.05). There was no difference between two groups in terms of rates of location of AMI. Anterior location AMI was observed in 29 cases in angioplasty group and 32 cases in thrombolysis group (Table 1).

Table 1. Baseline clinical characteristics in patients with primary angioplasty and thrombolytic groups.

	Angioplasty (n=54)	**Thrombolysis (n=60)**	***p Value***
Age(years)*	54±12	56±11	ns
Male	46(85%)	49 (81%)	ns
BMI(kg/m2)*	27.0±4.4	26.7±4.5	ns
Diabetes mellitus	15(28%)	12(20%)	ns
Hypertension	21(39%)	17(28%)	ns
Smoking	32(59%)	39(65%)	ns
History of family	18(33%)	18(30%)	ns
Hyperlipidemia	8(15%)	8(13%)	ns
LVMI (g/m2)*	92±34	105±42	ns
Heart rate(beats/min)*	75±13	78±14	ns
Peak CKMB (U/L)*	300±209	326±202	ns
Systolic blood pressure(mmHg)*	112±12	113±14	ns
Diastolic blood pressure(mmHg)*	70±8	69±10	ns
Anterior location of infarct	29(55%)	32(53%)	ns
Time from the onset of symptoms to initiation of treatment (hr)*	4.12±3.04	4.40 ±2.43	ns
Medication			
Beta-blocker	50(93%)	56(93%)	ns
Aspirin	54(100%)	60(100%)	ns
ACE inhibitor	47(87%)	55(92%)	ns

*Values are mean ± SD; BMI = Body mass index; ACE = Angiotensin converting enzyme; LVMI = Left ventricle mass index; CKMB = Creatin kinase isoenzyme MB; ns= p>0.05.

There was no statistical difference between two group according to success of reperfusion treatment (p=0.148). Successful revascularization (TIMI flow grade ≥ 2) was observed in 50 (92%) patients in angioplasty group. Successful thrombolysis was observed in 49 (81%) patients in thrombolysis group, which it was evaluated with clinical parameters such as relief of pain, ST segment resolution and early peak in CKMB level.

Systolic functions

WMSI was significantly lower in angioplasty group (1.31 ± 0.30) compared to thrombolysis group (1.45 ± 0.40) (p<0.01). LVEF did not differ between treatment groups (50 ± 9 % vs 47 ± 8 % p>0.05). The significant correlation was found between CKMB levels and WMSI in thrombolysis group (r =0.510, p<0.001), but this correlation was not observed in primary angioplasty group (p>0.05) (Fig. 1).

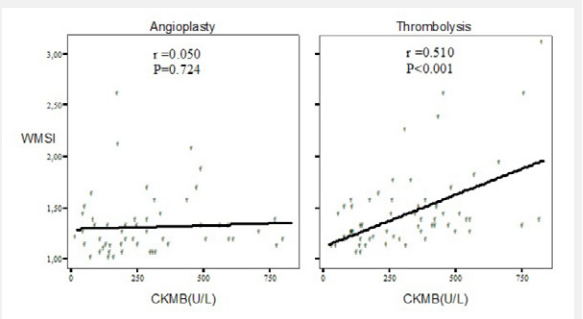

Fig. 1. The relationship between creatin kinase MB (CKMB) and wall motion score index (WMSI).

Diastolic functions and Doppler measurements

Table 2 shows the Doppler derived diastolic parameters. There was no difference between two groups according to E wave and A wave velocity. E wave velocity was 0.62± 0.16 m/s and 0.67± 0.18 m/s, (p>0.05) in angioplasty and thrombolysis group, respectively. Also A wave velocity was 0.65± 0.14 m/s in angioplasty and 0.62± 0.19 m/s in thrombolysis group (p>0.05). But, there was a significant difference for E/A ratio between two groups (0.99± 0.38 versus 1.20± 0.60, P<0.05). DT was 169 ± 61 ms in primary angioplasty group and 163 ± 59 ms in thrombolytic group (p>0.05).

Frequency of LV diastolic dysfunction is presented in Fig. 2. There was no difference between two groups in terms of frequency of diastolic dysfunction (p>0.05). LV diastolic dysfunction was observed in 27 patients (50%) in angioplasty group and 37 patients (62%) in thrombolysis group. The number of patients in different LV filling pattern is presented in Table 2. LV diastolic filling abnormality in patients treated with angioplasty was mostly impaired relaxation (n=13) and pseudonormal pattern (n=10), while it was equally distributed in patients treated with thrombolytic agents between impaired relaxation (n=11), pseudonormal pattern (n=13) and restrictive filling pattern(n=13). However the number of patients with restrictive filling pattern are very low (n=4) in angioplasty group. Primary angioplasty resulted in a reduced number of patient with LV restrictive filling pattern compared to thrombolytic therapy (p<0.05).

Table 2. Echocardiographic variables

Variable	Reperfusion strategy		
	Primary angioplasty (n=54)	Thrombolysis (n=60)	*p Value*
LVEF (%)	50±9	47±8	ns
WMSI	1.31±0.30	1.45±0.40	<0.01
E (cm/s)	0.62±0.16	0.67±0.18	ns
A (cm/s)	0.65±0.14	0.62±0.19	ns
DT(ms)	169±61	163±59	ns
E/A	0.99±0.38	1.20±0.60	<0.05
Diastolic dysfunction patterns (n,%)			
impaired relaxation pattern	13 (24%)	11 (18%)	ns
pseudonormal pattern	10 (19%)	13 (22%)	ns

Values are mean ± SD; E= Peak transmitral velocity of early rapid filling wave; A= Peak velocity of late filling wave; DT= mitral deceleration time; LVEF= left ventricular ejection fraction; WMSI= wall motion score index; ns= p>0.05.

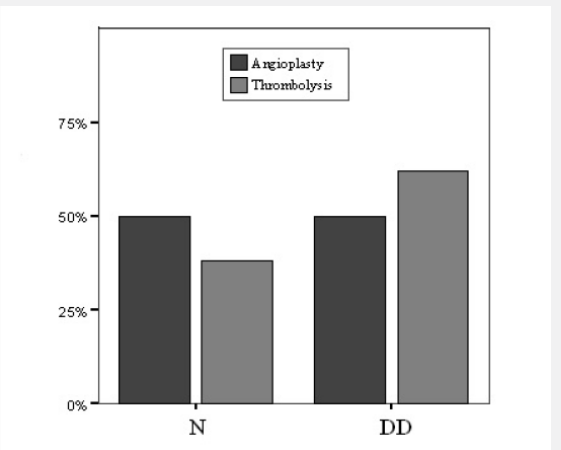

Fig. 2. The frequency of diastolic function in patients treated with primary angioplasty and thrombolytic agents. N: Normal diastolic function, DD: Diastolic dysfunction.

4. Discussion

Our study shows that primary PCI has a more beneficial effect on left ventricular functions using the echocardiogarphic index in STEMI patients. These favourable results has been observed especially systolic function by assesed WMSI and diastolic dysfunction by restrictive filling abnormalities.

Diastolic dysfunction after AMI has a prognostic information provided by the diastolic assessment independent from that derived from the systolic evaluation alone (Poulsen et al., 2001; Azevedo et al., 2004) and it has been shown that diastolic dysfunction plays an important role in the development of clinical heart failure following AMI (Poulsen et al., 1987). Moreover, ischaemic injury after AMI affects both systolic and diastolic function. Indeed, it has been demonstrated that the phenomenon of myocardial stunning has both a systolic and a diastolic component (Azevedo et al., 2004). Myocardial stunning and hibernation have been observed after PTCA and thrombolysis in AMI (Kloner and Jenning, 2001).

Mechanical reperfusion seems to exert more favorable effects on early LV filling abnormalities after AMI compared with thrombolysis, probably because of an anti-remodelling effect of the open infarct-related artery (Cerisano et al., 2001). In the present study, the effect of primary angioplasty on LV diastolic functions have been investigated in the early phase

of AMI using transmitral flow velocities by Doppler echocardiography. Two-dimensional echocardiography is an excellent method for diagnosing systolic dysfunction, and Doppler echocardiography has become well accepted as a reliable, reproducible and practical noninvasive method for diagnosing and longitudinal follow-up of patients with diastolic dysfunction (Nishimura and Tajik, 1997). In our study, the number of cases with diastolic dysfunction were lower in primary angioplasty group. But, there are no significantly differences between two group in diastolic dysfunction frequency. However the frequency of restrictive filling pattern were found higher in thrombolysis group than angioplasty group. Additionally, mean E/A ratio was significantly elevated in thrombolysis group. This is may be due to the high number with the restrictive filling pattern in these patients. However the deceleration time was decreased in thrombolysis group, indicative of a restrictive filling pattern, but it was not significant. The patients with a restrictive LV filling pattern after early phase of AMI have a poor clinical outcome, even if treated with primary angioplasty (Garcia-Rubira et al., 1997; Cerisano et al.,2001). Thus, our results suggest that primary angioplasty was more effective than thrombolytic therapy on preservation for restrictive filling pattern in early phase of AMI. The protective effect of primary angioplasty on restrictive filling pattern may contribute to the better clinical outcomes.

