Anatol J Clin Investig 2015;9(2):55-60

EVALUATION OF THE SHORT-TERM OUTCOMES OF PLATELET-RICH PLASMA INTRA-ARTICULAR INJECTIONS FOR TREATING PATIENTS WITH EARLY STAGE GONARTHROSIS

ERKEN EVRE GONARTROZ HASTALARINDA EKLEM İÇİ TROMBOSİTTEN ZENGİN PLAZMA TEDAVİSİNİN ERKEN DÖNEM SONUÇLARININ DEĞERLENDİRİLMESİ

Olcay GÜLER[1], Mahir MAHİROĞULLARI[2], Ferdi DÖNMEZ[3], Serhat MUTLU[4]
Selami ÇAKMAK[4], Harun MUTLU[5]

[1] Özel Nisa Hastanesi, Ortopedi ve Travmatoloji Polikliği,İstanbul.
[2] Özel Medipol Mega Hastaneleri,Ortopedi ve Travmatoloji Polikliği,İstanbul.
[3] Özel Salihli Hastanesi, Ortopedi ve Travmatoloji Polikliği,Manisa.
[4] Kanuni Sultan Süleyman Eğitim ve Araştırma Hastanesi,Ortopedi ve Travmatoloji Kliniği,İstanbul.
[4] Gata Haydarpaşa Eğitim Hastanesi,Ortopedi ve Travmatoloji Kliniği,İstanbul.
[5] Taksim İlkyardım Eğitim ve Araştırma Hastanesi,Ortopedi ve Travmatoloji Kliniği,İstanbul.

Abstract
The aim of this study was to evaluate the short-term clinical outcomes of intra-articular platelet-rich plasma (PRP) treatment and to evaluate the increase in functional activity and quality of life in patients with early stage gonarthrosis. We planned our study retrospectively. Eighty-six patients (54 females and 32 males) with 108 knees (54 right and 54 left) who had pain and swelling for > 4 months due to all grades of knee osteoarthritis according to the Kellgren–Lawrence grading scale were evaluated. Our patients were homogenous in terms of age and body mass index. Three intra-articular PRP injections were administered once per week, and the patients were clinically evaluated prospectively before treatment and at 2 and 6 months after treatment with the visual analogue scale (VAS), the Knee Society Score (KSS), and the Short Form-36 (SF-36). No major complications due to treatment were observed. Seventeen patients had transient swelling and pain for 2 days. Significant improvements on the VAS, KSS and SF-36 scores were obtained at the 2- and 6-month follow-ups ($p < 0.05$). The VAS, KSS, and SF-36 scores improved significantly at the 6-month evaluation compared to those at the month 2 follow up. We believe that intra-articular PRP treatment is effective during the early stage of gonarthrosis and increases the quality of life and functional activity of recipients.
Key words: Platelet-rich plasma, Intra-articular injection, gonarthrosis.

