Comparison of Efficacy and Safety of Duloxetine and Nonsteroidal Anti-inflammatory Drugs in Subacromial Impingement Syndrome

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Research article

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Abstract

Background: Subacromialimpingement syndrome (SIS) is characterized by shoulder pain and restriction in range of motion (ROM), which lead to debility and decrease quality of life (QoL). Duloxetine could provide persistent long-term pain relief in chronic musculoskeletal pain. Therefore, we aimed to investigate the efficacy of duloxetine in stage I or II SIS patients through comparing the nonsteroidal anti-inflammatory drugs (NSAIDs) treatment.

Methods: The patients diagnosed with stage I or II SISwere randomly assigned into the duloxetine group (N= 37) and NSAIDs group (N= 37). Duloxetine group patients started on oral duloxetine 40 mg per day for one week and then titrated up to 60 mg per day for one week. NSAIDs group patients received oral loxoprofen sodium tablets 60mg3 times a day for two weeks. The standard measures for investigating the efficacy include pain intensity (VAS), ROM, shoulder functional status, and the QoL at baseline, end of treatment, and at 1 and 3 months follow-up.

Results: 74 eligible patients completed the treatment and evaluation. Both treatment groups improved significantly from baseline over time. And all parameters of pain intensity, shoulder functionalstatus and QoL in the duloxetine group were significantly better than those in the NSAIDs group.And no one manifested SIS recurrence and side effects during the entire follow-up period.

Conclusions: Both duloxetine and NSAIDs can be beneficial in the rehabilitation of stage I or II SIS patients. Moreover, duloxetine resulted in improvements in outcomes greater than NSAIDs for the treatment of SIS. The current results indicated that duloxetine treatment might be used as a new safe and effective alternative for SIS. Given the encouraging results of this study, it would be worthwhile to confirm our findings in randomized placebo-controlled multicentre clinical trials.

Background

Subacromial impingement syndrome (SIS) is one of the most common disorders of the shoulder in adults age groups and is characterized by shoulder pain and restriction in range of motion (ROM), especially with overhead activities.(1, 2) Although SIS is generally self-limiting, the cuff lesions and complications caused by SIS often exacerbate over time and lead to debility and decreased quality of life (QoL) of SIS patients.(3, 4) Many conservative treatment modalities have been demonstrated to be beneficial in relieving subacromial inflammation and shoulder pain and improving the shoulder functional status in SIS,(5–8) including systemic nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, activity modification, electromagnetic radiation, therapeutic exercises, and corticosteroid injections. There is wide agreement that NSAIDs treatment is the first choice for stage I or II SIS.(1, 9)

Duloxetine is a selective serotonin norepinephrine reuptake inhibitor (SNRI) that is commonly prescribed for treatment of depression and anxiety disorders.(10)In addition, many studies have shown that duloxetine could provide persistent long-term pain relief in chronic musculoskeletal pain,(11, 12) including fibromyalgia, osteoarthritis and musculoskeletal pain. Moreover, some studies have shown that

duloxetine could improve the quality of recovery and relieve acute postoperative pain after knee replacement surgery and spine surgery.(13, 14) More importantly, the results they observed were consistent with this study. Given the absence of other effective pharmacological treatments for SIS, any medication which could provide effects for SIS patients has to be investigated. In this study, we aimed to investigate and present the efficacy of duloxetine on pain, shoulder functions and QoL in stage I or II SIS patients through comparing the NSAIDs treatment.

Materials And Methods

Patients

This is a retrospective study which conducted between January 2018 and December 2019. The study was approved by the Medical Ethics Committee of The Affiliated Yantai Yuhuangding Hospital of Qingdao University (Ref: 20180120), (Additional file 1) and conducted in accordance with the Helsinki Declaration. The written informed consent form was obtained from each outpatient, (Additional file 2).The diagnosis of SIS was made on clinical examination (shoulder pain with limited range of motion, positive Neer and Hawkins-Kennedy impingement tests) and confirmed by magnetic resonance imaging (MRI).(15, 16) All the patients received a three-month follow-up period after the 2-week duloxetine or NSAIDs treatment.

Inclusion criteria were as follows:(17, 18) aged 20–65 years, presented with shoulder pain which had been ongoing for one-three months, patients were diagnosed of SIS and characterized as stage I or II SIS based on MRI findings.