LV diastolic function is determined by the energy dependent deactivation of contractile elements in the sarcomere (relaxation) and the passive properties of the ventricle during filling (compliance) (Bayata et al., 2000; Moller et al., 2003). Both myocardial relaxation and compliance are affected by ischemia, but the predominant diastolic abnormality is the impaired relaxation (Poulsen et al., 1997). The effect of percutaneous transluminal coronary angioplasty (PTCA) on LV diastolic function has been investigated in a number study. The studies showed that early or late improvement in LV diastolic function following PTCA. A study by Schanwell et al. (2001) showed an early improvement of LV diastolic function 48 hours after stent implantation. They reported that there was no significant short-term (48 hours) improvement of diastolic function. Joserich et al. (1990) found that LV diastolic filling is more pronounced within 24 hours after angioplasty, compared to 3 hours after PTCA. Klisiewicz et al. (2002) reported that LV diastolic functions were improved following angioplasty in 1 to 6 months after AMI, these patients were evaluated with the tissue Doppler Imaging. In contrast, Ricou et al. (1992) reported the persistence of diastolic filling abnormalities 3 months after angioplasty in patients with isolated coronary stenosis and normal systolic function. However the primary angioplasty and thrombolysis were not compared in these studies and there are limited information available regarding to diastolic functions in the early phase of AMI.

Despite the greates. reperfusion rates associated with primary angioplasty, a difference in left ventricular ejection fraction have not always revealed among patients treated with primary angioplasty and lytics (Berger and Gersh, 2001). In our study, primary angioplasty brings out a better preserved myocardial systolic function compared to patients who received thrombolytic therapy. This systolic preservation has been observed as wall motion score index, though left ventricular ejection fraction was slightly increased in primary angioplasty group. Semiquantitative assessment of regional systolic function using wall motion score index is an alternative to LVEF for the assessment of left ventricular systolic function. Moller et al. (2006) were found a close negative correlation between LVEF and WMSI in AMI patients and they have showed the predictive power of WMSI for prognostic information is greater than LVEF.

In study by Ottervanger et al. (2001), the patients treated with primary angioplasty showed a significant improvement almost 50% in left ventricular systolic functions after 6 months. But no data was available about diastolic dysfunction in their study.

In our study, the enzymatic estimation of infarct size by CKMB was significantly correlated with WMSI in thrombolysis group, but no correlation was observed in angioplasty group. The preservation of systolic functions associated with angioplasty may be independent of enzymatic elevations. In addition, the elevation of enzymes in patients with primary angioplasty may not reflect the severity of myocardial damage.

Some trials reported that the primary angioplasty showed a more beneficial effect in patients with anterior infarct location (de Boer et al., 1994; Ottervanger et al., 2001). However, the almost equal number of patients in two groups with anterior wall AMI in our study, may show that the effect of primary angioplasty on LV diastolic function are independent of the location of AMI.

Limitations

In the current study, diastolic functions were assessed only by standart traditional Doppler filling indices. We did not use the new echocardiographic applications such as flow propagation velocity by colour M-mode Doppler echocardiography, mitral annulus velocities by tissue Doppler echocardiography and pulmonary venous flow velocities. Furthermore, invasive haemodynamic measurements were also not performed. Echocardiographic examination was not performed before and after angioplasty or thrombolysis because this treatment regimens were urgent. Therefore diastolic functions did not compared before and after the procedures.

Conclusions

Primary angioplasty is more effective than thrombolytic therapy in reducing short-term and long-term major adverse cardiac events. The primary mechanism of benefit of primary angioplasty may be related to early restoration of coronary flow. However, differences in outcomes is influenced not only by systolic functions, but also by the diastolic functions; especially restrictive filling pattern. In consequence, the primary angioplasty seems to have more favorable effects on restrictive filling abnormalities after early phase of AMI. This protective effect may contribute to better clinical outcomes in patients with AMI treated by primary angioplasty.

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Comparison of efficacy of epidural triamsinolone and betamethasone injection on blood glucose and pain in non-diabetic patients

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Triamcinolone

ABSTRACT

The aim of this study is to compare the effects of two different steroid medication on pain and blood glucose for non-diabetic patients suffering from low back and leg pain for the purpose of providing epidural analgesia. ASA I-II classified non-diabetic 60 patients were involved into this study. In group 1, betamethasone 6 mgr+10 mgr bupivacaine and in group 2, triamcinolone 40 mgr+10 mgr bupivacaine were applied with epidural injection. VAS scores, blood glucose measures, and satisfaction scales were analysed. In the comparison of VAS values with initial VAS values of patients in group 1 and group 2, there was significant decrease for all time-points. VAS scores for the group 1 were found low, comparing to group 2, in the second, fourth and sixth hours after the injections, but it was found as high in the second week and first month. In the comparison of blood glucose values with its initial scores for group 1 patients, there was significant increase in the fourth hour. For group 2, significant difference was not observed. When the blood glucose values were compared between group 1 and 2 patients, there was significant increase for group 1 in the second and the fourth hour after injections. In the sense of patient satisfaction scale, significant difference cannot be observed between groups. Epidural betamethasone and triamcinolone were observed that both of them are effective for low back and leg pain. It was found that epidural betamethasone was more effective in the early period, and triamcinolone was more effective in the later period. Epidural betamethasone injection increased blood glucose levels in the early period. It was found that epidural triamcinolone injection did not cause any significant changes in blood glucose level. Triamcinolone not changing blood glucose levels can be regarded as an advantage of this treatment.

1. Introduction

Low back pain is one of the common causes of referral to physicians and its life-long incidence is 40-60% (Priffman et al., 2001; Tong et al., 2003; Lee et al., 2006). Spinal stenosis and lumbar intervertebral disc herniation are the most common causes of low back pain, leading to serious limitations in the social life of patients (Helliova et al., 1987; Bush et al., 1992; Botwin

et al., 2002; Vad et al., 2002; Karaeminoğulları et al., 2005; Jeong et al., 2007). The majority of the patients benefit from conservative treatments such as bed rest, oral medications, lifestyle changes, corset use, physical therapy and exercise. Epidural steroid injection is a low-risk treatment option that can be used in patients who do not benefit from conservative treatment. It has been suggested that the most important factor playing a role in the development of radicular symptoms is inflammation in nerve roots. Steroid administered to the epidural region exerts its effect by reducing inflammation. Epidural steroid application for low back pain was first described by Robecchi and Capra in 1952. Success rates of epidural steroid applications ranging from 20% to 100% have been reported (Lutz et al., 1998). Although initial success rates in acute and chronic pain were found to be equal, the 6-month success rate dropped to 34% in acute pain and to 12% in chronic pain. Studies have shown that epidural steroid and local anesthetic injections are effective and safe methods of reducing radicular pain in patients with lomber radiculopathy.

Steroid agents have been shown to increase blood glucose in non-diabetic and diabetic patients. Historically, steroid administration is under debate in patients with Type-I and Type-II diabetes. There are not enough prospective studies describing epidural steroid administration in diabetic and non-diabetic patients and the effect of various steroid-type drugs on blood glucose. In this study, we aimed to compare the effect of two different steroid preparations administered with epidural method on blood glucose levels and chronic low back and leg pain related to radiculopathy in non-diabetic adult patients aged 18-65 years.

2. Materials and methods

60 patients aged 18-65 years and ASA grade I-II, who applied to the Algology clinic of Ondokuz Mayıs University Medical Faculty for complaints of leg pain and low back pain for more than 6 weeks due to radiculopathy, who were not previously operated were included in the study. After receiving the approval of the Ondokuz Mayıs University Local Ethics Committee and written consent of patients, the patients were randomly assigned two groups. Patients with Type I-II diabetes and preoperative blood glucose levels outside 70-100 mg/dl, endocrine diseases, morbid obesity (BMI> 30), patients using drugs that affected sugar metabolism, patients with more than three failed epidural application attempts, patients with hemorrhagic disorder and receiving anticoagulant therapy, patients with infection in the treatment area and those who did not come to controls were excluded from the study. During the study, patients with blood glucose ≥ 160 were excluded from the study after initiating a GIK solution (5% dextrose + 8 ug insulin + 10 mEq potassium).

Patients were randomly divided into two groups.

Group 1; Betamethasone 6 mg + 0.5% 10 mg bupivacaine (reconstituted with saline as total 5 cc)

Group 2; Triamcinolone 40 mg + 0.5% 10 mg bupivacaine (reconstituted with saline as total 5 cc)

All patients were monitored on 3-lead ECG, pulse oximetry and non-invasive blood pressure measurements after being taken to the operation table after 8 hours fasting before the procedure. Patients were given 6 l/min oxygen with a mask. The vein was opened with 18-20 gauge cannula on the back of the hand. During the procedure, heart rate, mean arterial pressure and peripheral oxygen saturation were monitored.

