



## RESEARCH ARTICLE

## Sustainability and Clinical Effectiveness of Inpatient Rehabilitation in Painful Shoulder Diseases

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### Abstract

**Objective:** Complaints of the shoulder are often accompanied with pain, function lease and impaired quality of life. Inpatient rehabilitation in Austria acts as a powerful non-operative intervention to improve shoulder function and to reduce pain. The aim of this presented study was to observe the long-lasting effects of rehabilitation on shoulder complaints in a follow up trial.

**Design:** The impact of three-week inpatient rehabilitation on pain, sleep quality and shoulder function, respectively biomarkers for stress and pain was investigated in a multi-center study.

**Patients:** 150 inpatient rehabilitation patients with painful shoulder disorders were recruited to a follow up study (baseline, three weeks, three months, and six months).

**Methods:** Data were collected by standardized questionnaires concerning function and sleep quality. Pain intensity was determined by Visual Analogue Scale (VAS). Additional biomarkers for stress, pain and inflammation (CRP, Serotonin, ACTH, Dynorphin,  $\beta$ -Endorphin) were analyzed by ELISA technique or HPLC.

**Results:** Many investigated parameters, mainly pain (VAS) and function (Quick Dash/Constant Murley score) improved significantly during and after the rehabilitation program. Fewer effects could be seen in the biomarkers in serum. Furthermore, the reduction of pain was not gender dependent.

**Conclusion:** The improvement of our main outcome parameters showed that an inpatient rehabilitation program has a long-lasting effect on pain and function in shoulder disabilities and is therefore very important for the improvement in quality of life.

### Keywords

Rehabilitation, Shoulder, Pain, Function, Sustainability

### Introduction

Painful shoulder impairments results in substantial difficulties in daily activities. Shoulder pain, as a common musculoskeletal disease, often arises due to dysfunction in the complex network of structures, which is crucial for the extensive mobility of the shoulder joint. Treatment of shoulder problems has also an effect on economic costs. Disorders increase the demand on health care; affected people show decreased working capacity and substantial absence due to sickness. Sometimes these factors lead to early retirement or job loss [1].