Özet
Bu çalışmanın amacı eklem içi Trombositten Zengin Plazma (TZP) tedavisinin, gonatroz hastalarının erken dönemde hayat kalitesine, fonksiyonlarına ve diz ağrısı şikayetlerine etkisini ve kısa dönem klinik sonuçlarını değerlendirmektir. Çalışmamız retrospektif olarak planlandı. Dizinde 4 aydan daha uzun süren ağrı ve şişlik şikayeti olan, Kellgren ve Lawrence sınıflamasına göre erken ve ileri evre gonartrozlu 86 hastanın (54 kadın, 32 erkek) 108 dizi (54 sağ, 54 sol) değerlendirildi. Hastalarımız yaş ve BMI açısından homojen olarak değerlendirildi. Hastalarımıza birer hafta arayla üç kez eklem içi TZP tedavisi uygulandı. Hastalar tedavi öncesi ve sonrası 2. ve 6. aylarda Görsel Analog Skor(GAS), Diz Cemiyet Skoru(KSS) ve Kısa Form-36(SF-36) skorlama sistemleri ile değerlendirildi. Tedaviye bağlı hiçbir hastada majör komplikasyon ortaya çıkmadı. Onyedi hastada ortalama iki günde düzelen geçici eklemde şişlik ve ağrı meydana geldi. Hastalarımıza uyguladığımız eklem içi TZP tedavi sonrası ikinci ve altıncı aylardaki GAS, KSS ve SF-36 değerleri tedavi öncesi değerlere göre istatiksel olarak anlamlı derecede iyileşme elde edildi($p<0.05$). Ayrıca tedavi sonrası altıncı aydaki GAS, KSS ve SF-36 değerleri tedavi sonrası ikinci aydaki değerler göre istatiksel olarak anlamlı iyileşme tespit edildi. Eklem içi TZP tedavisinin, erken evre gonartroz hastalarının tedavisinde kolay uygulanan, ağrıyı azaltan ve erken dönemde hayat kalitesini ve fonksiyonları arttıran etkin bir tedavi yöntemi olduğunu düşünmekteyiz.
Anahtar kelimeler: Trombositten zengin plazma, eklem içi enjeksiyon, gonartroz

Introduction

The incidence of articular cartilage problems increases with average life span and more vigorous sporting activities [1]. Self-repair of the articular cartilage is difficult due to the low cellular mitotic activity of chondrocytes and its avascular nature [2]. Therefore, treatment of articular cartilage lesions is a major challenge for orthopedic surgeons [3].

A variety of non-invasive techniques are available to treat articular injuries and osteoarthritis (OA)[4]. Besides oral and topical non-steroidal anti-inflammatory agents (NSAIDs), glucosamine, chondroitin sulfate, and hyaluronic acid have been used to treat symptoms such as pain and motion difficulties that result from articular cartilage injury [3,4].

Recent studies have focused on novel methods of stimulating healing or repairing damaged cartilage, such as matrix metalloproteinase inhibitors, gene therapy, cytokine inhibitors, and growth factors [1,3,9]. The healing-promoting effects of growth factors on damaged tissue have long been known, and the effects of growth factors on cartilage repair have been demonstrated by *in vivo* and *in vitro* studies [4,9,13-15]. Several *in vivo* studies have shown

Olcay GÜLER
Özel Nisa Hastanesi, Ortopedi ve Travmatoloji Polikliniği, İstanbul.
E-posta: olcayguler77@gmail.com

Received: 22.02.2014 Accepted: 08.03.2015

that growth factors affect chondrocyte metabolism, healing and chondrogenesis, proliferation, migration, and differentiation of cells through matrix synthesis [4,10].

Platelet-rich plasma (PRP), which can promote tissue regeneration and stimulate biological healing similar to the normal healing process after injury, has been used in many fields [1,4,10,11]. PRP is a simple, cost effective and minimally invasive method [1,3] that was first used by Ferrari et al. in 1987 to reduce bleeding following open-heart surgery [4,12]. However, today, its use has extended to include plastic, esthetic and maxillofacial surgery, dermatology, ophthalmology, dentistry, and sports medicine [4,10,11,16].

The purpose of our study was to evaluate the short-term clinical efficacy outcomes of intra-articular PRP injections to treat patients with early stage gonarthrosis and to demonstrate whether PRP therapy is easy to use, increases quality of life and functionality, and reduces pain during the early period of gonarthrosis.

Material and Methods

A total of 108 knees from 86 patients with complaints of swelling and pain for > 4 months and who had stage 1 or 2 knee OA according to the Kellgren–Lawrence grading scale were included. This study was designed retrospectively after patient files and records were reviewed.