Patients were lyed down on their side with the pain. Sterile treatment and covering of the intervention area was performed with antiseptic solution (10% povidone iodine). The reference anatomical points were determined so that the intervention could be made in the middle line and from the most appropriate intervertebral range (L2-3, L3-4 or L4-5). Local anesthesia was established with 2-3 mL of 2% prilocaine in the area of skin, subcutaneous and supraspinous ligament at the specified intervention point. An epidural injection was made with a median approach at the epidural distance from interlaminary distance with a 18 G (1.3 mm) Touhy needle (Perican, 88 mm) using the 'resistance loss' method with 3-5 ml sterile saline. Blood glucose levels of the patients were recorded before epidural injection, at 2nd, 4th, 6th, 48th hours, 2nd week, and 1st month after the injection, by measurements from the fingertip. Visual Analog Scale (VAS) scores were recorded before and after the injection at 2nd, 4th, 6th, 48th hours, 2nd week, and 1st month. Patients were followed-up regarding side effects and complications such as nausea-vomiting, itching, restlessness, tinnitus, numbness in the mouth, palpitations, metallic taste, dizziness, headache, hematoma at the injection site, infection, rash, weight gain, subarachnoid damage, arachnoiditis, paralysis, paraplegia, loss of strength, bladder dysfunction, meningitis, and flushing. Patients were also assessed at the end of the first month by a satisfaction scale. Satisfaction was assessed as follows: 0 = very bad, 1 = bad, 2 = good, 3 = very good, 4 = excellent. Satisfaction score of at least 2 was considered successful.

Statistical analysis

"SPSS for Windows 20.0" package program was used for statistical analysis. Shapiro Wilk test was used for checking normal distribution of continuous data. Student T test was used to compare groups. Anova test was used in the analysis of repeated measurements. Binary comparisons were made for repetitive measurement analysis in intra-group comparisons. Pearson Chi-Square independence test was used for the inter-group comparison of the data obtained by

census. Mann Whitney-U test was performed since VAS and SpO2 values did not fit normal distribution. Other continuous variables were expressed as Mean ± Standard Deviation as they were normally distributed. Significance level was accepted as $p < 0.05$.

3. Results

There was no significant difference between groups in terms of demographic characteristics and ASA classification (p>0.05) (Table 1).

Table 1. Demographic characteristics of groups and ASA Classification (Mean ± Standard Deviation).

Variable		Group 1	Group 2	P
Age		54.76±11.61	51.80±11.34	0.321
Gender	**Female**	12 (% 40)	15 (%50)	0.604
	Male	18 (% 60)	15 (%50)	
Weight		77.20±9.27	76.86±11.61	0.903
Height		168.13±8.61	168.33±8.82	0.930
ASA	**ASA I**	17 (%56.6)	16 (% 53.3)	1.000
	ASA II	13 (%43.4)	14 (% 46.7)	

There was no significant difference between the groups in terms of HR, MAP and SpO2 values. (p > 0.05).

When VAS scores of the patients were compared with the baseline VAS scores in Group 1 and Group 2, VAS scores were significantly lower at all time points ($p < 0.05$) (Table 2).

Table 2. Comparison of VAS scores with Baseline VAS Scores (Mean ± Standard Deviation).

VAS	Group 1	P	Group 2	P
Pre-Injection	7.33±0.75	-	7.26±0.90	-
2nd Hour	3.9±1.24	<0.001	5.40±1.27	<0.001
4th Hour	3.7±0.95	<0.001	5.16±1.11	<0.001
6th Hour	3.73±1.11	<0.001	4.96±1.21	<0.001
48th Hour	5.26±1.48	**<0.001**	4.83±1.17	<0.001
2nd Week	5.26±1.48	**<0.001**	4.7±0.98	<0.001
1st Month	5.3±1.31	**<0.001**	4.56±1	<0.001

The comparison of VAS scores between groups. is shown in Figure 1. Although the VAS scores of group 1 were lower than group 2 for post-injection hours 2, 4 and 6, VAS scores of group 2 were lower than group 1 on the 2nd week and 1st month after the injection ($p < 0.05$) (Fig. 1).

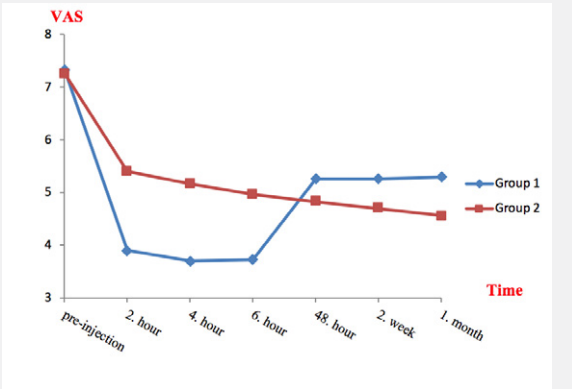

Fig. 1. VAS scores of Group 1 and Group 2

Comparison of blood glucose levels of patients in Group 1 and Group 2 with baseline blood glucose levels is shown in Table 3. Accordingly, only Group 1 had a statistically significant increase in blood glucose levels at 4 hours after injection ($p < 0.05$).

Table 3. Comparison of blood glucose levels in Group 1 and Group 2 with baseline blood glucose levels (Mean ± Standard Deviation).

Blood Glucose	Group 1	P	Group 2	P
Pre-Injection	94.60±7.44	-	93.60±10.56	-
2nd Hour	106.56±19.60	0.064	99.40±14.20	0.075
4th Hour	111.76±30.23	0.043	96.56±9.87	1.000
6th Hour	102±20.56	1.000	94.03±8.42	1.000
48th Hour	90.46±9.37	**0.054**	94±15.25	1.000
2nd Week	94.56±11.65	**1.000**	92.3±10.08	1.000
1st Month	94.53±6.61	**1.000**	92.13±7.97	1.000

When blood glucose levels were compared between groups, it was found that 2nd and 4th hour measurements were significantly higher in Group 1 in comparison with Group 2 ($p< 0.05$).

There was no significant difference between the groups in terms of patient satisfaction (Table 4) (p > 0.05).

Table 4. Comparison of patient satisfaction scale between groups.

	Group 1	Group 2
Bad (0-1)	%13.3(4)	%13.3(4)
Good (2)	%43.3(13)	%33.3(10)
Excellent (3-4)	%43.3(13)	%53.3(16)
P	0.704	

4. Discussion

In this study, we compared the effect of two different steroid preparations combined with local anesthesia administered by epidural method on blood glucose levels and chronic low back and leg pain related to radiculopathy in non-diabetic adult patients aged 18-65 years.

Injection of corticosteroids into the epidural space is a non-surgical interventional method that is used the treatment of pain. The use of this method in the treatment of low back and leg pain was first reported in 1925 by caudal procaine injection. In 1952, Robecci and Kapra reported the injection of hydrocortisone to the first sacral canal in patients with low back and leg pain, and Lievre reported lumbar epidural hydrocortisone injection for the treatment of low back pain in 1957 (Güldoğuş, 2007). Epidural steroids are used because of abnormal nociceptive formation around the lesion and secondary neuroradiculitis caused by inflammatory mediators (Güldoğuş, 2007). Corticosteroids inhibit prostaglandin synthesis, stabilize cellular membranes, and block the delivery of nociceptive C fibers. The point of effect of corticosteroids on eicosanoid synthesis is the step in which arachidonic acid forms from membrane phospholipids, and they exert their effect by inhibiting phospholipase A2 enzyme catalyzing this step (Saal and Saal, 1989; Güldoğuş, 2007). Epidural steroids can be applied in 3 different regions (cervical, thoracic and lumbar) by 2 different ways (interlaminar and transforaminal epidural) and caudally. In this study, steroid medication was administered to the lumbar epidural area via interlaminar way.

VAS is a simple, reliable, and quick method of measuring pain severity in the clinic. It is highly sensitive in evaluating efficacy of pharmacologic and nonpharmacologic treatments that reduce pain. Its correlation with verbal and numerical pain scales is good. Akbaş et al. (2009) examined 30 patients with radiculopathy for the efficacy of transforaminal epidural steroid injection. Patients were injected at the level of disc herniation, and pain severity was assessed with Verbal Numerical Rating Scale (VNRS) and satisfaction level was assessed with a 4-point scale at the end of the study. It was found that transforaminal epidural steroid injection significantly reduced pain for up to 3 months in the treatment of patients with radiculopathic pain (Akbaş et al., 2009). Interlaminar epidural injection method was chosen in our study because efficacy of epidural injection is not observed since there is no previous epidural injection; the transforaminal procedure is performed under fluoroscopy and includes radiation, is more difficult and may cause more neuronal damage. Our study suggests that betamethasone and triamcinolone cause a significant decrease in VAS values compared to pre-intervention values and may be administered epidurally in patients with chronic low back pain. In a study conducted by Gelalis et al. (2009), 40 patients with radiculopathy due to L4-L5 and L5-S1 disc herniation were treated with three epidural steroid injections consecutively every 24 hours via spinal catheter, and the other group was treated with three epidural steroid injections intermittently over 10 days via epidural needle. The VAS score of all patients decreased with respect to baseline at 1st month of follow-up and there was no significant difference between the two groups. VAS scores were found to be significantly lower in the group that was injected with epidural needle at 2nd month of follow-up (Gelalis et al., 2009). In a study by Ho-Joong Kim et al. (2012), the efficacy of transforaminal epidural steroid injection in lumbar disc herniation was examined. Fifteen patients with lateral herniation of the lumbar disc and 70 patients with interspinal lumbar disc herniation were included in the study. No difference was found between the two groups for VAS and Oswestry disability index (Kim et al., 2012). In the study of Benoist et al. (2012), the efficacy and safety of epidural steroid injection in the treatment of low back pain caused by radiculopathy was examined, and Cochrane performed a literature review. As a result, epidural steroid injections were generally well tolerated and most of the complications were due to technical problems (Benoist et al., 2012). No complications were observed in our study. In the study conducted by Ho-Jong Kim et al. (2013), the efficacy of two different methods for herniated lumbar disc-induced pain, epidural neuroplasty and transforaminal epidural steroid injection were compared. VAS and functional measurement index were assessed before treatment and at 2nd, 4th, and 8th weeks after treatment. VAS and functional measurement index decreased markedly after both treatments. As a result, they concluded that epidural neuroplasty and transforaminal epidural steroid injection were equally effective treatments for lumbar disc herniation (Kim et al., 2013a). In two different controlled studies conducted by Kraemer et al. (1997) on 182 patients, epidural perineural injection, conventional posterior epidural injection, and paravertebral local anesthetic were administered as control group in patients with lumbar radicular syndrome. Epidural perineural injections were found to be more effective than conventional posterior epidural injections. They reported that both groups administered with epidural injections had better results than the group receiving paravertebral local anesthetic injection. There were no serious complications or side effects in any group. Studies have shown that single shot epidural injection is effective in treating lumbar radiculopathy