Subjects with the presence of any of the following were excluded:(17, 18) patients with stage III SIS, complete tear of the rotator cuff on MRI, a history of acute shoulder trauma, adhesive capsulitis, any rheumatic disorder (such as rheumatoid arthritis or spondyloarthropathy), history of steroid injection therapy for shoulder, patients taking regular systemic NSAIDs or steroids. Other exclusion criteria were: a history of neck and shoulder surgery, or radicular neck pain within previous three months, diabetes mellitus, use of anticoagulants, pregnant or breastfeeding mothers and malignancy.

Treatments

Before treatment, the following baseline measurements were assessed: (1) blood pressure; (2) blood glucose; (3) visual analog scale (VAS) scores for pain intensity with overhead activities; (4) shoulder ROM (includes flexion, abduction and external rotation); and (5) quality of life and shoulder functional status questionnaires. After the baseline measurements, the patients were randomly assigned into the duloxetine group and NSAIDs group using the numbered envelopes method. Then the duloxetine group patients started on oral duloxetine (Cymbalta; Eli Lilly & Company, Indianapolis, IN 46285, USA) 40 mg per day for one week and then titrated up to 60 mg per day for one week.(19, 20) NSAIDs group patients received oral loxoprofen sodium tablets (Daiichi Sankyo Co., Ltd. H20030769, Japan) 60 mg3 times a day for two weeks.(21)A home-based standardized exercise program (10 repetitions of 1 set daily for

eachexercise) including Codman pendulum exercises, aswell as pain-limited, active shoulder ROM and strengthening (isometric) exercises, weregiven to all patients after the baseline assessment.(22) The treatment regimen would be stopped if any severe side effect occurred, such as dizziness, insomnia, hypertension.(18) Each day of the treatments, and then 1 and 3 months post-treatment, the following tests were performed: (1) VAS scores for pain intensity with overhead activities; (2) shoulder ROM (includes flexion, abduction and external rotation); (3) quality of life and shoulder functional status questionnaires; (4) blood pressure; (5) blood glucose; and (6) side effects.

Assessments

Pain

The pain intensity with overhead activities was assessed by a 10-cm VAS, which is a regular method for measuring the pain. The measurement is performed on a 10-cm horizontal line with “no pain” written at the left end and the “worst imaginable pain” written at the right end.(23, 24) The patients were asked to mark their current pain state. According to the changes of patients’ VAS scores at the end of treatments, we divided all the patients into three groups including total relief group (100% decrease in VAS scores), major relief group (a decrease of at least 50% in VAS scores), and poor relief or worse pain group (VAS scores decreased by less than 50% or increased).(25)

ROM

Shoulder ROM was assessed using a goniometry.(26) To measure shoulder ROM for coronal abduction and sagittal flexion, patients kept a standing position and actively raised their arms against the pull of gravity in the coronal and sagittal plane respectively. To measure shoulder ROM for external rotation, the patients were placed in the supine position with the tested arms were abducted to 90°, the elbow flexed to 90°. And then each patient actively brought their arm back into external rotation.

Questionnaires

Two questionnaires were used to evaluate the shoulder functional status and QoL of patients, respectively. The questionnaires include the Shoulder Pain and Disability Index (SPADI) and the McGill Pain Questionnaire Short Form (MPQSF).

1. Shoulder functional status questionnaire

We selected the Chinese validated version of Shoulder Pain and Disability Index (SPADI) questionnaire to assess functional status of the shoulder.(27) The SPADI is the shortest self-administered instrument and widely used because of the high reliability and validity. The SPADI consists two scales including shoulder pain (five items) and disability (eight items), all items are assessed on a VAS with “no pain/ no difficulty” written at the left end and the “worst imaginable pain/ difficulty requiring assistance” written at the right end. Higher SPADI scores indicated higher degree of shoulder pain and disability.(28, 29)

2. QoL questionnaire

The MPQSF is a multidimensional pain questionnaire used to assess the acute and chronic pain sensory, affective and intensity.(30, 31) This questionnaire includes VAS scores of pain intensity and 15 descriptors (11 sensory, 4 affective) which are rated on a four-point verbal scale as 0 = none, 1 = mild, 2 = moderate, or 3 = severe. The reliability and validity of MPQSF for evaluating the effectiveness of pain interventions are well documented.

