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Dexmedetomidine for chronic pain patients with anxiety and depression: a propensity score matching cohort study

Yiting Ren[1†], Peng Huang[1†] and Xiaohong Jin[1*]

Abstract

Background Chronic pain patients often experience moderate to severe anxiety and depressive symptoms. Growing evidence supporting dexmedetomidine as a potential treatment for mental health conditions, research on its application in chronic pain patients with comorbid anxiety and depression remains limited.

Methods Patients who received intravenous infusions of dexmedetomidine during their interventional pain management procedures from January to July 2024 were compared to those who underwent similar procedures without dexmedetomidine infusion during the same period, utilizing propensity score matching.

Results A total of 290 patients were included in the analysis from January to July 2024. Propensity score matching resulted in 92 matched pairs for further analysis. At the one-month follow-up, the perioperative application of dexmedetomidine was associated with a greater improvement in anxiety and depression disorders, as measured by the Generalized Anxiety Disorder 7-item scale, showing a reduction of -4.43 points (95% CI, -4.98 to -3.88) compared to -2.42 points (95% CI, -2.97 to -1.87) for the local analgesia group and the Patient Health Questionnaire-9 scores indicated a reduction of -6.19 points (95% CI, -6.84 to -5.55) for the dexmedetomidine group versus -3.92 points (95% CI, -4.56 to -3.28) for the local analgesia group. The use of dexmedetomidine was also associated with a greater improvement of pain(-3.32 points vsurs -2.62 points).

Conclusions Intraoperative dexmedetomidine significantly improves anxiety and depression in patients with chronic pain. Therefore, dexmedetomidine may serve as a promising adjunctive treatment for chronic pain patients, particularly those with comorbid anxiety and depression.

Clinical trial number Not applicable.

Keywords Dexmedetomidine, Chronic pain, Anxiety, Depression

Background

Chronic pain is a major public health issue, being a leading cause of disability worldwide and affecting millions [1]. Epidemiological studies estimate that the prevalence of chronic pain varies between 8% and 43% [1–5]. Chronic pain impacts individuals not only physically but also emotionally and psychologically [6, 7]. Studies indicate that most chronic pain patients also experience moderate to severe anxiety and depressive symptoms (~87%). Moreover, patients suffering from chronic

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pain-induced depression exhibit a poorer prognosis than those without depression and anxiety [7, 8]. Since anxiety and/or depression can negatively impact the body's pain processing mechanism, these patients are at greater risk of developing chronic pain and experiencing more intense pain due to increased pain sensitivity [9–11], thereby suggesting a bidirectional relationship between chronic pain symptoms and psychopathological conditions [12, 13]. In treating chronic pain with comorbid anxiety and depression, addressing pain alone could be insufficient. Instead, a holistic treatment targeting both conditions is crucial for improving outcomes and quality of life [14].

Dexmedetomidine (DEX) is a highly selective α2-adrenoreceptor (α2-AR) agonist commonly used as an analgesic and anxiolytic drug in perioperative care [15]. DEX functions by modulating the noradrenergic system that regulates neuroinflammation and oxidative stress [16]. Randomized clinical trial (RCT) studies have shown DEX administration in the early postpartum period significantly reduces the incidence of positive postpartum depression [17]. Sublingual film formulation of DEX has high efficacy in treating bipolar disorder (BPD)-associated acute agitation and has received U.S. Food and Drug Administration's approval for adult BPD stages I/II and schizophrenia, as well [18].

Despite growing evidence of DEX's potential in managing mental health conditions, research on its use in chronic pain patients with comorbid anxiety and depression remains limited. Therefore, this study aims to fill this gap by evaluating the clinical outcomes of chronic pain patients receiving DEX during their interventional procedures, focusing on its effects on pain relief and mental health improvement.

Methods

Study overview and clinical measures

This is a single-center retrospective study of patients who received DEX intravenous infusion (the DEX group) during their interventional pain management procedures from January through July 2024. The DEX cohort was compared with a control local analgesia group (the LA group) who underwent similar procedures without the DEX infusion during the same period. The study was approved by The First Affiliated Hospital of Soochow University Ethics Committee (No.2024-678), Written informed consent was obtained from all participants prior to the commencement of the study. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [19].

Enrolled patients were diagnosed with chronic pain, defined as pain persisting for more than three months, according to the International Classification of Diseases 11 th Revision (ICD-11) [20]. For this cohort, interventional pain management procedures included radiofrequency ablation, neuromodulation, endoscopic lumbar discectomy, and vertebral augmentation. Eligible patients presented mild to severe anxiety or depressive symptoms, as assessed either by the 7-item Generalized Anxiety Disorder scale (GAD-7) or the 9-item Patient Health Questionnaire (PHQ-9), with scores exceeding 5. Patients with incomplete clinical data or unaccomplished follow-up criteria were excluded from the analysis.