(Kraemer et al., 1997). In a meta-analysis of 12 randomized clinical trials conducted by Koes et al. (1995), six of the studies showed that epidural steroids were more effective, while the other six reported that they were no better or worse than the reference treatment. In a meta-analysis of 11 placebo-controlled studies conducted by Watts and Silagy (1995), improvements were observed in both short-term (1-60 days) and long-term (12 weeks-1 year). In our study, the fact that betamethasone lowered VAS value more than triamcinolone in the early post-injection period can be attributed to the faster initiation of analgesic and antiinflammatory effect of betamethasone combined with local anesthetic than triamcinolone. On the other hand, in the late period, although the duration of action of betamethasone was longer, triamcinolone caused a further decrease in VAS values.

The effects of steroid agents on blood glucose are known; glucocorticoids stimulate gluconeogenesis to increase blood glucose, and the hypothalamo-hypophyseal axis is blocked by negative feed-back. Even et al. (2012) studied the effect of epidural steroid injection on blood glucose levels in diabetic patients. In diabetic patients, epidural steroid injection significantly increased blood glucose and these effects did not last longer than 2 days. In our study, the effect of betamethasone and triamcinolone on blood glucose was investigated. Betamethasone significantly increased blood glucose in the early period after epidural injection, and there was no significant difference in subsequent measurements. In triamcinolone treated patients, there was no change in blood glucose levels. In the study of Zufferey et al. (2011), the systemic effects of epidural injection of methylprednisolone on glucose tolerance in diabetic patients were investigated. The aim of the study was to investigate the effect of intra-articular or epidural 80 mg methylprednisolone acetate on glycemic profile in diabetic patients. In five patients treated with epidural injection, the glycemic profile did not change or the change was negligible, and blood glucose was increased by 3 mmol/lt for the next two days in the group given intraarticular steroids. Significant differences were observed in each individual treated with intraarticular injection. This is the first study to show that single dose epidural injection of depot methylprednisolone has no effect on glycemic control in diabetic patients. The absence of glycemic control changes was highly correlated with the low urinary excretion of the drug after epidural injection. In the study of Younes et al. (2007), systemic effects of epidural and intraarticular glucocorticoid injections were evaluated in diabetic and non-diabetic patients. Basal blood glucose increased significantly on day 1. In 12 patients, blood glucose levels significantly increased at day 7 compared to baseline levels. Plasma ACTH, cortisol and urinary cortisol increased markedly in the entire population on days 1 and 7. On day 21, these values were decreased in the epidural injection group whereas they were normal in the intraarticular group (Younes et al., 2007). In a prospective cohort study performed by Gonzales et al. (2009), lumbosacral or caudal epidural betamethasone was administered to 12 diabetic patients for neurogenic claudication or radicural pain. Fingertip blood glucose level was measured 2 times a day for 3 days before the injection, on the injection day, and for 3 days after the injection. A significant increase was found in blood glucose levels for the next 3 days after injection. It was found that this increase peaked on injection day and ended in about 2 days (Gonzales et al., 2009). In Kim et al.'s study (2013b), the effect of two different epidural steroid doses on blood glucose level and pain control in diabetic patients was examined. In one thousand diabetic patients, lumbar transforaminal, lumbar interlaminar, or caudal epidural thiramycinolone injection was performed at 20 mg and 40 mg doses for radiculopathy and spinal stenosis. On the next day after the injection, a significant increase in fasting blood glucose levels was found in the group administered with 40 mg dose, and a significant increase was found in postprandial blood glucose levels in both groups. High doses of triamcinolone increased fasting and postprandial blood glucose levels more, but there was no difference in pain control. Accordingly, 20 mg triamcinolone was found to be more recommendable than 40 mg in diabetic patients in terms of blood glucose and pain control. In our study, there was no change in blood glucose in non-diabetic patients who received triamcinolone. Our results suggest that triamcinolone may be more likely to be recommended in both diabetic and nondiabetic patients, as it causes less irregularity in blood glucose levels compared to betamethasone. In a study conducted by Moon et al. (2014), 29 diabetic and non-diabetic patients with sciatic or shoulder pain were treated with epidural or intra-articular glucocorticoid injection on the shoulder, and the changes in blood glucose and cortisol levels were examined. In patients, the fasting plasma glucose level was significantly increased the next day after injection but returned to the baseline value on the 7th day after injection. Cortisol levels decreased significantly on days 1 and 7 after injection compared to baseline. Moon et al. (2014) demonstrated the necessity of paying close attention to glucocorticoid injection treatment in diabetic patients, especially epidural injections, but they did not find any difference between the groups in terms of patient satisfaction, and both groups were evaluated with perfect scores. In the study conducted by Çetin et al. (2012), the efficacy and safety of transforaminal lumbar

epidural steroid injection in patients with radiculopathy due to lumbar disc herniation were investigated. In the patient satisfaction questionnaire, 63.9% of the patients stated their satisfaction as 'good or excellent (Çetin et al., 2012).

In conclusion, it was observed that triamcinolone and betamethasone combined with local anesthetic were effective on chronic low back and leg pain due to radiculopathy. Betamethasone was found to be more effective in the short term after injection, whereas triamcinolone was more effective in the long term. Triamcinolone did not cause changes in blood glucose levels after epidural injection. On the other hand, betamethasone significantly increased blood glucose levels in comparison with triamcinolone in the early period after epidural injection. Triamcinolone and betamethasone resulted in similar levels of patient satisfaction in the treatment of chronic low back and leg pain associated with radiculopathy. Triamcinolone not changing blood glucose levels can be regarded as an advantage of this treatment.

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Hand preference in patients with acute coronary syndrome

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ABSTRACT

The relationship between left-handedness and morbidity and mortality of some disorders has been extensively studied in recent years. We aimed to investigate whether a relation with coronary artery disease proven with angiography and hand preference exist or not. This is a prospective cross-sectional study including a total of 633 patients admitted to the ED. Hand preference was assessed using the Edinburg Handedness Inventory. Patients whose hand lateralization could not be evaluated via Edinburg Handedness Inventory and whose coronary angiography detection were unable were excluded. All patients with angina pectoris admitted to ED were evaluated via current guidelines. Selective left and right coronary angiography was performed and the lesion severity and coronary anatomy were evaluated. A total of 633 patients were included in the study. Edinburg handedness inventory assessment showed that of the study population, 93.2 % was right-handers and 6.8% was non-right handers. For the patients ≥65 years, the ratio of right handers in patients with angiographically proven coronary artery diseases were markedly higher compared to patients with non-right handers.Physicians should give attention to this situation while evaluating coronary angiographies. Non-right handedness seems to have a protective affect against CAD in the elderly.

1. Introduction

Individuals can have either a weak or a strong preference for the contralateral hand. However, the left hand is consistently preferred only by a small percentage of individuals (about 12% of males and 8 – 10% of females) when performing a range of everyday tasks (Gilbert and Wysocki, 1992; Annett, 2004; Papadatou-Pastou et al., 2008). Left handers who show a mixed pattern, using their right hand for some activities and the left for others, are said to have a weak or mixed hand preference.

In recent years, there have been extensive studies of the association between left handedness and morbidity and mortality in various disorders, such as attention deficit disorder, Alzheimer's disease (cognitive deficits) and sleep apnea (Hoffstein et al., 1993; Doody et al., 1999). However, the notion of reduced longevity in left-handers has been disputed (Hoffstein et al., 1993; Doody et al., 1999).Thus, the aim of the present study was to investigate the potential relationship between hand preference and angiography-proven coronary artery disease (CAD).