Side effects

We used an adverse-effects checklist interview to collected duloxetine and NSAIDs related side effects during and after treatment.(32) The possible side effects include somnolence; nausea; peptic ulcer; dizziness; headache; vomiting; stomatitis; decreased appetite; constipation; dry mouth; hyperhidrosis; hypertension; insomnia; dysuresia; diarrhea; ventosity.(18)

Data Analysis

The statistical analysis was based on data obtained from all SIS patients, (Additional file 3). Categorical data were expressed using frequencies, and continuous data were described as mean ± SD. The Wilcoxon test was used to compare intra-group differences, and the Mann-Whitney U test was used to compare inter-group differences.(33) We used the SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY) to perform statistical analysis and $P < 0.05$ was considered statistically significant.

Results

Patients

In total, 102 patients were screened for the enrollment. 74 patients met the inclusion criteria and agreed to participate. All of the patients completed the treatment and evaluation. 37 patients were randomized to the duloxetine group, and 37 patients to the NSAIDs group and no one was lost to follow-up (Figure 1). The general demographic features of the patients and baseline measures are given in Table 1 and Table 2. There were no significant differences between both groups with respect to demographic characteristics or baseline measures (all $P> 0.05$).

Effects on shoulder pain

Both groups showed an improvement in pain intensity, shoulder functional status and QoL at the end of treatment and the entire follow-up period compared to their baseline values.

When comparing the VAS scores of improvement between groups, the improvements in duloxetine group (DVAS: 5.66 ± 1.02) were found to be statistically higher in patients receiving NSAIDs (DVAS: 4.80 ± 1.07) ($P= 0.001$) at the end of treatments (Table 3). And 35 of 37 (94.59%) patients in the duloxetine group rated total relief or major relief compared with 29 of 37 (78.38%) patients in the NSAIDs group after treatments (Figure 2).

Effects on ROM, functional status and QoL

Subgroup analysis of the ROM, SPADI and MPQSF scores demonstrated that the duloxetine group had a significant increase in abduction (DROM: duloxetine: 53.89 ± 10.53, NSAIDs: 46.27 ± 12.31, P=0.006), external rotation (DROM: duloxetine: 10.54 ± 4.27, NSAIDs: 7.84 ± 3.86, P=0.006), SPADI scores (DSPADI: duloxetine: 79.11 ± 9.77, NSAIDs: 70.86 ± 9.80, P=0.001) and MPQSF scores (DPRI-total: duloxetine: 25.27 ± 5.03, NSAIDs: 18.86 ± 3.99, P<0.001) compared to the NSAIDs group. Although shoulder ROM of flexion improvement was not statistically significant compared to NSAIDs (P=0.184), the mean improvement in the flexion at the end of treatment was 29.24 for the duloxetine group, which was higher than 25.19 for NSAIDs group(Table 3).

In the assessments at the one month and three months follow-up, significant improvement was observed in all parameters in both groups when compared to the baseline values. And all parameters of pain intensity, shoulder functional status and QoL in the duloxetine group were significantly better than those in the NSAIDs group(Table 4).

Side effects

No severe side effects were reported during or after the treatment period in both groups. The frequency of side effects during and after the treatment of duloxetine and NSAIDs in all the patients are shown in Table 5. 6 patients (16.22%) reported side effects concerning the duloxetine treatment, and 4 patients (10.81%) reported side effects concerning the NSAIDs treatment. The most frequently reported adverse events were nausea and decreased appetite. Side effects were generally of mild or moderate intensity, and no side effect was found in all patients during the entire follow-up period. Meanwhile, there was no significant difference between the groups regarding the side effects (P=0.496).

Discussion

In this study, our results indicated that duloxetine and NSAIDs treatment seems to be effective for stage I or II SIS patients. According to our findings, duloxetine more significantly relieved shoulder pain and improved shoulder ROM and functional status as well as QoL than NSAIDs. Furthermore, no patient reported symptom recurrence and side effect during the three-month follow-up period in duloxetine group.

SIS is one of the most common disorders of the shoulder in adults age groups, the cuff lesions and complications often exacerbate over time and lead to debility and decreased QoL of SIS patients. Many conservative treatment modalities have been demonstrated to be beneficial in SIS, Ruedi Steuri, et al. have been reported that oral NSAIDs appear to be more effective than placebo by systemic review and meta-analysis.(34) And the results of NSAIDs for SIS we observed were consistent with previous studies.