GAD-7 and PHQ-9 questionnaire used in our study has previously been published elsewhere. The PHQ-9 is a self-reported depression screening tool consisting of 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The total score is the sum of the individual item scores [21]. Similarly, the GAD-7 comprises 7 items and scores from 0 (not at all) to 3 (nearly every day), with the total score calculated by summing the responses. For both scales, a cutoff score of 5 indicates the presence of mild anxiety or depression [22].

The baseline characteristics included age, sex, symptom duration, educational background, primary diagnosis according to the ICD-11, use of anti-anxiety or antidepressive medications, the surgical method employed, and administration of perioperative DEX regimen. Also, another pain intensity measurement method called the numerical rating scale (NRS) - an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable', was employed to assess pain intensity over the past 24 h. All types of pain evaluations were conducted at the time of admission.

All patients were followed up one month after surgery, either in the outpatient clinic or by telephone, to assess their changes in anxiety, depression, and pain intensity levels.

DEX administration

The method of administration of DEX during perioperative procedures was extracted from the patient's medical records. All interventional surgeries at our center were performed under local anesthesia. DEX administration began 10 min before starting interventional procedures. The initial infusion consisted of a loading dose of 1 μg/kg over 10 min, followed by a continuous infusion of 0.5 μg/kg/h for another 30 to 60 min. For patients who did not receive DEX, only local anesthesia was employed.

Patient satisfaction evaluation

Patient satisfaction was assessed using a 0–10 scale, where 0 represented complete dissatisfaction and 10

represented complete satisfaction [23]. This scale was adapted from a previous study. Following their interventional pain management procedures, patients were asked to rate their overall satisfaction with the procedure. The satisfaction score was recorded immediately after the procedure, and participants were informed that their responses would be kept confidential to encourage honest reporting. The primary focus of the satisfaction assessment was to capture the combined impact of anxiety management, pain relief, and the overall procedural experience.

Statistical analysis

The sample size of the study was representative of patients who met the eligibility criteria based on their diagnoses and the presence of anxiety or depression. Continuous data are reported as means (standard deviation; SD or medians (interquartile range; IQR), depending on the distribution patterns of variables. Categorical data are presented as counts and percentages. Baseline characteristics comparisons between the groups were performed using the Student's t-test for normally distributed continuous variables or the Mann-Whitney U test for non-normally distributed continuous variables. For categorical variables, comparisons were made using chi-square (χ^2) tests or Fisher's exact tests, as appropriate.

To control potential confounding factors between the DEX and LA groups, the propensity score matching (PSM) method was applied. The propensity score was calculated using a logistic regression model (LRM) that included the aforementioned baseline characteristics. Patients in the DEX group were matched 1:1 with those in the LA group having similar propensity scores, using the nearest neighbor matching method with a caliper of 0.09. This matching procedure aimed to balance any covariates between the two groups and reduce the selection bias, thus ensuring a robust comparison of the effects of DEX on pain, anxiety, and depression.

We calculated the standardized mean difference (SMD) for each covariate to assess the balance of baseline characteristics between the two groups, with an SMD of less than 0.1 indicating an acceptable balance.

To assess the DEX efficacy in improving anxiety, depression, and pain, we conducted an analysis of covariance (ANCOVA) to compare changes in GAD-7, PHQ-9, or NRS scores between the two groups following PSM. Baseline scores of GAD-7, PHQ-9, and NRS were considered as covariates to adjust for potential baseline differences.

Two sensitivity analyses were conducted. First, subgroup analysis assessed between-group differences in GAD-7 and PHQ-9 score improvements among patients with both anxiety and depression. For patients who underwent different procedures and had different pain pathologies, the Welch's Two-Sample t-test was used to compare the outcome measures between the two groups. Second, ANCOVA was used in the unmatched cohort to compare score improvements, verifying result stability. DEX use was the primary independent variable, with covariates including age, sex, symptom duration, education, ICD-11 diagnosis, use of anti-anxiety or antidepressant medications, surgical method, baseline GAD-7 and PHQ-9 scores, and pain intensity.

The mediation analyses examining the alleviation of pain in the association between DEX and the improvement of GAD-7 and PHQ-9 scores were conducted using the R package'mediation'. These analyses aimed to estimate both the direct and indirect mediation effects of pain on the improvement of GAD-7 and PHQ-9 scores one month post-surgery. The analyses were performed using R-Studio software (version 2023.03.0), with a significance level set at $P < 0.05$.

Results

Demographic characteristics

During January - July 2024, a total of 686 patients underwent interventional surgeries for chronic pain symptoms at our center. Of these, 306 patients met the inclusion criteria; however, 16 patients were lost to follow-up, resulting in 290 patients for analysis. Among them, 106 patients (37 men and 69 women) received intravenous infusions of DEX (the DEX group), while 184 patients (64 men and 120 women) received only local analgesia (the LA group) during the interventional surgery (Fig. 1). Patients who received the DEX infusion doses were significantly older than those in the LA group [mean (SD), 62 (13) years vs. 58 (15) years; $P = 0.037$]. There were no differences between the two groups in baseline NRS [(mean (SD)5.93 (1.90) vs. 5.56 (2.04)], GAD-7 [(mean (SD)11.61 (5.11) vs. 11.73 (5.42)], or PHQ-9 [(mean (SD)15.30 (5.33) vs. 14.56 (5.86)], or symptom duration [(mean (SD)11.5 (5.0) months vs. 11.8 (5.5) months)]. The mean duration of the infusion was 49(17) minitus(mean (SD)).