2. Materials and methods

Study design and population

This was a prospective cross sectional study of 633 patients aged more than 18 years who were admitted to the emergency department (ED) between 10

September 2013 and 10 August 2014 with a suspicion of acute coronary syndrome. Patients were excluded whose hand lateralization could not be evaluated via the Edinburg Handedness Inventory (Alzheimer's, demans, mental disorders) and coronary angiography detection were unable (n =17, n =42, respectly). The study was approved by the local ethics committee (Reg. no:B30.2.ATA.0.01.00/165).

The Edinburg Handedness Inventory was used to assess hand preference (Oldfield 1971). Subjects with handedness scores of over + 40 were considered right-handers, and those with scores lower than - 40 were considered left-handers. Subjects with scores between -40 and + 40 were considered ambidextrous. According to the Edinburg Handedness Inventory scale, 33 patients were left handers, and 10 were ambidextrous. In the study, the left handers and ambidextrous patients were combined to aid the statistical analyses.

All the patients with angina pectoris who were admitted to the ED were evaluated according to current guidelines (Langorgen et al., 2014). ST segment elevation myocardial infarction (STEMI) was defined as a ST segment elevation in two contiguous precordial leads (in V2-3, ≥ 2 mm for men and 1.5 mm for women; ≥ 1 mm in other leads) or new onset presumed left bundle branch block. Non-STEMI was defined as troponin exceeding the 99th percentile of a normal reference population (> 0.06 ng/ml for troponin I in our laboratory) and having at least one of the following: ischemic symptoms, electrocardiographic changes in the ST segment or T-wave, or evidence of new loss of viable myocardium on imaging. Unstable angina was defined as ischemic symptoms without troponin elevation, ST segment or T-wave changes in electrocardiography, or evidence of new loss of viable myocardium on imaging.

All the coronary angiography procedures were performed using the femoral artery route. Selective left and right coronary angiography was performed, and the severity of the lesion and coronary anatomy were evaluated. Coronary lesions from at least two nonforeshortened angiographic views were evaluated. Angiographic CAD was defined as more than 50% stenosis in major epicardial coronary arteries and was graded as one vessel, two vessel, or three vessel disease.

Statistical analysis

Numeric variables were expressed as the mean ± standard deviation, and categorical variables were given as percentages. The distribution of numerical variables was assessed using the Kolmogorov Smirnov test. In comparing the right and left handed groups, a Student's t-test was used for normally distributed numerical variables, and the Mann–Whitney U test was used for non-normally distributed numerical variables. A chi square test was used for categorical variables. A p value of < 0.05 was accepted as statistically significant. All statistical analyses were done by SPSS 20.0 (SPSS Inc., Chicago, IL) for Windows.

3. Results

The study consisted of 633 patients (mean age, 61.1 ± 12.2; 74.2%, male). The diagnoses of the patients were as follows: 26.7% STEMI, 24.1% Non-STEMI, and 49.2% unstable angina pectoris. The coronary angiography results revealed normal coronary arteries in 28.4%, single vessel disease in 35.5%, two vessel disease in 20.4%, and three vessel diseases in 15.6% of cases. The Edinburg Handedness Inventory assessment showed that 93.2% of the population were right handed and that 6.8% were nonright handed (5.2% left handed and 1.6% ambidextrous). In the group with normal coronary arteries, the ratio of left handers was 10%, whereas the ratio was 6.8% among patients with at least one vessel disease (p = 0.131) (Table 1).

Table 1. Baseline characteristics and coronary angiography results of patients according to the hand preference. Results are n (%), mean ± standard deviation, or median (interquartile range).

	all patients n:633	right handers n:586	nonright handers n:47
Baseline characteristics			
Age, years	61.1±12.2	61.3±12.4	58.6±10.6
Male/female	470/163	431/155	39/8
Coronary angiography			
normal coronary arteries	28.4%	27.6%	38.3%
single-vessel disease	35.5%	35.7%	34%
two-vessel diseases	20.4%	21.2%	10.6%
three-vessel diseases	15.6%	15.5%	17%

In the group with proven angiographic CAD, there were more right handers than in the group with normal coronary arteries, with statistically borderline significance (94.3% vs. 90.6%, p = 0.095, OR = 0.58, 95% CI 0.31–1.10). Nevertheless, no relationship was found between hand preference and the severity of angiographic CAD (no disease, single vessel, two vessel, and three vessel: 90.6%, 93%, 97%, and 88%, respectively; p = 0.161).

After categorizing the study population according to age (older age, ≥ 65 years), the analyses for hand preference were repeated (Table 2). Accordingly, for patients of < 65 years, the incidence of right handers did not differ between patients with and without angiographically proven CAD (92.1% vs 92.9%, p = 0.793, OR = 1.11, 95% CI 0.49 – 2.52). In the same age group, the relationship between the severity of angiographically proven CAD and hand preference was comparable (no disease, single vessel, two vessel, and three vessel: 92.9%, 90.9%, 95.4%, and 91.1%, respectively; p = 0.694).

Table 2. Baseline characteristics and coronary angiography results of patients according to the age group. Results are n (%), mean ± standard deviation, or median (interquartile range).

	<65, n:384	≥65, n:249
Baseline characteristics		
Age, years	53.5±8.6	72.9±6.3
Male/female	295/89	175/74
Coronary angiography		
normal coronary arteries	33.1%	21.3%
single-vessel disease	37.5%	32.5%
two-vessel diseases	17.7%	24.5%
three-vessel diseases	11.7%	21.7%

However, for the patients of ≥ 65 years, the ratio of right handers was markedly higher in those with angiographically proven CAD than the ratio of left handers (Table 3). Similarly, a significant relationship was found between hand preference and the severity of angiographically proven CAD (no disease, single vessel, two vessel, and three vessel: 84.9%, 98.7%, 98.4%, and 92.5%, respectively; p = 0.003).

Table 3. Coronary angiography results of over 65 years old patients according to the hand preference. Results are n (%), mean ± standard deviation, or median (interquartile range).

	right handers n:233	nonright handers n:16
Baseline characteristics		
Age, years	73.2±6.2	69.9±5.1
Male/female	162/73	14/2
Coronary angiography		
normal coronary arteries	19.1%	50%
single-vessel disease	33.2%	18.8%
two-vessel diseases	26.4%	6.3%
three-vessel diseases	21.3%	25.0%

When the analyses of hand preference were reanalyzed according to gender, the results revealed no relationship between the existence of CAD and hand preference or the severity of angiographically proven CAD and hand preference.

4. Discussion

Previous studies indicated on the relationship between lateralization and testosterone, a sex hormone that is believed to play a role in heart disease (Lalumière et al., 2000; Tan and Tan, 2001). According to earlier research, androgen levels could explain the protective effect of left handedness against CAD, especially in the elderly (Lalumière et al., 2000). However, debate continues about the effect of this hormone on heart disease, with some studies reporting that the levels were lower in left handers compared to right handers and others claiming that they were higher (Lalumière et al., 2000; Tan and Tan, 2001; Schwarcz and Frishman, 2010). Indeed, population studies reported a rise in all cause and cardiovascular mortality in patients with low testosterone levels (Ponikowska et al., 2010) and within a population of male patients with proven CAD (Malkin et al., 2010). As we did not measure the testosterone levels of patients in the present study, we are unable to express an opinion about whether this hormone has a protective effect against cardiac disease. Further studies of hand preference, cardiac arteries, and blood testosterone levels are needed to shed light on this issue.

Genetic factors and the early fetal environment are both thought to contribute to phenotypic variations in hand preference (Daniel and Yeo, 1993). In some individuals, developmental instability and pathological consequences of obstetric complications or early cerebral insults were reported to be responsible for an increased preference for the left hand (Rasmussen and Milner, 1977; Daniel and Yeo, 1993). Stellman et al. (1977) reported a diminishing percentage of left handers in older age groups. The coronary angiography results of our patients revealed normal coronary arteries in 28.4%, single vessel disease in 35.5%, two vessel disease in 20.4%, and three vessel diseases in 15.6% of cases. Our patients were 93.2% right handed and 6.8% nonright handed. We have detected in this study that left handedness seemed to confer a protective effect against CAD, especially among those older than 65 years.

Zamrini et al. (1990) reported a significantly increased prevalence of left handedness in elderly people with heart disease and provided considerable evidence of shorter longevity among left handers that appeared to be associated with increased heart disease. The results of the our study demonstrated that angiographically proven CAD was significantly higher in right handers older than 65 years and that there was no correlation with the severity of CAD and hand preference in any group. The strong points of this study are the large patient population and the detection of CAD via angiography, which is accepted as the gold standard.

According to Zamrini et al. (1990) cerebral dominance may contribute to differences in the cardiovascular responses of right-handers and left handers to autonomic stressors. In that study, the right hemisphere was associated with chronotropic effects on the heart, as well as with sympathetic activation (Rasmussen et al. 1977; Zamrini et al., 1990). The opposite was found in our study of an elderly population, with left handed patients having fewer coronary occlusions on angiography than right handed patients.

Consequently, in patients aged 65 years and older, the probability of detecting a lesion in coronary angiography was higher in patients with right hand predominance compared to those with left hand predominance. Physicians should pay attention to the handedness of patients when evaluating coronary angiographies. Left handedness seems to have a protective effect against CAD in the elderly.