Duloxetine is a potent and selective SNRI in the central nervous system in vitro and in vivo.(35)In addition, duloxetine has been approved for the treatment of chronic musculoskeletal pain and neuropathic pain in

the United States as well as other countries.(36)The mechanism of the analgesic effect of duloxetine may be explained by its ability to enhance both serotonin and norepinephrine neurotransmission in descending inhibitory pain pathways in the central nervous system.(37) Given the similar pharmacokinetic profiles of duloxetine between Chinese and Caucasians,(38) it is thought that duloxetine may also prove effective in the treatment of chronic pain in Chinese patients. To the best of our knowledge, there are few studies on duloxetine in SIS patients. In this study, we aimed to present our results regarding the comparison of duloxetine and NSAIDs in the treatment of SIS, which may bring a new perspective into the treatment strategy.

In the present study, the ongoing shoulder pain intensity decreased significantly in both groups compared to the baseline measurements. The decrease was more pronounced in the duloxetine group. After the duloxetine treatment, four (10.81%) patients obtained total shoulder pain relief, and 83.78% of the patients (31/37) achieved major shoulder pain relief, and this proportion increased to 97.30% (36/37) at three-month post duloxetine treatment, which was higher than that reported in NSAIDs group.

Subgroup analysis of the ROM and SPADI scores demonstrated that the duloxetine group had a significant increase in abduction, external rotation and SPADI scores (all $P < 0.05$) compared to the NSAIDs group. Although shoulder ROM of flexion improvement was not statistically significant compared to NSAIDs ($P = 0.184$), the mean improvement in the flexion degrees at the end of treatment was 29.24 for the duloxetine group, which was higher than 25.19 for NSAIDs group.

The efficacy of treatments for SIS can be measured not only in terms of the amount of pain and restricted ROM the patient experiences, but also in terms of their overall physical and emotional well-being (quality of life). Pain is known to reduce the quality of life, including mood and physical and social functioning. This study used a validated instrument, the MPQSF questionnaire, to measure quality of life. Duloxetine-treated patients scored significantly better than NSAIDs-treated patients for all domains. For all of the domains (pain scale and disability), the difference was statistically significant.

In addition, the duloxetine and NSAIDs treatment were well tolerated. Consistent with the previous clinical studies of duloxetine and NSAIDs,(19, 39) the most common side effects were nausea and decreased appetite. All patients did not receive the necessitating specific treatment for side effects and opted to remain on duloxetine or NSAIDs treatment with these side effects being mild to moderate in intensity. Moreover, no side effect was found in all patients during the entire follow-up period. Meanwhile, there was no significant difference between the groups regarding the side effects ($P = 0.496$).

Taken together, the persistent existence of pain relief and improvement in ROM and QoL indicated that duloxetine is an effective and safe treatment of SIS, although, the involved mechanisms are not clear.

In this study, there are some important limitations that should be noted. Firstly, patients were followed up for a short-term period (three months). Therefore, we cannot comment on the long-term effects of these different modalities. Secondly, we did not include a placebo group, which limits the interpretation of our

results and conclusion. Therefore, long-term randomized placebo-controlled trials are required to confirm our findings and conclusion.

Conclusion

In summary, both duloxetine and NSAIDs can be beneficial in the rehabilitation of stage I or II SIS patients. Moreover, duloxetine resulted in improvements in outcomes greater than NSAIDs for the treatment of SIS. The current results indicated that duloxetine treatment might be used as a new safe and effective alternative for SIS. Given the encouraging results of this study, it would be worthwhile to confirm our findings in randomized placebo-controlled multicentre clinical trials.

Abbreviations

SIS
subacromial impingement syndrome; ROM:range of motion; QoL:quality of life; NSAIDs:nonsteroidal anti-inflammatory drugs; SNRI:selective serotonin norepinephrine reuptake inhibitor; MRI:magnetic resonance imaging; VAS:visual analog scale; SPADI:Shoulder Pain and Disability Index; MPQSF:McGill Pain Questionnaire Short Form

Declarations

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Authors' contributions

Li Zhao, Li Teng, Feng Xu, Huayun Zhang, Zhigang Xie, Bin Huang conceptualised and designed the study. Li Zhao, Li Teng, Feng Xu, Huayun Zhang collected field data and carried out the analysis. Li Zhao, Li Teng drafted the manuscript. Bin Huang, Li Zhao reviewed and edited the drafted manuscript. Li Teng, Feng Xu, Zhigang Xie were responsible for the collection of data and administration of study participants. Li Zhao, Li Teng, Zhigang Xie provided methodological guidance on research statistics. All authors approved the final manuscript for submission.