Patients with early stage gonarthrosis who were admitted to the outpatient clinic and received three 2 cc intra-articular PRP injections using an appropriately sized needle through an anterolateral portal at 1-week intervals were enrolled in the study. After diagnosis, patients were assessed at baseline, and at 2- and 6-month follow-up visits using the visual analogue scale (VAS), the Short Form-36 (SF-36) health survey, and the Knee Society Score (KSS). In addition, patient body mass index (BMI), baseline hemogram, microbiological test results, standing anteroposterior and lateral radiographs of the knee and feet, and magnetic resonance imaging were also evaluated.

The mean age of the pateints was 55 years (range, 25–70 years); 54 patients were females and 32 were males. A total of 108 knees (54 right knees and 54 left knees) including the unilateral knee joint in 64 patients and bilateral knee joints in 22 patients were treated. A variety of analgesics and anti-inflamatory agents had been prescribed to all patients prior to treatment. Ethical approval for this study was granted by the Ethics Committee, and informed consent was obtained from all patients.

The exclusion criteria were: patients with diabetes mellitus, rheumatic diseases, hematological diseases (coagulopathy), major axial deviation (varus > 5, valgus > 5), severe cardiovascular disease, infections, immunosuppressive diseases, those taking anticoagulant therapy, use of anti-inflammatory drugs during the 5 days before blood collection, patients with abnormal hemoglobin levels, patients with KSS,VAS, and SF-36 scores not evaluated before and after the intra-articular injections, those who refused to sign the informed consent form, and patients with advanced-stage gonarthrosis (Kellgren–Lawrence grades 3 and 4).

Preparation of the PRP

Approximately 15 ml of peripheral venous blood were drawn from an upper extremity of the patients, and 1.5 ml was reserved for the platelet count. The remaining 13.5 ml of blood were mixed with 1.5 ml 3.2% sodium citrate in a 15-ml sterile centrifuge tube and centrifuged for 10 min at 4000 rpm (Rotofix 32, Hettich, Germany). After centrifugation, 2.5 ml of PRP were taken from the space between the erythrocytes at the bottom and the plasma at the top of the tube. Approximately 0.5-ml PRP was collected for platelet counting. Approximately 2 ml of PRP were injected inside the knee joint. No commercial kit was used to obtain the PRP.

Treatment Method and Assessment

The injection site was covered with a sterile dressing, and the PRP was injected into the knee joint through an arthroscopic anterolateral portal using an appropriately sized needle. After the procedure, the patient was asked to flex and extend the knee for a short duration. The patients were permitted to perform limited activity for 24 h and were advised to rest if they had severe pain. Patients were also asked to refrain from using NSAIDs or applying cold therapy for 1 week after the injection to prevent a reduction in the effectiveness of the PRP. Furthermore, patients were given an exercise program and were advised to resume normal activities as tolerated. All complications and adverse effects were recorded.

Statistical Analysis

The statistical analysis was performed using SPSS for Windows 15.0. Descriptive values such as the arithmetic mean, standard deviation, confidence intervals, range, frequency, percentage and coefficient of skewness were calculated.

The Kolmogorov–Smirnov test and graphics were used to determine the normal distribution of the data. The t-test was used for pre- and post-injection paired groups, and Spearman's correlation coefficient and partial correlation coeficients were calculated for relationships. The results were evaluated with a 95% confidence interval, and a p-value < 0.05 was considered to indicate a significant difference.

Results

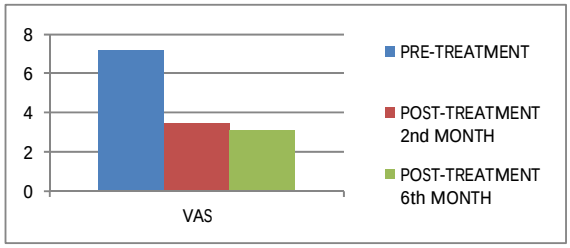
It was observed that of the nurses working in the In total, 48 knees had grade 1 OA and 59 knees had grade 2 OA according to the Kellgren–Lawrence classification. Mean BMI was 28.7 kg/m^2 (range 22.43–35.4 kg/m^2). The patients showed statistical homogeneity for age and BMI.
The mean platelet count before centrifugation was 238 × 10³/µl (range, 156 × 10³–351 × 10³/µl), whereas that after centrifugation was 987 × 10³/µl (range, 685 × 10³–1373 × 10³/µl). The mean change in platelet count was 4.3 (range, 3.6–4.6). The mean leukocyte count before centrifugation was 6.77 × 10³/µl (range, 5.25 × 10³–10.25 × 10³/µl), whereas that in the PRP was 30.5 × 10³ µl (range, 22.1 × 10³– 44.4 × 10³/µl). The mean change in leukocyte count was 4.7 (range, 4.1–5.4).