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Case Report

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Treatment of a clavicular aneurysmal bone cyst with fibula allograft: A case report

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ABSTRACT

Aneurysmal bone cyst (ABC) is defined as an expansile and osteolytic lesion, containing cystic cavities full of blood, which although benign, has a locally destructive course. The most preferred treatment method is surgery. Curettage and bone grafts are often used. The case is here presented of an ABC located in the clavicle, which was successfully treated with fibula allograft.

1. Introduction

Aneurysmal bone cyst (ABC) is defined as an expansile and osteolytic lesion, containing cystic cavities full of blood, which although benign, has a locally destructive course (Jaffe and Lichtenstein, 1942). They constitute 1% of all bone tumours and 80% of cases are aged below 20 years. They are often seen in the metaphyseal sections of the long bones, in vertebra posterior elements and in the iliac bone (Arata et al., 1981). Clavicle is a very rare site for aneurysmal bone cyst with only few cases reported in literature (Yashavntha et al., 2014). The case is here presented of an ABC located in the clavicle, which was successfully treated with fibula allograft.

2. Case

A 7-year old male patient was brought to the orthopedic department with complaints of pain and swelling in the right shoulder which had started 6 months previously and was worsening. It was learned from the patient history that there had been no response from non-narcotic analgesics for the pain but shoulder movement had increased. In the physical examination no deformity was seen in the shoulder or clavicle. In the distal clavicle,

swelling was felt and sensitivity was determined with palpation. Cervical, axillary or supraclavicular lymph nodes were not determined. Shoulder range of movement was full but movements were painful. The radial, ulnar and median nerves were evaluated as normal in motor and sensory examinations. On direct radiographs, eccentric, radiolucent destructive lesions were seen which were widening the cortex and causing expansion in the distal clavicle (Fig. 1).

A fine sclerosis was seen around the lesion and within the lesion, septa and trabeculations. Although evident cortical thinning was seen on computed tomography (CT) (Fig. 1) , the lesion was not seen to have extended beyond the cortex. On magnetic resonance imaging (MRI) a cystic lesion was observed of fluid-fluid levels with multiple septa, 30 x 16 x 14.5mm in dimension, located at the distal end of the clavicle, which was causing significant expansion in the bone and thinning of the cortex. As an initial diagnosis, ABC, giant cell tumour, non-ossifed fibroma, eosinophilic granuloma and osteomyelitis were considered. A neddle biopsy was applied to the patient for diagnostic purposes. In the histpathological evaluation giant cells with multi-nuclei were seen and a histiocytic, fibroblastic thin membrane rich in capillaries.

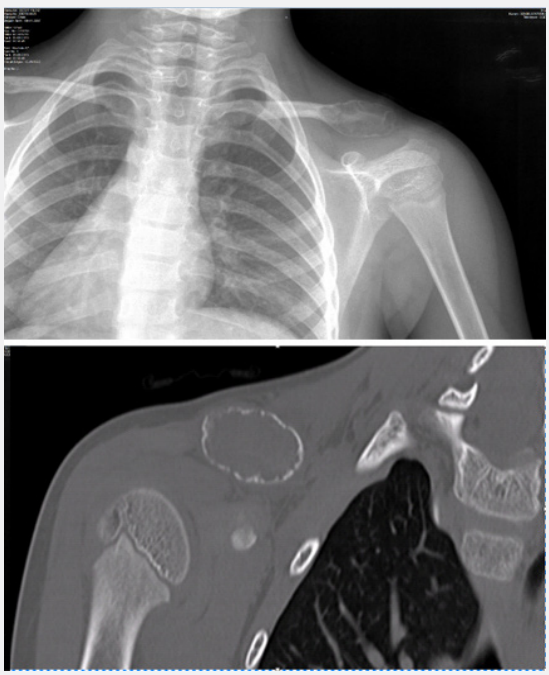

Fig. 1. On the left side preoperative direct radiography and right side computed tomography: Eccentric, radiolucent destructive lesions were seen which were widening the cortex and causing expansion in the distal clavicle.

Surgery was planned for the patient and the opertion was performed under general anaesthesia. The mass was reached by entering over the right clavicle. The cortex around the lesion was very thin and there was seen to be leakage from within of fluid of serohaemorrhagic consistency. Following curettage of the inside of the lesion, reconstruction of the distal clavicle was made with 4 cm fibula allograft. Fixation of the allograft was made with K-wires (Fig. 2). During the 24-month follow-up period, no recurrence was determined (Fig. 2). The remodelling using the fibula allograft showed pleasing results.

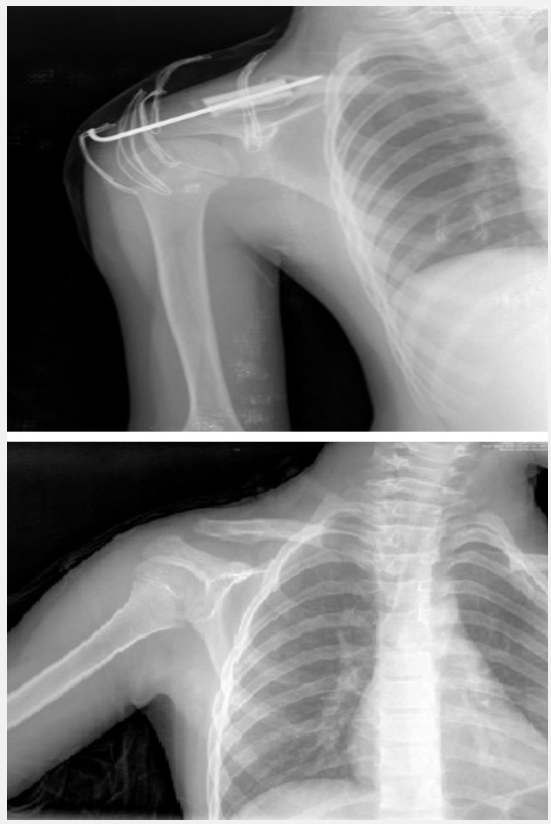

Fig. 2. Following curettage of the inside of the lesion postoperative radiograph and postoperative radiography after 24-month follow-up period.

3. Discussion

As ABCs are destructive and recurrent lesions, treatment must be adequate and complete. The most preferred treatment method is surgery (Gitelis and McDonald, 1998). Curettage and bone grafts are often used. Recurrence rates following this treatment have been reported as 14%-34% (Gitelis and McDonald, 1998). To reduce recurrence, aggressive curettage or total resection of the involved segment can be applied in patients with a destructive extensive lesion. Reconstruction following resection can be made with autogenous or allogenous bone grafts. In serious structural defects, strut graft may be used. In cases where it is necessary, graft fixation can be applied using conventional plate, screw or intramedullary rods (Jaffe and Lichtenstein, 1942).

Reconstruction with the fibula following resection of the radius with a tumour was first applied as an autogenous structural bone graft by Walther (Springfield, 1996). In terms of length, geometric shape and strength, the fibula is a suitable bone to be transferred to a tubular bone (Doi et al., 1997). Although there has been evidence of better results from autogenous grafts than allografts, many studies have reported better results from allografts (Cheng and Gebhardt, 1991). The use of allografts has the advantages of no donor site morbidity, a change in several sizes and limited source. In a study by Marco and Miller, good treatment of permanent stability of large cystic cavities was reported to have been provided with fibular allograft in a young population (Kapoor et al., 2004).

Reconstruction with non-vascularised bone grafts can be applied without the need for special training or equipment, is an inexpensive and simple procedure and results are good (Başarır, 2005). In the long bones of patients aged below 15 years, in centrally located lesions, particularly those which are active and have an aggressive course, surgically insufficient curettage has been reported together with high rates of recurrence (Dormans et al., 2004). To reduce the risk of recurrence in the current case of a locally aggressive ABC in the clavicle, the bone defect occurring after extensive curettage was treated with fibula allograft and at the end of a 2-year follow-up period, no recurrence was observed.

In conclusion, the application of aggressive treatment is useful to prevent recurrence in patients with a large, destructive lesion. In a young population, to provide stability in large cystic cavities, fibula allograft can be considered for use in the reconstruction of defects occurring after extensive curettage.

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Kyphoplasty for osteoporotic fractures: Experience of a single center

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ABSTRACT

Osteoporosis increases the risk of spontaneous fractures of skeleton by enhancing the microstructure of the bones. Kyphoplasty is preferred for decreasing the pain and disability in treatment of spinal fractures. We aimed to report our clinical experience in kyphoplasty for spinal fracture treatment and to express a brief literature review. We performed balloon kyphoplasty in 14 patients with osteoporotic spinal fractures between January 2012 and July 2015. Nine of the patients were women and 5 were men. Age of the patients ranged between 59 to 81 years. We think that spinal fractures should be initially treated with conventional methods, however, kyphoplasty should be done without a delay because it is very effective in pain and other complications of the fracture and a relatively safer method than other interventions.