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Availability of data and materials

Datasets are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of The Affiliated Yantai Yuhuangding Hospital of Qingdao University (Ref: 20180120) and conducted in accordance with the Helsinki Declaration. The written informed consent form was obtained from each outpatient.

Consent for publication

Not applicable.

Competing interests

The authors report no conflicts of interest in this study.

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Tables

Table 1 Baseline demographic and clinical characteristics of both groups.

Characteristics	Duloxetine group (n=37)	NSAIDs group (n=37)	F	P-value
Age (years), mean (SD)	57.16 (6.10)	57.81 (6.32)		0.66
Gender, M/F	22/15	19/18	0.64	0.32
Duration of symptoms (days), mean (SD)	53.97 (17.31)	54.27 (17.01)		0.94
Affected shoulder, n (%)			1.00	0.50
Dominant	25 (67.57%)	26 (70.27%)		
Non-dominant	12 (32.43%)	11 (29.73%)		
Baseline pain in activity (VAS 0-10) , mean (SD)	7.41 (0.69)	7.46 (0.69)		0.76

Notes: Data are given as mean (SD) or ratio.

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; M, male; F, female; VAS, visual analog scale.

Table 2 The comparison of baseline clinical parameters of the groups.

Clinical parameters	Duloxetine group (n=37)	NSAIDs group (n=37)	P-value
VAS (0-10, activity)	7.41 ±0.69	7.46 ±0.69	0.76
ROM (degrees)			
Flexion	123.27± 15.20	122.41 ± 14.88	0.81
Abduction	68.81 ± 9.49	68.19 ± 9.14	0.78
External rotation	64.30 ± 7.76	63.70 ± 7.37	0.74
SPADI scores			
Pain scale	36.68 ± 3.64	36.59 ±3.66	0.92
Disability	59.38 ± 5.60	59.24 ± 5.64	0.92
Total	96.05 ± 9.05	95.84 ± 9.12	0.92
MPQSF scores			
Sensory	22.41 ± 3.48	22.54 ± 3.56	0.87
Affective	7.05 ± 1.87	7.30 ± 1.78	0.57
PRI-total	29.46 ± 5.23	29.84 ± 5.01	0.75
VAS	7.41 ± 0.69	7.46 ± 0.69	0.76
PPI	3.62 ± 0.72	3.81 ± 0.78	0.28

Notes: The Mann-Whitney U test was used to compare the baseline clinical parameters of both groups. No significant differences between both groups with respect to baseline clinical parameters (all P> 0.05).Data are expressed as mean ± SD.

Abbreviations: VAS, visual analog scale; ROM, range of motion; SPADI, Shoulder Pain and Disability Index; MPQSF, McGill Pain Questionnaire Short Form; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 3 Comparison of change in outcome measures from baseline to end of treatment.

Change in outcome	Duloxetine group (n=37)	NSAIDs group (n=37)	P-value
DVAS (activity)	5.66 ± 1.02	4.80 ± 1.07	0.001
DROM (degrees)			
Flexion	29.24 ± 12.28	25.19 ± 13.67	0.184
Abduction	53.89 ± 10.53	46.27 ± 12.31	0.006
External rotation	10.54 ± 4.27	7.84 ± 3.86	0.006
DSPADI scores			
Pain scale	28.49 ± 5.18	24.97 ± 5.04	0.004
Disability	50.35 ± 5.54	46.43 ± 6.52	0.007
Total	79.11 ± 9.77	70.86 ± 9.80	0.001
DMPQSF scores			
Sensory	19.24 ± 3.39	14.70 ± 3.08	< 0.001
Affective	5.92 ± 1.93	4.19 ± 1.45	< 0.001
PRI-total	25.27 ± 5.03	18.86 ± 3.99	< 0.001
VAS	5.66 ± 1.02	4.80 ± 1.07	0.001
PPI	2.65 ± 0.86	2.24 ± 0.68	0.028

Notes: When comparing the change in outcome measures between groups, the improvements in duloxetine group were found to be statistically higher in patients receiving NSAIDs at the end of treatments, only ROM of flexion improvement was not statistically significant compared to NSAIDs group (P=0.184). Data are expressed as mean ± SD.