No patient had major complications (infection, deep vein thrombosis, or muscle atrophy) associated with the intra-articular injections. Seventeen patients had knee-joint effusion and pain, but the complaints resolved spontaneously within 2 days.

The mean KSS was 58.77 ± 4.67 before treatment, 80.75 ± 5.58 at the 2-month follow-up, and 86.54 ± 6.58 at the 6-month follow-up. A significant increase was noted in both the 2- and 6-month post-treatment KSS compared to the baseline values (p < 0.05). In addition, a significant increase in the KSS was observed between months 2 and 6 post-treatment (p < 0.05) (Table 1).

Picture 1. Correlation of Knee Society Score (KSS) and evaluation time.

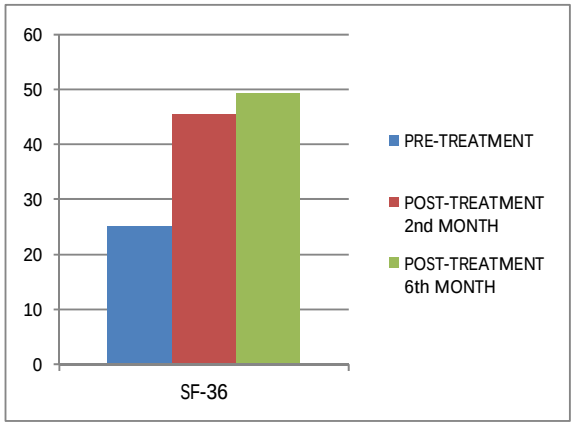
The mean VAS scores were 7.19 ± 1.26 before treatment, 3.48 ± 1.14 at the 2-month follow-up, and 3.06 ± 0.87 at the 6-month follow-up. A significant decrease was observed in both the 2- and 6-month post-treatment VAS scores compared to those at baseline (p < 0.05). Furthermore, a significant decrease in VAS scores was observed between the 2- and 6-month post-treatment follow-ups (p < 0.05) (Table 2).



Picture 2. Correlation of Visual Analogue Scale(VAS) and evaluation time.

The mean SF-36 score was 25.03 ± 5.67 before treatment and 45.39 ± 5.20 and 49.18 ± 5.29 at the 2- and 6-month follow-ups, respectively. A significant increase was observed in both the 2- and 6-month post-treatment KSS values compared to those at baseline (p < 0.05). Furthermore, a significant increase in SF-36 scores was observed between the 2- and 6-month post-treatment follow-ups (p < 0.05) (Table 3).

Picture 3. Correlation of SF-36 scores and evaluation time.



Discussion

Due to the distinctive function and structure of hyaline cartilage and its low healing potential, treating articular cartilage lesions and degeneration remains a major challenge for both orthopedic surgeons and physical therapy and rehabilitation specialists [17,18]. More recent treatment protocols have focused on maintaining normal cartilage homeostasis and preventing

progression of cartilage lesions instead of symptomatic treatment such as analgesics and NSAIDs [1].

Of the invasive treatment modalities, intra-articular corticosteroid injections show short-term benefit for reducing pain and restoring function in a limited patient group [5]. Intra-articular injections of hyaluronic acid have yielded satisfactory results in many studies [4,6,7]. Despite available treatment options, the optimal treatment for cartilage lesions has not been established [1,8].
An increasing number of studies have addressed the positive effects of cellular and humoral mediators obtained from autologous blood products on tissue healing. This method relies on activating growth factors in blood [1,19]. Growth factors consist of various polypeptide groups that regulate the growth of all cells, including chondrocytes [1,3].