PSM with a 1:1 ratio resulted in 92 matched pairs for further analysis. The imbalance in baseline characteristics was significantly reduced following PSM. The baseline characteristics of both the study and PSM cohorts are presented in Table 1. Following PSM, no significant differences were observed between the two groups.

Clinical outcomes of DEX

At the one-month follow-up, the perioperative application of DEX was associated with a greater improvement in anxiety disorders, as measured by the GAD-7, with a reduction of −4.43 points (95% CI, −4.98 to −3.88)

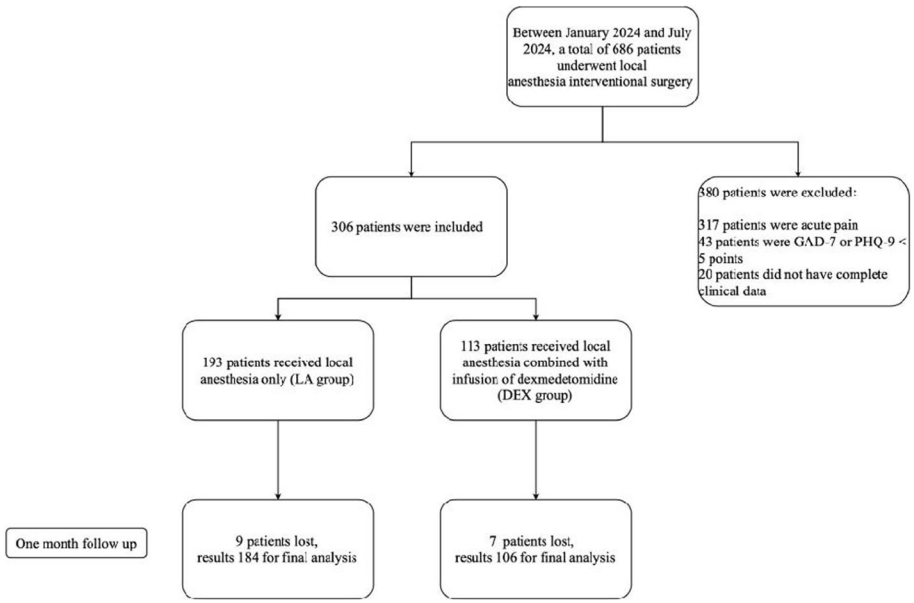

Fig. 1 Overview of analysis and study population

compared to −2.42 points (95% CI, −2.97 to −1.87) for the LA group. A significant between-group difference was observed in the mean change from baseline in PHQ-9 scores for depression. The DEX group exhibited a reduction of −6.19 points (95% CI, −6.84 to −5.55), while the LA group showed a decrease of −3.92 points (95% CI, −4.56 to −3.28). A similar effect was noted in the improvement of pain, with the DEX group showing a reduction of −3.32 points (95% CI, −3.58, −3.05) compared to −2.62 points (95% CI, −2.88, −2.36) for the LA group (Table 2 and Fig. 2).

Sensitivity outcomes

Among the 290 patients, 158 exhibited both anxiety and depression symptoms. The baseline characteristics are described in Table 3. The analysis of these patients revealed a significant between-group difference in the improvement of GAD-7 [−2.49 (−3.88, −1.10); $P < 0.001$], PHQ-9 [−2.27 (−4.00, −0.53); $P = 0.012$], and NRS [−0.67 (−1.23, −0.12); $P = 0.020$] (Table 4).

ANCOVA analysis for the unmatched cohort also demonstrated a significant difference in the improvement of GAD-7, PHQ-9, and NRS scores between the DEX and LA groups. This difference remained statistically significant even after adjusting for covariates (Table 5).

To further explore the relationship between pain and mood, we conducted a mediation analysis. The results indicated a significant direct and indirect effect of alleviation of pain on the association of DEX and improvement of GAD-7. The portion mediated by pain improvement for the association between DEX and GAD-7 was 18.2% (95% CI: 0.7, 56.7, $P < 0.001$). For PHQ-9, The portion mediated by pain improvement for the association between DEX and PHQ-9 one month after surgery was 32.3% (95% CI:. 4.8, 66.2, $P < 0.001$) (Table 6).

In the statistical analysis of patients with different procedures and diagnoses, it was found that patients who received radiofrequency procedures and were diagnosed with musculoskeletal pain showed the most significant improvement in anxiety and depression after receiving DEX infusion (Table 7 and Table 8).