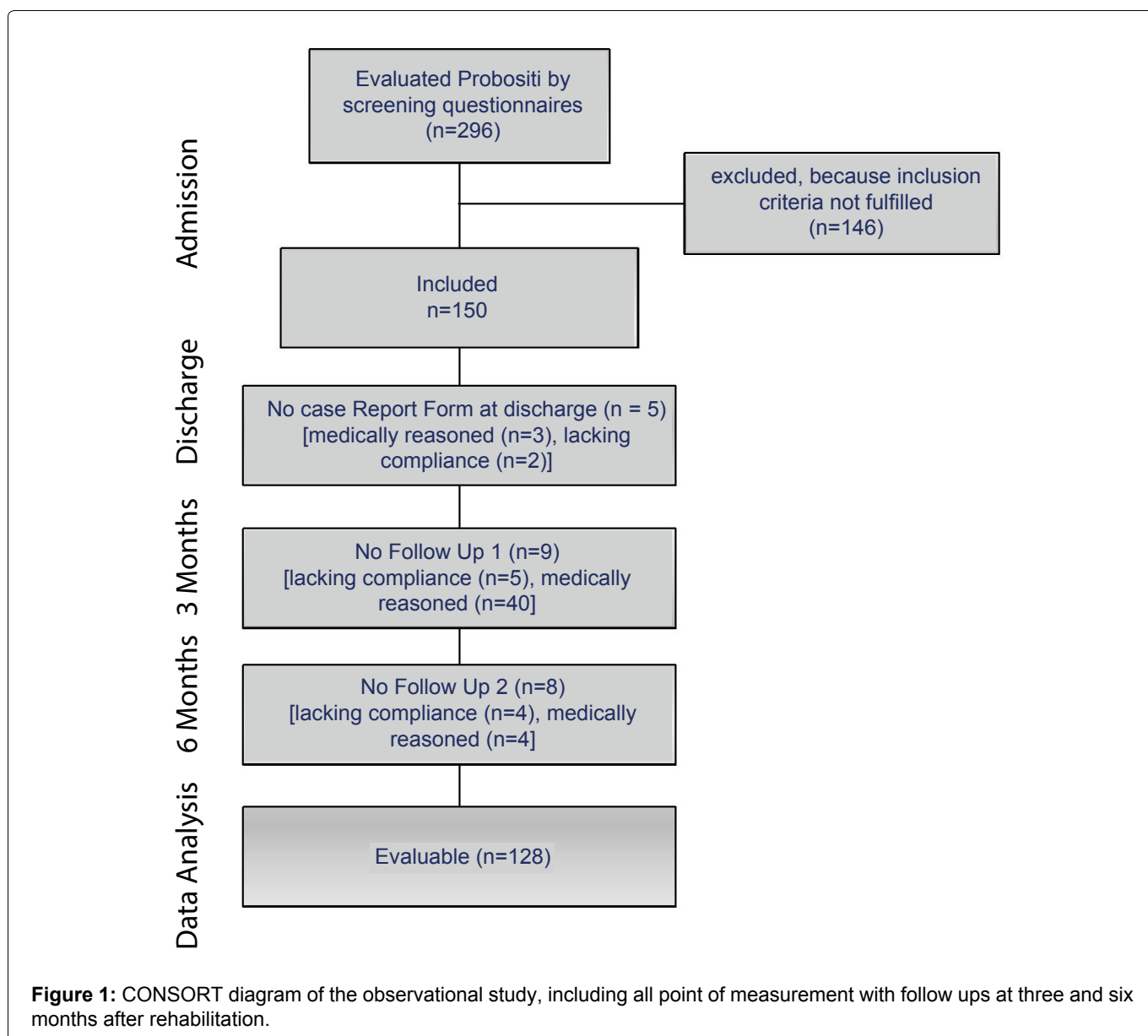
Therefore, in Austria the social security system enables patients with loss of function or physical handicap to undergo 3-week inpatient rehabilitation within a rehabilitation center of a social insurance carrier. The goal of non-operative interventions used in the rehabilitation programs refer to: (i) Pain reduction, (ii) Help in recovery and maintain a passive range of motion, (iii) To strengthen the rotator cuff in a non-impingement range of motion, and (iv) To prevent the occurrence of progressive pathological changes.

Therapies to treat musculoskeletal disorders of the shoulder are amongst others the manual therapy, the therapeutic ultrasound, low-level laser therapy, acupuncture and the pulsed or static electromagnetic field therapy, applied alone or in combination [2]. Kuhn summarized the outcome of eleven randomized, controlled trials to demonstrate that exercise (as applied in rehabilitation programs) in the treatment of rotator cuff impingement has statistically and clinically benefits on pain reduction and improvement of function [3]. Conventional therapy within a rehabilitation center is composed of exercise, physiotherapy, acupuncture, rehabilitation, etc. By contrast, for medical therapy intra-articular corticoids or oral Non-Steroidal Anti-Inflammatory Drugs (NSAID), topic NSAIDs or Capsaicin are applied but result only in the reduction of the symptoms and often do not prevent disease-progression in connection with significant side-effects. Circumvention of joint surgery as a result of failed conventional therapy is of utmost urgency and therefore, there is an exceptional need of rehabilitation-programs with long term effects.

To document a possible effect of multi-week inpatient shoulder rehabilitation the use of validated specific questionnaires to record the functional change is supportive, like the Quick Dash and the Constant Score. A documentation of these questionnaires was made in combination with the evaluation of changes of pain behavior.

## Methods

In multicenter study 150 patients suffering from painful shoulder disorders in four Austrian rehabilitation centers of the Pension Insurance (PVA) were recruited (Figure 1). The inclusion criteria were: painful affection of rotator cuff without rupture (tendinitis, impingement-syndrome), painful partial rupture, and painful osteoarthritis of the shoulder, painful bursitis, and sonography of the shoulder, VAS  $\geq 4$ , age between 30 and 75 years and sufficient knowledge of the German language. At the beginning of the study all approvals from the ethical review committee of the different states (Salzburg, Upper Austria, and Styria) were given.



The exclusion criteria were: fracture of the scapula and/or upper arm, systematic inflammatory rheumatic diseases, fracture of the clavicle and other periarticular fractures, fresh (non-operated) total rupture of the rotator cuff, rupture of biceps, frozen shoulder, cervical discopathy with radicular symptomatic, patients with acute infections, tumor, HIV, liver diseases, alcohol- or drug dependency, pregnancy and lactation period and implanted pacemaker, defibrillators, pain- or insulin pumps.