PRP is obtained from a small fraction of autologous blood [4]. Platelets contain alpha granules that store large numbers of growth factors such as transforming growth factor-β (TGF-β), fibroblast growth factor, platelet-derived growth factor (PDGF), epidermal growth factor, and vascular endothelial growth factor. Autologous growth factors released from platelets stimulate mesenchymal tissue to regenerate. PRP also contains plasma proteins such as fibronectin and vitronectin, which act as mesenchymal cell adhesion molecules [4].

TGF-ß plays a role in cartilage regeneration and is an interleukin-1 (IL-1) antagonist that suppresses chondrogenic differentiation of mesenchymal stem cells and synthesis of cartilage-specific molecules [9,20].

In contrast, PDGF stimulates chondrocyte proliferation and proteoglycan synthesis and is a potent chemotactic factor for all cells of mesenchymal origin [15,21].

Insulin-like growth factor (IGF) is an anabolic factor that stimulates cartilage proliferation and proteoglycan synthesis and slows their catabolism by augmenting the effects of other growth factors in cartilage [9,22].

Other growth factors are also involved in cartilage regeneration and metabolism and have chondroinductive action with other factors [20,22]. PRP is a minimally invasive, simple to use, and inexpensive blood product that contains many growth factors [14,15]. Platelets contain many growth factors such as PDGF, TGF-β, and IGF-1, which play major roles in cartilage homeostasis and regeneration [10, 11, 13, 14, 15, 20]. PRP is obtained by centrifugation of autologous blood and contains a 4–5-fold higher concentration of platelets than normal blood [1,3,4,23]. Growth factors released from platelets have positive effects on tissues with low healing capacity, such as cartilage.

Numerous studies have reported the potential effects of blood-derived growth factors on cartilage repair [3,4,19,23,24]. In a study of experimentally induced OA in horses by Fisbie et al., intra-articular administration of autologous conditioned serum resulted in improved lameness, decreased synovial membrane hyperplasia, less cartilage fibrillation, and increased synovial fluid concentration of IL-1 receptor antagonist after treatment with autologous conditioned serum [24]. Gaissmaier et al. suggested that human platelets accelerate chondrocyte expansion but have no effect on chondrocyte differentiation [25]. Saito emphasized that gelatin hydrogel microspheres containing PRP have preventive effects against OA progression in rabbit knees [26]. In a study by Sanchez, PRP was administered to treat avulsion of knee articular cartilage in a soccer player; complete articular cartilage healing was reported [21]. A retrospective cohort study of 30 patients by Sanchez reported that intra-articular PRP therapy is safe and effective in knees with OA [19]. Sampson et al. reported that PRP injections administered to 14 patients with primary and secondary knee OA resulted in reduced pain and improvement of function [27]. In a study by Kon et al., PRP intra-articular injections were administered to 100 patients (115 knees) with chronic degenerative cartilage lesions and OA. They reported that intra-articular PRP was a safe method that reduced pain, improved quality of life, and articular function in patients with low-grade articular degeneration [1]. A series of 46 patients with severe chondropathies of the knee by Giannini et al. reported positive effects of intra-articular PRP injections in terms of reducing pain and improving function [28].

In a study by Kon et al., 150 patients with chronic degenerative lesions and OA were divided into three groups. Group 1 patients were treated with three intra-articular PRP injections, group 2 patients were treated with intra-articular injections of high-molecular-weight hyaluronic acid, and group 3 patients were treated with intra-articular injections of low-molecular-weight hyaluronic acid. They concluded that autologous PRP injections were more efficaceous than hyaluronic acid injections for reducing pain and restoring articular function during the early period [3]. In a study by Spakova et al., 60 patients with early stage OA

were treated with three intra-articular applications of PRP and 60 patients were given three injections of hyaluronic acid. A significant decrease in early stage complaints was observed in patients who received intra-articular PRP injections compared to those who received hyaluronic acid [4].