Adverse events

Although there was no statistically significant difference in the incidence of adverse events between the DEX and LA groups, incidences of bradycardia (3.3% vs. 5.7%), hypotension (4.9% vs. 6.6%), nausea (4.9% vs. 7.5%), and dizziness (3.8% vs. 6.6%) were relatively higher in the DEX group. Conversely, hypertension was more common in the LA group (12.0% vs. 4.7%). No serious adverse events occurred in either group (Table 9).

Patient satisfaction

Patient satisfaction was significantly higher in the group that received dexmedetomidine infusions during their interventional pain management procedures compared to those who received only local analgesia. [mean (SD), 8.6(2.2) vs. 5.7 (1.9); $P < 0.001$].

Table 1 Baseline characteristics before and after matching

Variables		Before Matching				After Matching			
		Group				Group			
		LA group (*n*=184)	DEX group (*n*=106)	*P* value[f]	SMD[a]	LA group (*n*=92)	DEX group (*n*=92)	*P* value[f]	SMD[a]
Age, mean (SD)		58.42 (14.51)	61.95 (13.39)	0.037	0.264	60.49 (13.62)	61.50 (13.76)	0.617	0.075
NRS[b] score, mean (SD)		5.57 (2.04)	5.93 (1.89)	0.127	0.192	5.82 (2.08)	5.82 (1.84)	>0.999	0.000
PHQ-9[c], mean (SD)		10.08 (5.84)	10.32 (5.27)	0.721	0.045	9.78 (5.62)	9.88 (5.28)	0.903	0.019
GAD-7[d], mean (SD)		6.88 (5.53)	6.58 (5.02)	0.648	−0.058	6.53 (4.92)	6.27 (4.86)	0.718	−0.052
Pain duration, mean (SD)		41.36 (75.20)	40.60 (53.12)	0.920	−0.014	40.63 (72.03)	44.14 (55.00)	0.711	0.066
Sex (%)				0.983				0.641	
	Female	120 (65.2)	69 (65.1)		−0.003	59 (64.1)	62 (67.4)		0.068
	Male	64 (34.8)	37 (34.9)		0.003	33 (35.9)	30 (32.6)		−0.068
Education background, n(%)				0.505				0.880	
	<High school	82 (44.6)	51 (48.1)		0.071	45 (48.9)	48 (52.2)		0.065
	>High school	34 (18.5)	14 (13.2)		−0.156	15 (16.3)	13 (14.1)		−0.064
	High school	68 (37.0)	41 (38.7)		0.035	32 (34.8)	31 (33.7)		−0.022
Use of antidepression, n(%)				0.633				>0.999	
	No	155 (84.2)	87 (82.1)		−0.056	75 (81.5)	75 (81.5)		0.000
	Yes	29 (15.8)	19 (17.9)		0.056	17 (18.5)	17 (18.5)		0.000
Diagnosis according to ICD-11[e], n(%)				<0.001				>0.999	
	Facial head pain	9 (4.9)	2 (1.9)		−0.221	3 (3.3)	2 (2.2)		−0.080
	Cancer pain	3 (1.6)	15 (14.2)		0.359	3 (3.3)	3 (3.3)		0.000
	Neuropathic pain	48 (26.1)	27 (25.5)		−0.014	25 (27.2)	26 (28.3)		0.025
	Musculoskeletal pain	124 (67.4)	62 (58.5)		−0.181	61 (66.3)	61 (66.3)		0.000
Interventional pain management, n(%)				<0.001				0.892	

Table 1 (continued)

Variables		Before Matching				After Matching			
		Group				Group			
		LA group (*n*=184)	DEX group (*n*=106)	*P* value[f]	SMD[a]	LA group (*n*=92)	DEX group (*n*=92)	*P* value[f]	SMD[a]
	Vertebral augmentation	6 (3.3)	7 (6.6)		0.135	5 (5.4)	5 (5.4)		0.000
	Endoscopy of the spine	3 (1.6)	6 (5.7)		0.174	3 (3.3)	5 (5.4)		0.094
	Radiofrequency	104 (56.5)	75 (70.8)		0.313	74 (80.4)	71 (77.2)		−0.072
	Neuromodulation	71 (38.6)	18 (17.0)		−0.575	10 (10.9)	11 (12.0)		0.029

[a] SMD, Standardized Mean Difference

[b] NRS, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

[c] PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression.

[d] GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety.

[e] ICD-11,International Classification Diseases 11 th Revision

[f] t Test for continuous variables, χ2 test for categorical variables.