Abbreviations: VAS, visual analog scale; ROM, range of motion; SPADI, Shoulder Pain and Disability Index; MPQSF, McGill Pain Questionnaire Short Form; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 4 Summary of treatments effects in both groups during the entire follow-up period.

	Duloxetine group (n=37)			NSAIDs group (n=37)		
	Baseline	**One-month follow-up**	**Three-months follow-up**	**Baseline**	**One-month follow-up**	**Three-months follow-up**
VAS (0-10, activity)	7.41 ±0.69	0.99 ± 1.03 [a]	0.36 ± 0.93 [b]	7.46 ± 0.69	1.82 ± 1.37 [c]	1.34 ±1.39 [d]
ROM (degrees)						
Flexion	123.27 ± 15.20	161.08 ± 10.95 [a]	162.68 ± 10.62 [b]	122.41 ± 14.88	158.76 ± 12.18 [c]	160.54 ± 11.92 [d]
Abduction	68.81 ± 9.49	142.78 ± 15.92 [a]	152.86 ± 14.94 [b]	68.19 ± 9.14	137.65 ± 22.92 [c]	149.11 ± 25.52 [d]
External rotation	64.30 ± 7.76	81.19 ± 6.72 [a]	83.14 ± 5.76 [b]	63.70 ± 7.37	79.76 ± 6.53 [c]	81.70 ± 5.92 [d]
SPADI scores						
Pain scale	36.68 ± 3.64	6.29 ± 3.42 [a]	5.57 ± 3.09 [b]	36.59 ± 3.66	9.67 ± 5.42 [c]	8.52 ± 4.39 [d]
Disability	59.38 ± 5.60	8.18 ± 2.41 [a]	7.25 ± 2.62 [b]	59.24 ± 5.64	10.65 ± 5.87 [c]	9.13 ± 4.76 [d]
Total	96.05 ± 9.05	14.47 ± 5.62 [a]	12.82 ± 5.49 [b]	95.84 ± 9.12	20.32 ± 11.11 [c]	17.65 ± 8.97 [d]
MPQSF scores						
Sensory	22.41 ± 3.48	2.65 ± 1.58 [a]	1.87 ± 0.92 [b]	22.54 ± 3.56	5.78 ± 2.16 [c]	4.62 ± 2.52 [d]
Affective	7.05 ± 1.87	1.04 ± 0.82 [a]	0.76 ± 0.45 [b]	7.30 ± 1.78	2.65 ± 1.52 [c]	1.57 ±1.49 [d]
PRI-total	29.46 ± 5.23	3.69 ± 2.32 [a]	2.63 ± 1.23 [b]	29.84 ±5.01	8.43 ± 5.45 [c]	6.19 ± 3.87 [d]
VAS	7.41 ±0.69	0.99 ± 1.03 [a]	0.36 ± 0.93 [b]	7.46 ± 0.69	1.82 ± 1.37 [c]	1.34 ±1.39 [d]
PPI	3.62 ± 0.72	0.82 ± 0.65 [a]	0.61 ± 0.48 [b]	3.81 ± 0.78	1.45 ± 0.83 [c]	1.21 ± 0.64 [d]

Notes: The Wilcoxon test was used to investigate the intra-groupdifferences.The SPADI consists two scales including shoulder pain (five items) and disability (eight items). Higher SPADI scores indicated higher degree of shoulder pain and disability.The MPQSF comprises five domains including sensory,

affective, PRI-Total, VAS, and PPI. Responses are summed and then transformed onto a scale for each domain. Lower scores in each domain indicate improved health status. Data are expressed as mean ± SD.

a: One-month follow-up vs. baseline in duloxetine group. P< 0.001.

b: Three-months follow-up vs. baseline in duloxetine group. P< 0.001.

c: One-month follow-up vs. baseline in NSAIDs group. P< 0.001.

d: Three-months follow-up vs. baseline in NSAIDs group. P< 0.001.