The platelet concentration should be 4–6-fold higher than the blood baseline [4,22]. In our study, a 4.3-fold average increase in platelet concentration was obtained. However, this value remains controversial; some authors advocate that the effect is suboptimal at lower concentrations, whereas others believe that extremely high concentrations may cause adverse effects.

In the present study, leukocyte concentration in the PRP exhibited an average 4.7-fold increase compared to blood baseline values. A number of studies have reported that increased concentrations of leukocytes help prevent infection and regulate the immune system and angiogenesis in patients receiving PRP treatment [4,29-33]. However, the positive effect of an increased concentration of leukocytes on the knee joint has not been demonstrated.

In an attempt to prevent a reduction in the effectiveness of the positive inflammatory response intended and desired with the PRP injections, our patients were advised not to use NSAIDs and to avoid applying cold therapy. Previous studies have reported a satisfactory biological response in clinical practice with three intra-articular injections, and no considerable improvement was observed in patients receiving four and more injections [27]. Therefore, the treatment was planned to consist of three injections in our study.

As PRP is developed from autologous blood, it is free of allergens or transmissible diseases. In addition, no studies have documented hyperplasia, a carcinogenic effect, or tumor growth associated with PRP [34]. In contrast, temporary knee complaints associated with PRP injections have been reported. In our study, 17 patients developed knee effusion and pain, but their complaints resolved spontaneously within 2 days. We believe that the development of knee effusion is a phase of treatment. At this point, one may ask whether clinical improvement is achieved in patients who do not develop effusion. This can be attributed to individual differences among patients. The outcomes of patients with and without effusion did not differ significantly. No patient had a major complication requiring the termination of the treatment.

A total of 108 knees from 86 patients were treated, and patients were assessed using the SF-36, VAS, and the KSS at the pre-injection visit and at the 2- and 6-month follow-ups. A significant difference was observed in all parameters at the 2- and 6-month follow-up visits compared to baseline. Maximum efficacy was observed at the 6-month follow-up.
Based on the KSS results, pain was reduced most signficnatly at the 6-month follow-up. There was also a dramatic improvement in knee range of motion and stair climbing due to the reduced pain.

According to the SF-36 results, patients presented a less restricted social life, which was accompanied by a substantial decrease in emotional problems and a substantial increase in work performance.

The patients showed statistical homogeneity in age and BMI; therefore, these parameters had no effect on the results of PRP therapy in this study. Previous studies have reported that better clinical outcomes are obtained with PRP injections in younger patients with gonarthrosis compared to that in older patients with gonarthrosis, and that the biological response to growth factors is lower in the more degenerated joints of older patients [1]. PRP therapy slows intra-articular catabolic processes, stimulates chondral anabolism, reduces synovial membrane hyperplasia, and modulates cytokine levels without affecting joint degenerative progression or changing the cartilage tissue structure, thus leading to an improved clinical outcome [1,2,4].

Early stage gonarthrosis can be influenced by a number of parameters. It is not reasonable to suggest that one injection of PRP will result in clinical improvement. The number of patients was small and there was no control group in our study. One of the main questions regarding PRP application for gonarthrosis is the duration of symptom improvement. We followed our patients for 6 months. Based on assessments made in the literature, standard scoring criteria, and the significant results obtained here, we consider that PRP intra-articular injections are a simple, cost effective, safe, and promising treatment option that improves the quality of life and knee function, and provide relief from pain.