Table 2 Dexmedetomidine and clinical outcomes in the matched cohort

Outcomes	Baseline Mean (SD)	One month after surgery Mean (SD)	Mean Change from Baseline Mean (95% CI)	Mean Difference in Change, Mean (95% CI)	*P* value[f]
GAD-7[a]					
DEX[d] group	6.3 (4.86)	2.0 (2.37)	−4.39 (−4.91, −3.87)	−1.98 (−2.72, −1.25)	< 0.001
LA[e] group	6.5 (4.92)	4.1 (4.03)	−2.40 (−2.93, −1.88)		
PHQ-9[b]					
DEX group	9.9 (5.28)	3.8 (3.34)	−6.10 (−6.72, −5.48)	−2.17 (−3.04, −1.30)	< 0.001
LA group	9.8 (5.62)	5.9 (4.81)	−3.93 (−4.55, −3.30)		
NRS[c] scores					
DEX group	5.8 (1.84)	2.5 (1.22)	−3.32 (−3.58, −3.05)	−0.70 (−1.06, −0.33)	< 0.001
LA group	5.8 (2.08)	3.2 (1.48)	−2.62 (−2.88, −2.36)		

[a] GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety

[b] PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression

[c] NRS score, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

[d] DEX, Dexmedetomidine

[e] LA, Local anesthesia

[f] Analysis of covariance, baseline values were included as covariates

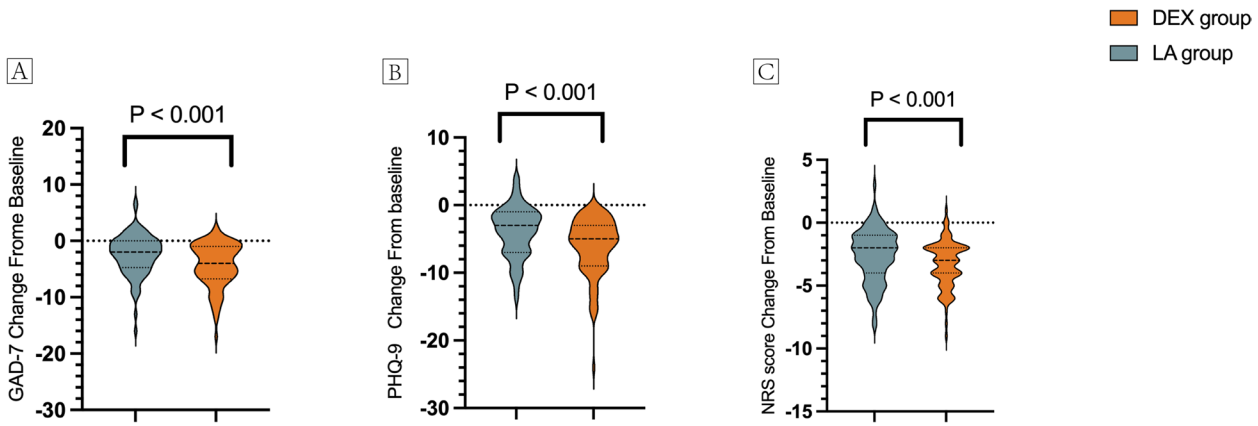

Fig. 2 Comparison of clinical outcomes between the DEX and LA groups after PSM. A: Difference in the improvement of GAD-7 scores from baseline [−4.43 (95% CI, −4.98 to −3.88) vs. −2.42 (95% CI, −2.97 to −1.87); $P < 0.001$]. B: Difference in the improvement of PHQ-9 scores from baseline [(−6.19 (95% CI, −6.84 to −5.55) vs. −3.92 (95% CI, −4.56 to −3.28); $P < 0.001$]. C: Difference in the improvement of NRS scores from baseline [−3.32 (95% CI, −3.58, −3.05) vs. −2.62 (95% CI, −2.88, −2.36)]. PSM, Propensity score matching. DEX, Dexmedetomidine. LA, Local anesthesia. GAD-7, 7-item Generalized Anxiety Disorder questionnaire, PHQ-9, 9-item Patient Health Questionnaire. NRS, numerical rating scale. CI, confidence interval

Discussion

To our knowledge, this is the first cohort study to investigate the potential application of DEX in managing chronic pain in patients with comorbid anxiety and depression disorders. The results suggest that intraoperative DEX administration is associated with greater improvements in anxiety and depression, as measured by GAD-7 and PHQ-9 scores through PSM. Additionally, the intraoperative DEX application correlated with a significant reduction in pain, with a mean difference of 0.59 (95% CI [0.15, 1.03], $P = 0.010$), although this difference is minimal and does not reach a clinically meaningful threshold.

Patients who received dexmedetomidine infusions during their interventional pain management procedures reported higher levels of satisfaction compared to those who received only local analgesia (8.6 Vs. 5.7). The mean satisfaction score for the dexmedetomidine group

Table 3 Baseline characteristics of patients exhibited both anxiety and depression