All patients received a standardized rehabilitation program with equal therapy units during their three weeks inpatient stay including physiotherapy with stretching, mobilization, manual therapy, therapeutically exercise training regarding coordination and force, medical gymnastic, underwater gymnastic, electrotherapy, therapeutic ultrasound, massages and compresses.

Blood samples were taken at admission (= baseline) and discharge (after 3 weeks). Beside typical laboratory routine parameters (blood sedimentation rate, CRP, leukocytes, and thrombocytes) parameters for the evaluation of stress and pain ACTH (Adrenocorticotrophic Hormone/Corticotropin),  $\beta$ -Endorphin, Dynorphin (all three Cusabio Biotech ELISA, GB) and Serotonin (High Pressure Liquid Chromatography (HPLC), Chromsystems, Germany) as well as the inflammatory marker VEGF (Vascular Epidermal Growth Factor) (R&D Systems ELISA, USA) were examined.

Pain intensity (pain at rest and pain on motion) was measured by Visual Analogue Scale (VAS) rating 0-10.

To ascertain the sleep quality, PSQI (Pittsburgh Sleep Quality Index) was used [4]. The PSQI consists of seven items and the total score lasts from 0 points (good sleep quality) to 21 points (insomnia).

Quick-DASH (Disability of the Arm, Shoulder and Hand) [5] was used to determine the *functio laesa* of the shoulder. PSQI and Quick-DASH were performed at admission, discharge, three and six months after the inpatient rehabilitation stay, respectively.

Further Constant-Murley Score shoulder function score [6] was conducted by physiotherapists. By reason of the fact that this score should be performed by medical professional staff it was only ascertained at baseline and discharge from inpatient rehabilitation.

At follow-up three and six months after inpatient rehabilitation the study questionnaires were sent by mail to the patients.

Statistical analyses were done by Microsoft Excel 2007 and SigmaPlot 12.3 (Systat Software Inc., USA).

## Results

From the 150 included patients 128 patients completed the study (57 female, 71 males, age  $56.7 \pm 9.3$ ). Most of the patients (63%) had combined shoulder disorders. 19% suffered from rotator cuff rupture and 13% had an impingement. All other affections of the shoulder showed prevalence beyond 3% within the study group. The results indicate that all parameters improve during the 3-weeks inpatient rehabilitation stay.

### Measurements of the pain intensity (pain on motion and pain at rest)

Mean intensity of pain at rest decreased consistently over six months. The major difference was observed between admission and discharge. Pain-intensity after three and six months compared to baseline was also significantly lowered ( $p < 0.001$ ).

The high mean baseline level of pain on motion (VAS  $6.1 \pm 2.0$ ) continuously decreased during and after rehabilitation, whereas the low VAS of  $2.9 \pm 2.5$  after 6 months was outstanding. The decrease in VAS, regarding pain on motion, of all measurements compared with admission values showed a high significance ( $p < 0.001$ ).

A subgroup analysis concerning gender indicates that subjective pain intensity perception differed between women and men. The mean VAS value of pain at rest in men was 3.5 and in women 4.1. At pain on motion pain intensity of men was higher than in women (6.3 and 5.8). In both sexes VAS decreased significantly ( $p < 0.001$ ). Mean difference in pain at rest and pain on motion did not distinguish significantly between men and women (Figure 2A and Figure 2B).