Abbreviations: VAS, visual analog scale; ROM, range of motion; SPADI, Shoulder Pain and Disability Index; MPQSF, McGill Pain Questionnaire Short Form; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 5 Summary of side effects.

Side effects	Duloxetine (N= 37), n (%)	NSAIDs (N= 37), n (%)	P-value
Patients with ≥ 1 side effect	6 (16.22)	4 (10.81)	0.496
Nausea	4 (10.81)	3 (8.11)	0.691
Decreased appetite	3 (8.11)	1 (2.70)	0.304
Dizziness	2 (5.41)	0	0.152
Somnolence	1 (2.70)	1 (2.70)	1
Constipation	1 (2.70)	0	0.314
Others	0	0	-

Notes: Data are presented as the number (percentage) of patients. Data were analyzed using chi square test and fisher's exact.

Abbreviation: NSAIDs, nonsteroidal anti-inflammatory drugs.

Figures

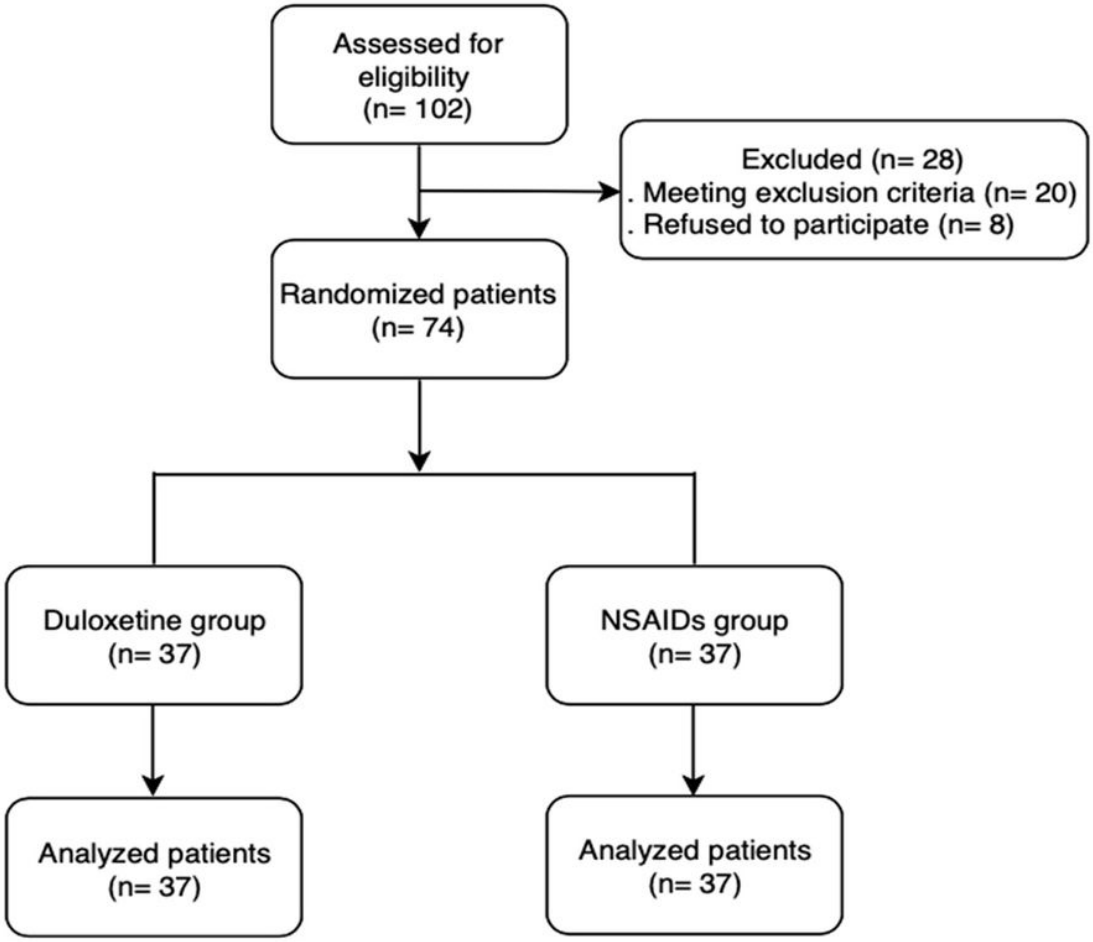

Figure 1

Flow diagram of the patients throughout the course of the study.