		Before Matching				After Matching			
		Group				Group			
		LA group (n = 100)	DEX group (n = 57)	*P* value	SMD[a]	LA group (n = 40)	DEX group (n = 40)	*P* value	SMD
Age, mean (SD)		57.23 (15.80)	62.86 (13.02)	0.017	0.432	61.52 (13.81)	61.60 (13.79)	0.981	0.006
NRS[b] score, mean (SD)		6.06 (2.01)	6.21 (1.89)	0.640	0.080	6.15 (2.13)	6.15 (1.85)	> 0.999	0.000
PHQ-9[c], mean (SD)		13.29 (5.81)	12.53 (5.50)	0.414	−0.139	13.62 (6.45)	13.03 (5.71)	0.661	−0.109
GAD-7[d], mean (SD)		10.46 (4.81)	9.81 (4.24)	0.379	−0.154	10.20 (5.05)	9.97 (4.43)	0.833	−0.053
Pain duration, mean (SD)		35.71 (60.62)	41.19 (55.61)	0.566	0.099	45.33 (79.52)	48.42 (61.87)	0.846	0.056
Sex (%)				0.084				0.626	
	Female	60 (60.0)	42 (73.7)		0.311	27 (67.5)	29 (72.5)		0.114
	Male	40 (40.0)	15 (26.3)		−0.311	13 (32.5)	11 (27.5)		−0.114
Education background, n(%)				0.259				0.942	
	< High school	46 (46.0)	30 (52.6)		0.133	22 (55.0)	22 (55.0)		0.000
	> High school	23 (23.0)	7 (12.3)		−0.327	6 (15.0)	7 (17.5)		0.076
	High school	31 (31.0)	20 (35.1)	0.907	0.086	12 (30.0)	11 (27.5)		−0.052
Use of antidepression, n(%)								0.785	
	No	78 (78.0)	44 (77.2)		−0.019	32 (80.0)	31 (77.5)		−0.060
	Yes	22 (22.0)	13 (22.8)		0.019	8 (20.0)	9 (22.5)		0.060
Diagnosis according to ICD-11[e],n(%)				< 0.001				> 0.999	
	Facial head pain	8 (8.0)	0 (0.0)		−0.369	0 (0.0)	0 (0.0)		0.000
	Cancer pain	3 (3.0)	12 (21.1)		0.443	3 (7.5)	2 (5.0)		−0.061
	Neuropathic pain	33 (33.0)	14 (24.6)		−0.196	14 (35.0)	14 (35.0)		0.000
	Musculoskeletal pain	56 (56.0)	31 (54.4)		−0.032	23 (57.5)	24 (60.0)		0.050
interventional pain management, n(%)				0.026				> 0.999	
	Vertebral augmentation	6 (6.0)	5 (8.8)		0.098	4 (10.0)	3 (7.5)		−0.088
	Endoscopy of the spine	2 (2.0)	4 (7.0)		0.196	2 (5.0)	3 (7.5)		0.098
	Radiofrequency	52 (52.0)	37 (64.9)		0.271	29 (72.5)	28 (70.0)		−0.052
	Neuromodulation	40 (40.0)	11 (19.3)		−0.525	5 (12.5)	6 (15.0)		0.063

[a] SMD, Standardized Mean Difference

[b] NRS, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

[c] PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression

[d] GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety

[e] ICD-11,International Classification Diseases 11 th Revision

[f] t Test for continuous variables, χ2 test for categorical variables

Table 4 Clinical outcomes in patients exhibited both anxiety and depression after matched

Outcomes	Baseline Mean (SD)	One month after surgery Mean (SD)	Mean Change from Baseline Mean (95% CI)	Mean Difference in Change from baseline, Mean (95% CI)	*P* [f] value
GAD-7 [a]				−2.49 (−3.88, −1.10)	< 0.001
DEX [d] group	10.0 (4.43)	3.0 (2.75)	−7.08 (−8.08, −6.09)		
LA [e] group	10.2 (5.05)	5.5 (4.73)	−4.59 (−5.59, −3.59)		
PHQ-9[b]				−2.27 (−4.00, −0.53)	0.012
DEX group	13.0 (5.71)	5.1 (4.14)	−8.02 (−9.27, −6.78)		
LA group	13.6 (6.45)	7.8 (6.34)	−5.75 (−7.00, −4.51)		
NRS [c] score				−0.67 (−1.23, −0.12)	0.020
DEX group	6.2 (1.85)	2.6 (1.08)	−3.58 (−3.97, −3.18)		
LA group	6.2 (2.13)	3.2 (1.64)	−2.90 (−3.30, −2.50)		

[a] GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety

[b] PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression

[c] NRS score, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

[d] DEX, Dexmedetomidine

[e] LA, Local anesthesia

[f] Analysis of covariance, baseline value were included as covariates

Table 5 ANOVA Analysis of All the Included Patients Before Matched

Outcomes	Baseline Mean (SD)	One month after surgery Mean (SD)	Mean Change from Baseline Mean (95% CI)	Mean Difference in Change from baseline Mean (95% CI)	*P* [f] value
GAD-7 [a]				−1.76 (−2.42, −1.10)	< 0.001
DEX [d] group	6.6 (5.02	2.4 (3.04)	−4.85 (−5.68, −4.02)		
LA [e] group	6.9 (5.53)	4.0 (3.95)	−3.09 (−3.95, −2.24)		
PHQ-9 [b]				−2.03 (−2.81, −1.25)	< 0.001
DEX group	10.3 (5.27)	4.2 (3.95)	−6.38 (−7.36, −5.39)		
LA group	10.1 (5.84)	6.0 (4.80)	−4.35 (−5.36, −3.34)		
NRS [c] scores				−0.67 (−0.99, −0.35)	< 0.001
DEX group	5.9 (1.89)	2.5 (1.23)	−3.68 (−4.08, −3.28)		
LA group	5.6 (2.04)	3.1 (1.45)	−3.01 (−3.42, −2.60)		