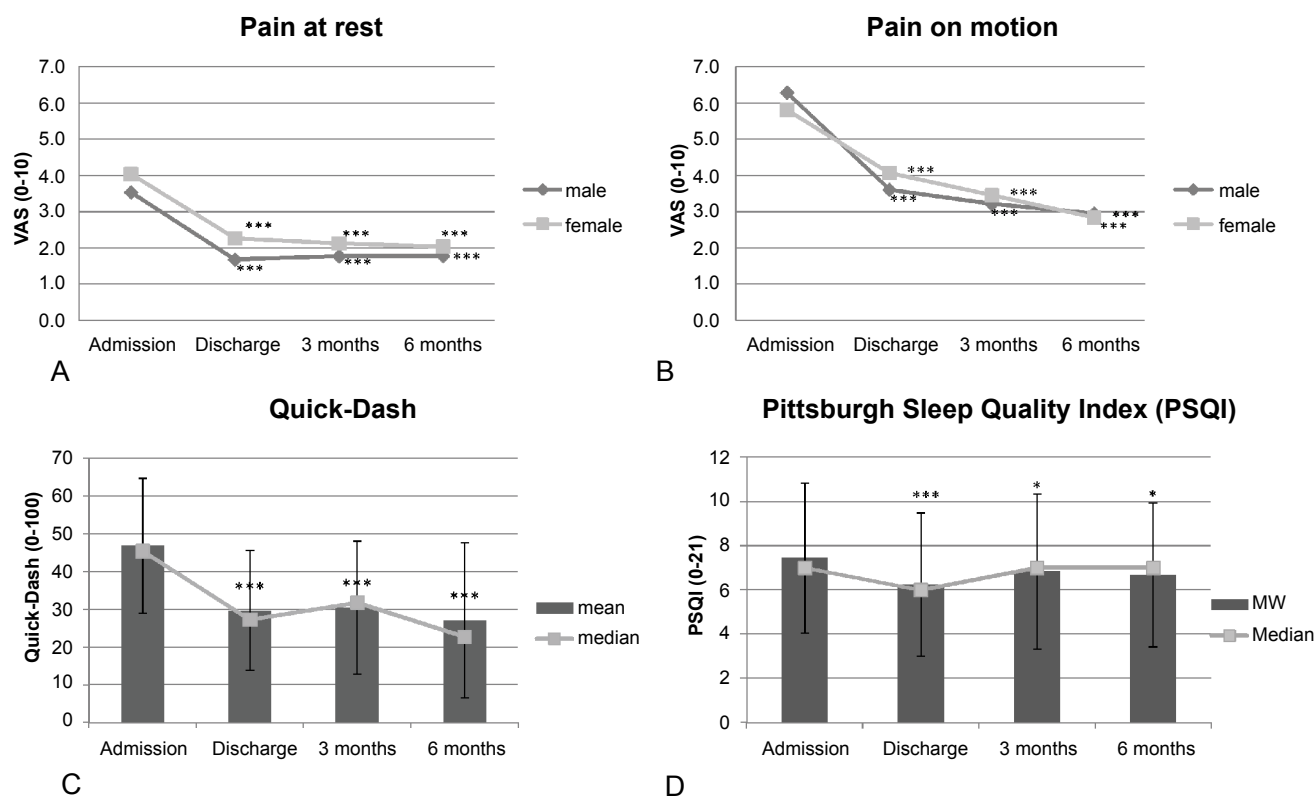
### Analysis of the serum samples for different biomarkers

Laboratory parameters ACTH, Serotonin, and Dynorphin decreased slightly.  $\beta$ -Endorphin increased from 131.3 pg/ml (baseline) to 225.8 pg/ml (discharge), with no significant difference partly due to the high standard deviation (Table 1). In the total group, the VEGF declined without significance (from 385.2 to 361.3 pg/ml) whereas the subgroup with rupture of the rotator cuff depicted a difference of VEGF more obvious but still without significance (baseline: 389.4; discharge 356.4 pg/ml).

**Table 1:** Development of pain and stress biomarkers during inpatient rehabilitation measured by immunoassays.

	n	Rehabilitation admission				Rehabilitation discharge (3 weeks)				p-value
		Mean	SD	Median	SEM	Mean	SD	Median	SEM	
<b>ACTH (pg/ml)</b>	123	51.3	32.7	39.7	3.0	50.5	28.9	41.4	2.6	n.s.
<b><math>\beta</math>-Endorphin (pg/ml)</b>	123	131.3	406.9	14.8	36.7	225.8	867.0	23.5	78.2	n.s.
<b>Dynorphin (pg/ml)</b>	123	4.3	6.2	1.9	0.6	4.1	6.0	2.2	0.5	n.s.
<b>Serotonin (ng/ml)</b>	124	123.3	66.5	114.2	6.0	120.0	71.1	109.9	6.4	n.s.

n: Number; ACTH: Adrenocorticotrophic Hormone; SD: Standard Deviation; SEM: Standard Error of the Mean; n.s: Not Significant.