References

1. Eatough EM, Way JD, Chang CH. Understanding the link between psychosocial work stressors and work – related musculoskeletal complaints. Applied Ergonomics 2012;43:554-563.
2. Castro AB. Handle with care: the American Nurses Association's campaign to address work-related musculoskeletal disorders. Online Journal of Issues in Nursing 2004; 9(3): [Cited 04 Oct 2011]. Available from URL: http://www.nursingworld.org/MainMenuCategories/ANAMarketplace/ANAPeriodicals/OJIN/TableofContents/Volume92004/No3Sept04/HandleWithCare.aspx.
3. June KJ, Cho SH. Low back pain and work-related factors among nurses in intensive care units. J Clin Nurs 2010; 20(3-4): 479-487.
4. Aksan AD. Ege Üniversitesi Tıp Fakültesi Hastanesinde çalışan hemşirelere yönelik iş kazası kayıt sisteminin geliştirilmesi ve izlenmesi (Development and follow-up of a registration system of work accidents for the nurses employed at the Ege University, Medical Faculty Hospital). Ph.D. diss., Ege University, Department of Public Health, Izmir, 2005. [Cited 04 Oct 2011]. Available from URL: http://tez2.yok.gov.tr/ (in Turkish).
5. Karwowski W, Jang RL, Rodrick D, Quesada PM, Cronin S. Self-evaluation of biomechanical task demands, work environment and perceived risk of injury by nurses: a field study. Occup Ergon 2005; 5(1): 13-27.
6. Fronteira I, Ferrinho P. Do nurses have a different physical health profile? A systematic review of experimental and observational studies on nurses' physical health. J Clin Nurs 2011; 20(17-18): 2404-2424.
7. Menzel NN, Brooks SM, Bernard TE, Nelson A. The physical workload of nursing personnel: association with musculoskeletal discomfort. Int J Nurs Stud 2004; 41(8): 859-867.
8. Yeung SS, Genaidy A, Levin L. Prevalence of musculoskeletal symptoms among Hong Kong nurses. Occup Ergon 2004; 4(3): 199-208.
9. Lagerstrom M, Wenemark M, Hagberg M, Hjelm EW. Occupational and individual factors related to musculoskeletal symptoms in five body regions among Swedish nursing personnel. Int Arch Occup Environ Health 1995; 68(1): 27-35.
10. Hernandez L, Genaidy A, Davis S, Guo L, Alhemoud A. A study of musculoskeletal strain experienced by nurses. Occup Ergon 1998; 1(2): 123-133.
11. Fanello S, Jousset N, Roquelaure Y, Chotard-Frampas V, Delbos V. Evaluation of a training program for the prevention of lower back pain among hospital employees. Nurs Health Sci 2002; (1-2): 51-54.
12. Smith DR, Wei N, Kang L, Wang RS. Musculoskeletal disorders among professional nurses in mainland China. J Prof Nurs 2004; 20(6): 390-395.
13. Trinkoff AM, Lipscomb JA, Geiger-Brown J, Brady B. Musculoskeletal disorders of the neck, shoulder and back and functional consequences in nurses. Am J Ind Med 2002; 41(3): 170-178.
14. Bos EH, Krol B, Van Der Star A, Groothoff JW. The effects of occupational interventions on reduction of musculoskeletal symptoms in the nursing profession. Ergonomics 2006; 49(7): 706-723.
15. Büker N, Aslan E, Altuğ F, Cavlak U. Hekimlerde kas-iskelet sistemi problemlerinin incelenmesi (Study of musculoskeletal system problems in physicians). In Sağlık Çalışanların Sağlığı 2. Ulusal Kongresi, Kongre Kitabı. Ankara: Genel-İş Matbaası, 2001; 174 (in Turkish).