[a] GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety

[b] PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression

[c] NRS score, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

[d] DEX, Dexmedetomidine

[e] LA, Local anesthesia

[f] Analysis of covariance, baseline values, age, sex, symptom duration, educational background, diagnosis according to ICD-11, use of anti-anxiety or anti-depression medications, surgical method employed, baseline GAD-7 and PHQ-9 scores, and pain intensity were included as covariates

ANOVA, analysis of covariance

CI, confidence interval

was notably higher, suggesting that the combination of improved anxiety management, pain relief, and overall procedural experience contributed to a more positive overall experience for these patients.

Consistent with our findings, previous trials have explored the efficacy of short-term DEX infusion in reducing depression. Zhou et al. reported that DEX effectively reduced postpartum depression symptoms, similar to our findings in chronic pain patients [17]. A meta-analysis focusing on the use of perioperative intravenous DEX for postpartum depression demonstrated improvements in both analgesia and sleep quality [24]. Additionally, a study comparing melatonin, DEX, and gabapentin for postoperative pain and anxiety following

Table 6 Adverse Events

	DEX [a] group	LA [b] group	*P* [c] value
Adverse Event			0.085
Bradycardia	6 (5.7%)	6 (3.3%)	
Hypotension	7 (6.6%	9 (4.9%)	
Nausea	8 (7.5%)	9 (4.9%)	
Vomiting	1 (0.9%)	10 (5.4%)	
Dizziness	7 (6.6%	7 (3.8%)	
Hypertension	5 (4.7%)	22 (12.0%)	
Adverse Event requiring treatment			0.005
Bradycardia requiring treatment	3 (2.8%)	0 (0.0%)	
Hypotension requiring treatment	3 (2.8%)	0 (0.0%)	
Hypertension requiring treatment	2 (1.9%)	7 (3.8%)	

[a] DEX, Dexmedetomidine

[b] LA, Local anesthesia

[c] Fisher's exact test

laminectomy found that DEX alleviated both pain and anxiety [25].

Chronic pain is a complex condition often accompanied by significant psychological distress, with anxiety and depression being common comorbidities [26]. The bidirectional relationship between pain and psychological disorders creates a vicious cycle where each condition exacerbates the other, complicating treatment [27]. In this retrospective cohort study, we evaluated DEX as an adjunct in managing chronic pain patients with anxiety and depression [28]. Our findings suggest that DEX may serve as a dual-purpose therapy, addressing both the physical and emotional aspects of chronic pain.

Interestingly, while pain relief was greater in the DEX group, we found that the improvement in anxiety and depression scores was more pronounced, indicating that the effects of DEX on mood may not be entirely attributable to pain relief. This suggests that DEX has an independent effect on mood regulation, likely mediated through its action on the α2-adrenoreceptor, which modulates the central nervous system's pain and emotional processing pathways.

Our mediation analysis showed that approximately18%—30% of the reduction in anxiety and depression could be attributed to the pain reduction, while the remainings seemed to be due to DEX's direct effects on mood regulation. This highlights the potential of DEX to address psychological distress independent of its analgesic effects.

Sub-group analysis revealed that patients who received radiofrequency procedures and were diagnosed with musculoskeletal pain experienced the most significant improvement in anxiety and depression symptoms following DEX infusion. Radiofrequency ablation (RFA) is a widely used interventional procedure for managing chronic pain, particularly in conditions such as osteoarthritis or facet joint pain. Previous studies have shown that RFA not only provides effective pain relief but also improves the overall quality of life of patients by reducing the psychological burden of chronic pain [29]. In our study, the combination of DEX infusion with radiofrequency procedures may have enhanced this effect, contributing to the observed reduction in both anxiety and depression.

Musculoskeletal pain, especially when chronic, is often accompanied by heightened levels of anxiety and depression, which can exacerbate the perception of pain and impair recovery [30]. The anxiolytic and sedative effects of DEX, as seen in this study, may play a crucial role in addressing these comorbid psychological symptoms. By targeting both pain and psychological distress, DEX may provide a more holistic approach to managing chronic musculoskeletal conditions.

DEX alleviates both chronic pain and psychological symptoms primarily through its central action on the brainstem and spinal cord [31]. By reducing norepinephrine release, DEX decreases sympathetic nervous system activity, which contributes to the amplification of both pain and anxiety, this effect may continue beyond the immediate postoperative period, leading to a prolonged reduction in anxiety and depressive symptoms [32]. Furthermore, its anxiolytic and sedative effects are thought to be mediated by its action on the locus coeruleus, a brainstem region involved in regulating arousal, anxiety, and pain perception [33]. In chronic pain, this central modulation helps restore balance to the overactive stress and pain pathways common in patients with comorbid anxiety and depression.