**Figure 2:** Results of Scores for pain, function and sleep: A) VAS-Course of pain at rest in male and female, significant difference refers to baseline (\*\* $p < 0.001$ ); B) VAS-Course of pain on motion in male and female, significant difference refers to baseline (\*\* $p < 0.001$ ) no significant difference between men and women; C) Alteration of Quick Dash (shoulder function); D) Pittsburgh Sleep Quality Index (PSQI) during rehabilitation and follow ups; p value refers to change between measurement point and baseline.

## PSQI

The total score improved from 7.4 at baseline to 6.3 at the end of the rehabilitation stay. Improved sleep quality lasted up to six months after rehabilitation (mean value 6.7). The best sleep quality could be observed after the rehabilitation, which is statistically verified ( $p < 0.001$ ). The alteration from baseline to three and six months after rehabilitation was also remarkable ( $p < 0.05$ ) (Figure 2D).

## Quick-DASH

The Quick-DASH values decreased significantly (from 48.1 (baseline) to 31.5 (discharge), 33.1 (3 months) 30.4 (6 months)). There was a highly detectable improvement in shoulder function when measurements at admission were compared to all later points of measurements. Quick-Dash values improved in 82% of the shoulder patients, 12% decreased and 3% did not change (Figure 2C). The Quick Dash changes correlated significantly with the changes of pain at rest ( $p < 0.02$ ) and pain on motion ( $p < 0.001$ ).

## Constant murley

The Constant Murley Score for evaluation of shoulder function [6] improved significantly during the inpatient rehabilitation stay ( $p < 0.001$ ). We observed an improvement of shoulder function in 87% of the patients. Only 5% showed deterioration in their shoulder function and 8% continued unchanged. We noticed a

high correlation between the Constant Murley and the Quick-Dash score ( $r = -0.351$ ,  $p < 0.001$ ).

## Discussion

A Cochrane review updating a series of reviews about physiotherapy in shoulder pain showed that physiotherapeutic interventions and exercise - as performed in our rehabilitation program - is similar to an intervention with drugs (e.g. glucocorticoid injection) [2]. Studies that consider physiotherapy for treating shoulder pain and function showed that active physiotherapy has a significant benefit to the patients in short- and long-term compared to non- or placebo-treatment. Physiotherapy intervention after surgical intervention results in a better outcome compared to physiotherapy alone.

In this present study on patients with painful shoulder affections we found an improvement of function, disability and sleep quality during the 3-weeks inpatient rehabilitation including various physiotherapeutically methods and exercise. All therapies together - especially exercise in the rehabilitation program - can help to retain mobility and enable again some disease disabled activities of daily living.

Inflammatory mechanisms might be responsible for shoulder pain too. Data of Savitskaya, et al. [7] indicate a correlation between VEGF levels and the advanced stage of the disease proven by power Doppler ultrasound.

In our investigations, we found a tendency for VEGF levels to decrease during the 3-week inpatient rehabilitation. Because of the large standard deviation, no significant difference was detectable.

Our findings in the increasing  $\beta$ -Endorphin levels correlate with the results of the literature, where it was demonstrated that modalities of physiotherapy can induce  $\beta$ -Endorphin release due to motion exercise [8].

ACTH and  $\beta$ -Endorphin are POMC (pro-opiomelanocortin)-derived peptides [9] expressed as prohormones that are expressed in the adenohypophysis. Stress induces  $\beta$ -Endorphin and ACTH release via POMC cleavage by corticotropin-releasing hormone which is released under stress conditions.  $\beta$ -Endorphin release tends to result in pain relief as could be observed in physical therapy which leads to endorphin-induced analgesia [8]. Dynorphin is an endorphin that autoregulatory counter-regulates pain [10]. In case of a noxa the intracellular  $\text{Ca}^{2+}$  increase inhibits the binding of DREAM (Downstream Regulatory Element Antagonist Modulator) whereby dynorphin binds and activates the opioid receptor. Leading to a reduction of pain transmission thereby a chronification of pain is prevented [11]. Unfortunately, our Dynorphin measurements showed no statistical change in serum levels.