1. Introduction

Osteoporosis increases the risk of spontaneous fractures of skeleton by enhancing the microstructure of the bones (Peck et al., 1993). Although it is more prevalent in postmenopausal women (Khuwaja et al., 2005; Spencer, 2007), osteoporotic fractures could be more troublesome in elderly men compared to age matched women (Kellie and Brody, 1990; Melton et al., 1992). Spinal fractures are disabling complications of osteoporosis. It may cause pulmonary dysfunction, nutritional problems and pain (Garfin et al., 2001). Its prevalence in postmenopausal women has been estimated about 16% (Galibert et al., 1987). Surgeons prefer Kyphoplasty for decreasing the pain and disability in treatment of spinal fractures (Garfin et al., 2001).

In present case series, we aimed to report our clinical experience in kyphoplasty for spinal fracture treatment and to express a brief literature review.

2. Cases

We performed balloon kyphoplasty in 14 patients with osteoporotic spinal fractures between January 2012 and July 2015. Nine of the patients were women and 5 were men. Age of the patients ranged between 59 to 81 years. All patients have been previously diagnosed

with osteoporosis in internal medicine clinics of our institution. Radiologic images (MRI and CT) obtained from all patients before procedure. Three of the patients had T12 fracture while others had lumbar fractures in different levels. All patients with mild to moderate pain have been advised for conventional procedures for at least 3 months before surgery decision. Early surgery considered in patients with either following conditions: serious pain that cause malfunction, necessity of high dose analgesic for pain relief, acute severe wedging or progressive vertebral collapse. We performed kyphoplasty under general anesthesia in all cases. Patients located on prone position on operating table. After a small incision made, a narrow tube placed through fractured area under the guidance of fluoroscopy. We placed special balloon through the tube into the vertebrae and inflated it for returning the pieces into more normal position. After that, we filled the cavity with polymethylmethacrylate, a special cement. There were no complications related to the surgical procedure in postoperative period. Only two patients needed re-operation with kyphoplasty; one after a month and the other one after 2 years from the first operation due to fracture of upper level fracture. None of the patients described problems related to surgery in follow up period.

3. Discussion

Spinal fractures associated with osteoporosis have important morbidity and mortality (Buchbinder et al., 2009). About a quarter of population over 50 years of age will have suffer from spinal fracture in their life (Jones et al., 1996). Currently, standard care for spinal compression fractures include, pain medication, brace immobilization, progressive mobilization, and time. Compression fractures have a high rate of success in terms of healing although it may take a while (about three months). Generally, most clinicians will wait to see if the fracture will heal on its own. Surgical interventions; such as vertebroplasty and kyphoplasty may yield important improvement in pain and debility especially in patients whom not respond to conventional approaches (Buchbinder et al., 2009). These two minimal invasive interventions are generally performed in cases with severe, disabling pain after spinal fracture, in particular, when conventional measurements (pain medication, brace immobilization, bed rest) failed to relieve symptoms. Literature data suggest they are effective interventions especially in relieving pain (Ploeg et al., 2006). Kyphoplasty have been introduced as successful as open surgery and it have been provided a shorter hospital stay in vertebral fractures (Fuentes et al., 2010). Kyphoplasty could be used as a safe and effective method in treatment of spinal fractures in cases with true indicaitons and with standardized procedure (Huber et al., 2009).

The goals of a kyphoplasty should be listed as follows: relief of the pain caused by a spinal fracture, stabilization of the vertebrae, and maintenance of vertebral body height. Indications of kyphoplasty are spinal hemangiomas, osteoporotic or meatastatic spinal fracture. A relative indication for kyphoplasty could be that prophylactic augmentation before development of pathological fracture or severe pain (Mut and Nader, 2008). All of the patients in present report reached required indications for kyphoplasty surgery. Cord compression, neurologic deficit, coagulation disorders, and vertebral burst fractures are some of the contraindications of kyphoplasty. None of the patients in our report had such contraindications.

Unfortunately, kyphoplasty is not an uncomplicated process. It carries a number of complications, included; anesthesia related complications, cord injury or nerve damage (due to malpositioned instruments), cement leakage, allergic reactions to the radiocontrast agents (Watts et al., 2001). Patients we reported here had not suffered from any of these complications.

It is controversial that whether kyphoplasty increase the risk of upper level spinal fracture. Some authors reported that rate of vertebral fracture increased after kyphoplasty especially within 2 months of the surgery (Fribourg et al., 2004). On the other hand, data from literature suggest that kyphoplasty reduce the risk of subsequent spinal fractures (Harrop et al., 2004). Two patients had been re-operated due to upper level spinal fracture in our case series; one a month and other two years after first intervention. We speculate that, upper level fracture should be a consequence of ongoing chronic course of osteoporosis rather than a complication of kyphoplasty.

Another serious, however luckily a rare complication of kyphoplasty is cement embolization in to veins that result in pulmonary embolization. This complication may lead severe morbidity and even death (Krueger et al., 2009). We have not reported such complication in our cases.

In conclusion, we think that spinal fractures should be initially treated with conventional methods, however, kyphoplasty should be done without a delay because it is very effective in treatment of pain and other complications of the fracture and a relatively safer method than other interventions.

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Case Report

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Two multiple sclerosis cases developed herpes zoster during use of fingolimod

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ABSTRACT

Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system. Immunosuppressive and immunomodulating drugs are used during disease monitoring. Fingolimod is one of the immunomodulatory treatments used in MS patients. It is a therapeutic agent acting on lymphocytes. Latent varicella-zoster virus infections may occur in MS patients receiving fingolimod therapy. In this article, the information of two cases with varicella-zoster virus reactivation during fingolimod use were presented.

1. Introduction

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system. In patients with relapsing remitting MS (RRMS), immunomodulator and immunosuppressive therapies are administered within certain rules based on the clinical and radiological course of disease. Fingolimod is an oral immunomodulator agent that has been recently started to use. The most commonly observed side effect in patients receiving fingolimod is first-dose bradycardia (Kappos et al., 2010) Lymphocyte counts of patients may decrease and rarely, lymphopenia may develop. Some opportunistic infections may occur due to decrease in lymphocyte count (Kappos et al., 2010, Cohen et al., 2010).

Varicella-zoster virus is an acute dermatomal viral infection that may cause chickenpox in children and shingles in adults by reactivation of latent virus (Brody and Moyer, 1997). Conditions causing increase in frequency of shingles include decreased cellular immunity and advanced age (Grann and Whitley, 2002). Latent viruses lead to shingles in result of reactivation

either by reinfection or effects of other factors (Cohen et al., 1999). Risk factors for reactivation of zoster include history of varicella, vaccination, age above 50 years, immunocompromised condition, immunosuppressants, chronic steroid administration, AIDS, bone marrow-organ transplantation, cancer, trauma and psychological stres (Bennett 1994; Gnann and Whitley, 2002).
Inthisarticle, wepresenttwo RRMS cases that developed varicella-zoster virus reactivation during theuse of fingolimod.

2. Cases

Case 1:

First complaints of a 50-year old woman have been started as weakness in left arm and leg six years ago. Patient was diagnosed with MS due to her attacks as pyramidal involvement repeated within the same year. Treatment with interferon beta was initiated but then, discontinued at the end of 3 years due to frequent attacks of patient and side effects. Patient was followed up without medication for about one year and afterwards, fingolimod therapy was initiated. At the month 6 of this therapy, pain occurred in back andchest of patient, and then rashes were observed (Fig. 1).

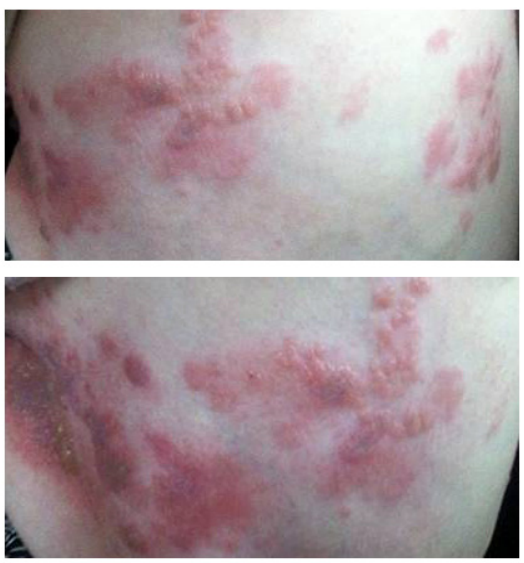

Fig. 1. Hyperemic, maculopapulovicularular lesions limited to the midline of a thoracic dermatome.

While white blood cell/lymphocyte counts of patient before fingolimod therapy were detected to be 7.6/1.8 K/μL, same counts were found to be 4.5/0.4 K/μL during the period that the patient had rashes. Maculo-papulovesicular lesions were observed in dermatologic examination and patient was diagnosed with herpes zoster. Immunomodulator therapy was continued for patient who was in clinical remission period with clinical and radiological fingolimod therapy and symptomatic treatments were arranged for her complaints. A significant improvement was observed in rashes with these treatments (Fig. 2).