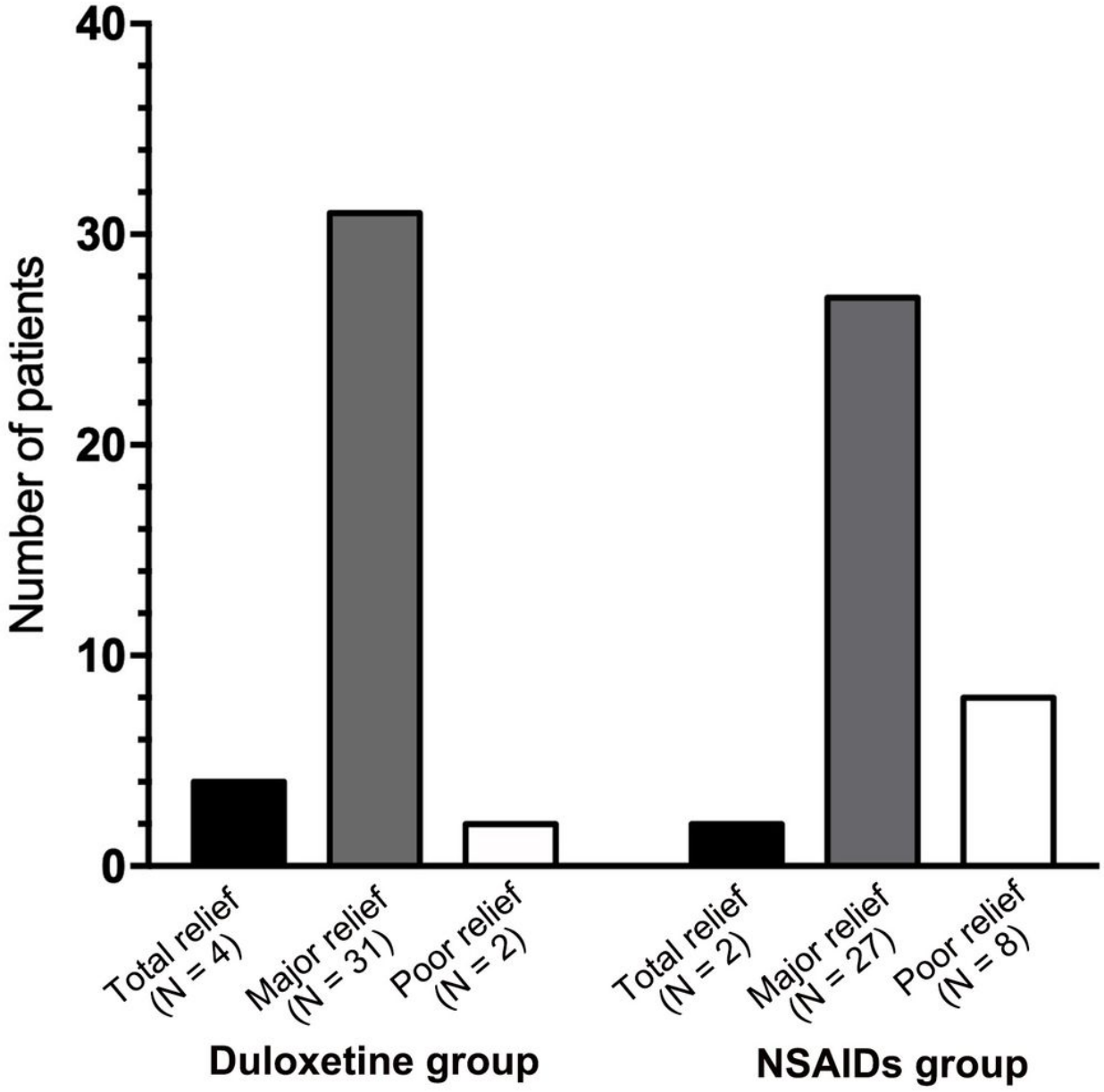

Figure 2

The number of patients reporting total (100%), major (≥ 50%), and poor (< 50%) shoulder pain relief compared with baseline in both groups, as measured by VAS scores, at the end of duloxetine and NSAIDs treatments.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.jpg
- Additionalfile2.docx

- Additionalfile3.xlsx