It is known that Serotonin alterations could be observed in chronic pain patients [12] but our results did not indicate a clear alteration of serotonin-levels in serum after the 3-weeks rehabilitation program. Compared with the observational study of Tafelski, et al., we found no difference neither between the genders nor in dependence on age [13]. Tafelski, et al. found that the difference of pain-intensity regarding genders is age-dependent. The older the patients the bigger and more diverse the subjective experienced pain intensity. Contrary to the common presumption that women are more sensitive to pain our results accompany with the findings of Racine, et al. In a systematic literature review, most of the investigations observed in this review concerning pain in men and women showed no difference between genders [14].

The shoulder with her very complex structure can be affected by different disorders. There are existing guidelines how to treat shoulder pain [15]. It can be said that a standard rehabilitation program which consists of various therapies and aspects has a positive and sustainable (up to 6 months) effect on shoulder disorders regarding pain, sleep quality and disabled shoulder function which again influences life quality in a positive way and justify the costs for rehabilitation in the social security system.

Maintaining a full independent life is the aim of a successful rehabilitation in patients with functional deficits of joint diseases like painful shoulder diseases. The results point to a quicker return to work after the inpatient rehabilitation stay. So, in painful shoulder diseases the multidisciplinary rehabilitation program exerts clear positive effects for health economics. Further research to the effects and the sustainability of effective rehabil-

itation program is required.

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## References

1. Linaker CH, Walker-Bone K (2015) Shoulder disorders and occupation. *Best Pract Res Clin Rheumatol* 29: 405-423.
2. Page MJ, Green S, McBain B, Surace SJ, Deitch J, et al. (2016) Manual therapy and exercise for rotator cuff disease. *Cochrane Database Syst Rev*.
3. Kuhn JE (2009) Exercise in the treatment of rotator cuff impingement: A systematic review and a synthesized evidence-based rehabilitation protocol. *J Shoulder Elbow Surg* 18: 138-160.
4. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 28: 193-213.
5. Hudak PL, Amadio PC, Bombardier C (1996) Development of an upper extremity outcome measure: The DASH (disabilities of the arm, shoulder, and hand). *Am J Ind Med* 29: 602-608.
6. Constant CR, Murley AH (1987) A clinical method of functional assessment of the shoulder. *Clin Orthop Relat Res* 160-164.
7. Savitskaya YA, Izaguirre A, Sierra L, Perez F, Cruz F, et al. (2011) Effect of angiogenesis-related cytokines on rotator cuff disease: the search for sensitive biomarkers of early tendon degeneration. *Clin Med Insights Arthritis Musculoskelet Disord* 4: 43-53.
8. Bender T, Nagy G, Barna I, Tefner I, Kadas E, et al. (2007) The effect of physical therapy on beta-endorphin levels. *Eur J Appl Physiol* 100: 371-382.
9. Böhm M, Grassel S (2012) Role of proopioidmelanocortin-derived peptides and their receptors in the osteoarticular system: From basic to translational research. *Endocr Rev* 33: 623-651.
10. Luo MC, Chen Q, Ossipov MH, Rankin DR, Porreca F, et al. (2008) Spinal dynorphin and bradykinin receptors maintain inflammatory hyperalgesia. *J Pain* 9: 1096-1105.
11. Cheng HYM, Penninger JM (2003) When the DREAM is gone: From basic science to future perspectives in pain management and beyond. *Expert Opin Ther Targets* 7: 249-263.
12. Patetsos E, Horjales-Araujo E (2016) Treating chronic pain with SSRIs: What do we know? *Pain Res Manag* 2020915.
13. Tafelski S, Kerper LF, Salz AL, Spies C, Reuter E, et al. (2016) Prospective clinical observational study evaluating gender-associated differences of preoperative pain intensity. *Medicine (Baltimore)* 95: e4077.
14. Racine M, Tousignant-Laflamme Y, Kloda LA, Dion D, Dupuis G, et al. (2012) A systematic literature review of 10 years of research on sex/gender and experimental pain perception-part 1: Are there really differences between women and men? *Pain* 153: 602-618.
15. Klintberg IH, Cools AM, Holmgren TM, Holzhausen AC, Johansson K, et al. (2015) Consensus for physiotherapy for shoulder pain. *Int Orthop* 39: 715-720.