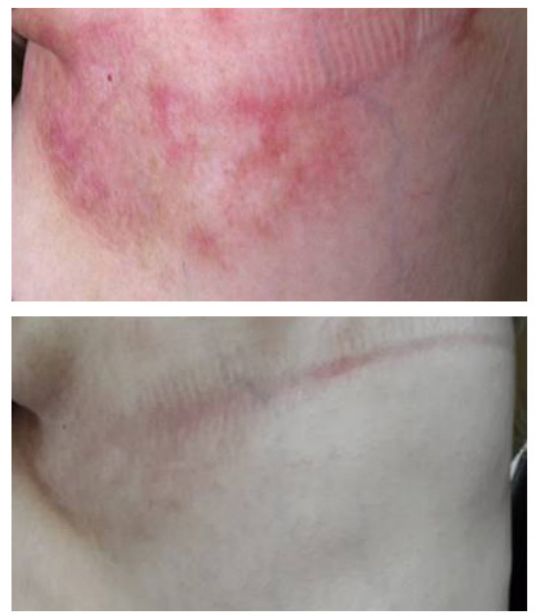

Fig. 2. Hyperemic, macular lesions during recovery.

Case 2:

A 30-year old male patient applied to our clinic with the complaintsof weakness in right arm and leg in 2007. Neurological examination revealed loss of strength in right upper and lower extremities, increased deep tendon reflexes in lower extremities and positive Babinski sign in right lower extremity. Patient was diagnosed with MS according to McDonald diagnostic criteria with the neurological examination and cranial MRI images. Attacks of the patient couldn't be controlled under subcutaneous immunomodulatory therapies with the diagnosis of RRMS and oral fingolimod therapy was initiated on February 2012. No new attack was observed in patient during this treatment period. No new and active lesion was detected in cranial MRI imaging. At month 15 of fingolimod therapy, patient applied to our outpatient clinic due to painful rashes at the front left chest and left side of his back which were developed within a few days. History of patient revealed that the rashes have been originated from lower left chest and radiated to the back. Eruption of grouped vesicles upon an erythematous base in a dermatomal distribution which originated from lower left chest and radiated to lower left shoulder blade was observed in examination (Fig. 3). Lesions did not pass the midline and there was no axillary lymphadenopathy. History of patient revealed that he had varicella infection when he was 7 years old. Varicella Zoster IgG was detected to be positive.

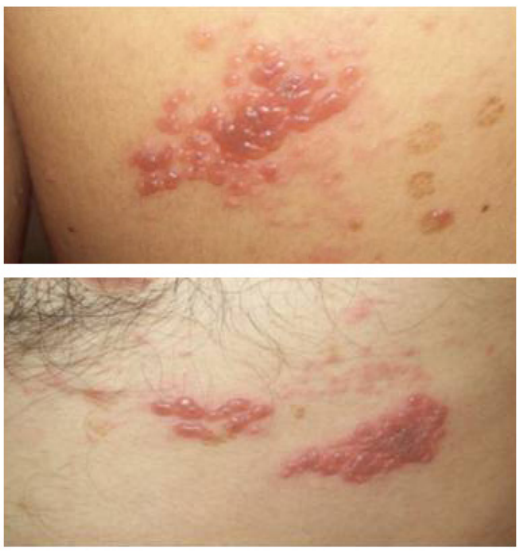

Fig. 3. Vesicular lesions on erythematous ground.

Patient was diagnosed with herpes zoster based on his history and clinical findings. Oral fingolimod therapy was continued and symptomatic treatment was initiated for patient and a significant improvement was observed in rashes at week 2 of therapy (Fig. 4).

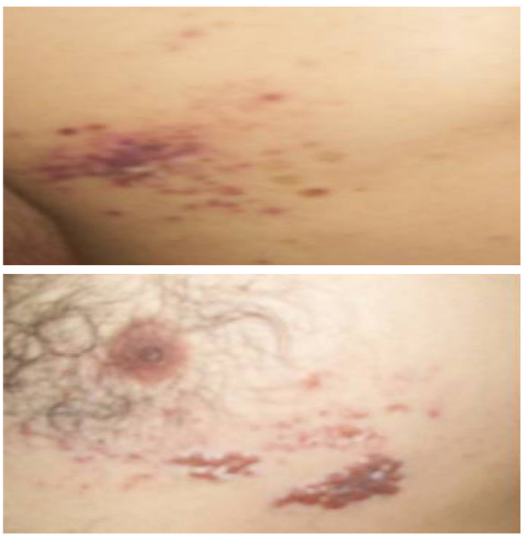

Fig. 4. Crusted, vesicular lesions during recovery.

3. Discussion

Varicella zoster virus (VZV) belongs to the family of herpes viruses. It usually causes two forms of infection. First one is infectious, benign chickenpox disease of childhood. And the second one is herpes zoster caused by latent virus in dorsal root ganglion (Strauss, 1994). In susceptible people, first pain and then, maculo-papularvesicular lesions occur across dermatome. Particularly, conditions where immune system is suppressed lead to the risk of herpes zoster (Brody and Moyer, 1997; Grann and Whitley, 2002; Weinberg 2007).

Fingolimod is an immunomodulatory agent that has been recently started to use in MS patients. It acts through sphingosine-1-phosphate receptor which is located at many systems including cardiovascular system, nervous system and immune system (Winkelmann et al., 2012). Release of T lymphocytes from lymph nodes are inhibited resulting in decreased peripheral T lymphocyte counts in patients (Kappos et al., 2010). Thus, increase in opportunistic infections may be observed. Studies with fingolimod have shown an increase in lower respiratory tract infections compared to placebo (Kappos et al., 2010). Two patients have developed primary VZV and herpes simplex encephalitis and prognosis of these patients have resulted in death. It is worthy of note that these patients were in the group of patients receiving high-dose fingolimod (1.25 mg) (Cohen, 2010).

Care must be taken for primary or latent VZV infections in MS patients receiving fingolimod therapy. VZV antibody must be looked for prior to therapy in these patients. If patients have no immunity to VZV, treatment must be initiated after vaccination. For both of our patients, VZV Ig G, which was checked prior to therapy, was found to be positive. Although herpes zoster developed in our patients is common in immunosuppressive patients, it has been very rarely reported in MS patients receiving fingolimod (Uccelli et al., 2011; Winkelmann et al., 2012). Our patients achieved a course without attacks after clinically and radiologically active course due to previous use of injectable immunomodulatory therapies. Oral immunomodulatory drug was not discontinued in our patients as herpes zoster could be controlled with symptomatic treatment and a good clinical response to fingolimod was obtained.

Shingles is diagnosed with classical prodromal pain-burning and shingles rash. Rashes are observed throughout the unilaterally affected dermatome (Bennett, 1994). Cytopathological assessment and polymerase chain reaction may be useful for atypical rashes (Strauss et al., 1994; Weinberg 2007). Virus may stay in lesions occurred for a few days and skin dissemination is not common except for the people whose immune system is suppressed (Strauss 1994). Rashes were painful and at thoracic region in both of our patients. Also in literature, thoracic involvement is observed in 50% of the patients while trigeminal nerve is involved in 10-15% of the patients (Weinberg, 2007). Dermatomes from T3 to L3 are frequently affected (Bennett, 1994). Local pain is severe in shingles.

Frequency of shingles is increased in immunosuppressive patients and recurrence of shingles is observed more frequently in this population

(Weinberg, 2007). History of our cases included use of fingolimod with the diagnosis of MS and these clinical pictures may be observed due to decreased lymphocyte counts because of effect of fingolimod to hold lymphocytes in the lymph node (Ricklin et al., 2013).

Postherpetic neuralgia, ophthalmic involvement and secondary infection of rashes are also important in shingles in addition to severe pain. Postherpetic neuralgia is increased with the age and observed at a rate of 8-70% within a period of 30-60 days (Weinberg, 2007). Initiation of treatment within 3 days of occurrence of rashes ensures a better clinical response in shingles (Dworkin et al., 2007). The aim of the therapy is to ensure rapid improvement, pain control and to reduce the risk of complications as much as possible. Early initiation of antiviral therapy accelerates the healing of rashes, reduce their severity and prevents some complications (Ahmed et al., 2007). Oral treatment is sufficient. Valacyclovir, famciclovir, acyclovir and brivudine may be used in the treatment. However, combined antiviral therapy may reduce the future pain and other complications (Tring et al., 2007). In case of disseminated infection, very severe immune system suppression and eye involvement, treatment with intravenous acyclovir must be considered if oral uptake is insufficient (Dworkin et al., 2007). Topical antiviral therapy is not relevant. Corticosteroids may only be useful in pain relief when used in combination with antiviral therapy (Dworkin et al., 2007, Ahmed et al., 2007). We also used oral antiviral therapy with the symptomatic treatment for pain in both of our cases and observed a significant improvement in clinical picture within a short period of time.

Fingolimod is a sphingosine-1-phosphate receptor modulator. It is very effective in treatment of multiple sclerosis. However, fatal herpes infections are observed during fingolimod therapy in the literature. Therefore, vaccination is recommended for VZV seronegative patients prior to initiation of fingolimod therapy.

A risk factor for reactivation of zoster is use of an immunosuppressant. Fingolimod, an immunosuppressant, is also important for reactivation of zoster. Therefore, it is important for clinical course of patients to monitor MS patients receiving fingolimod therapy for reactivation of zoster and early initiation of antiviral and symptomatic treatments in case of a potential reactivation.

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