16. Karadağ M, Yıldırım N. Hemşirelerde çalışma koşullarından kaynaklanan sırt/bel ağrıları ve risk faktörleri (Upper/lower back pains in nurses stemming from working conditions and risk factors). In Sağlık Çalışanların Sağlığı 2. Ulusal Kongresi, Kongre Kitabı. Ankara: Genel-İş Matbaası; 136 (in Turkish).
17. Karahan A, Bayraktar N. Hemşirelerde klinik ortamda vücut mekaniklerini kullanma ve bel ağrısı görülme durumlarının belirlenmesi (Determination of the use of body mechanics in nurses in a clinical environment and prevalence of lower back pain). In Sağlık Çalışanların Sağlığı 2. Ulusal Kongresi, Kongre Kitabı. Ankara: Genel-İş Matbaası, 2001; 171 (in Turkish).
18. Özcan E, Samancı N, Balcı N. Sağlık çalışanlarında bel ağrısı. (Lower back pain in health workers). In Sağlık Çalışanlarının Sağlığı 2. Ulusal Kongresi, Kongre Kitabı. Genel-İş Matbaası, Ankara, 2001; 135 (in Turkish).
19. Tezel A. Musculoskeletal complaints among a group of Turkish nurses. Int J Neurosci 2004; 115(6): 871-880.
20. Alçelik A, Deniz F, Yeşildal N, Mayda AS, Şerifi BA. AİBÜ Tıp Fakültesi Hastanesinde görev yapan hemşirelerin sağlık sorunları ve yaşam alışkanlıklarının değerlendirilmesi (Health survey and life habits of nurses who work at the Medical Faculty Hospital at Abant İzzet Baysal University [AIBU]). TSK Koruyucu Hekimlik Bülteni 2005; 4(2): 55-65 (in Turkish).
21. Malone RE. Ergonomics, policy, and the ED nurse. J Emerg Nurs, October 515, 2000. [Cited 04 Oct 2011]. Available from URL: http://www.jenonline.org/issues?issue_key=S0099-1767(05)X7007-6.
22. Torp S, Moen BE. The effects of occupational health and safety management on work environment and health: a prospective study. Appl Ergon 2006; 37(6): 775-783.
23. Yılmaz CM. Hemşirelerde çalışma koşullarından kaynaklanan sırt/bel ağrıları ve korunma önlemleri (Upper/lower back pains stemming from working conditions in nurses and preventive measures). In Sağlık Çalışanlarının Sağlığı 2. Ulusal Kongresi, Kongre Kitabı. Ankara: Genel-İş Matbaası, 2001; 172 (in Turkish).
24. Beevis D, Slade IM. Ergonomics-Cost and benefits. Appl Ergon 2003; 34(6): 413-418.
25. Griffiths H. Manual handling risk management: critical care beds and support systems. Nurs Stand 2006; 20(32); 45-53.
26. Güler C. Ergonomiye Giris (Ders Notları) Kitabı (Introduction to ergonomics (course notes) book). Ankara: Ankara Tabip Odası, 2001 (in Turkish).
27. Simon M, Tackenberg P, Nienhaus A, Estryn-Behar M, Conway PM, Hasselhorn HM. Back or neck-pain-related disability of nursing staff in hospitals, nursing homes and home care in seven countries—results from the European NEXT-Study. Int J Nurs Stud 2008; 45(1): 24-34.
28. Taloni S, Cassavia GC, Ciavarro GL, Andreoni G, Santambrogio GC, Pedotti A. An index for back pain risk assessment in nursery activities. Occup Ergon 2004; 4(4): 281-290.
29. Özcan E. İşe bağlı kas iskelet hastalıkları ve tedavisi (Job-related musculoskeletal disorders and treatment). Nobel Medicus Online Journal. 2006. [Cited 04 Oct 2011]. Available from URL: http://www.nobelmedicus.com/contents/200623/41.pdf (in Turkish).
30. McFarlane AC. Stress- related musculoskeletal pain. Best Practice & Research Clinical Rheumatology 2007;21(3):549-565.
31. Hedge A. Cornell musculoskeletal discomfort questionnaire: human factors and ergonomics laboratory at Cornell University. Female. 1994. [Cited 04 Oct 2011]. Available from URL: http://ergo.human.cornell.edu/ahmsquest.html