Table 7 Clinical outcomes between patients with different diagnoses

	Facial head pain, *N* = 5			Cancer pain, *N* = 6			Neuropathic pain, *N* = 51			Musculoskeletal pain, *N* = 122		
	LA GROUP *N* = 3	DEX GROUP *N* = 2	*p*-value2	LA GROUP *N* = 3	DEX GROUP *N* = 3	*p*-value	LA GROUP *N* = 251	DEX GROUP *N* = 26	*p*-value	LA GROUP *N* = 61	DEX GROUP *N* = 61	*p*-value
GAD-7 Change from baseline Mean (SD)	−7.67 ± 5.03	−2.00 ± 0.00	0.190	−5.33 ± 0.58	−1.33 ± 2.31	0.088	−2.6 ± 3.8	−4.2 ± 3.6	0.145	−2.0 ± 3.4	−4.6 ± 4.0	<0.001
PHQ-9 Change from baseline Mean (SD)	−8.67 ± 1.53	−10.00 ± 7.07	0.835	−7.00 ± 3.00	−2.67 ± 1.15	0.116	−4.0 ± 3.0	−6.3 ± 3.6	0.012	−3.5 ± 3.9	−6.1 ± 4.5	<0.001
NRS score Change from baseline Mean (SD)	−6.00 ± 2.00	−7.00 ± 1.41	0.561	−4.00 ± 1.73	−3.00 ± 3.00	0.649	−2.36 ± 2.00	−3.81 ± 2.06	0.014	−2.49 ± 1.99	−3.00 ± 1.53	0.116

GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety

PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression

NRS score, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

DEX, Dexmedetomidine

LA, Local anesthesia

Table 8 Clinical outcomes between patients who received different procedures

	Vertebral augmentation, *N* = 10			Endoscopy of the spine, *N*=8			Radiofrequency, *N* = 145			Neuromodulation, *N* = 21		
	LA GROUP *N* = 5	DEX GROUP *N* = 5	*p*-value	LA GROUP *N* = 3	DEX GROUP, *N* = 5	*p*-value	LA GROUP *N* = 74	DEX GROUP, *N* = 71	*p*-value	LA GROUP *N* = 10	DEX GROUP *N* = 11	*p*-value
GAD-7 Change from baseline Mean (SD)	−2.20 ± 4.82	−2.20 ± 2.86	>0.999	−5.00 ± 3.61	−6.60 ± 3.21	0.562	−2.5 ± 3.7	−4.3 ± 3.9	0.004	−1.8 ± 2.5	−4.2 ± 4.4	0.139
PHQ-9 Change from baseline Mean (SD)	−4.00 ± 5.34	−3.00 ± 0.71	0.699	−7.67 ± 1.15	−6.80 ± 3.96	0.666	−3.8 ± 3.7	−6.2 ± 4.4	<0.001	−3.8 ± 3.2	−6.8 ± 3.9	0.065
NRS score Change from baseline Mean (SD)	−1.80 ± 1.10	−1.80 ± 0.84	>0.999	−4.00 ± 2.65	−4.00 ± 1.22	>0.999	−2.58 ± 2.16	−3.15 ± 1.80	0.084	−2.90 ± 1.52	−4.73 ± 1.79	0.021

GAD-7, 7-item Generalized Anxiety Disorder questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 7 items are summed to yield a total score. scores exceeding 5 points indicates mild anxiety

PHQ-9, 9-item Patient Health Questionnaire, a self-report depression screening tool comprising 9 items, each scored on a scale from 0 (not at all) to 3 (nearly every day). The scores for these 9 items are summed to yield a total score. scores exceeding 5 points indicates mild depression

NRS score, numerical rating scale, which is an 11-point scale where'0'indicates'no pain'and'10'signifies'the most severe pain imaginable'

DEX, Dexmedetomidine

LA, Local anesthesia

Table 9 Adverse events

	DEX [a] group	LA [b] group	*P* [c] value
Adverse Event			0.085
Bradycardia	6 (5.7%)	6 (3.3%)	
Hypotension	7 (6.6%	9 (4.9%)	
Nausea	8 (7.5%)	9 (4.9%)	
Vomiting	1 (0.9%)	10 (5.4%)	
Dizziness	7 (6.6%	7 (3.8%)	
Hypertension	5 (4.7%)	22 (12.0%)	
Adverse Event requiring treatment			0.005
Bradycardia requiring treatment	3 (2.8%)	0 (0.0%)	
Hypotension requiring treatment	3 (2.8%)	0 (0.0%)	
Hypertension requiring treatment	2 (1.9%)	7 (3.8%)	

[a] DEX, Dexmedetomidine

[b] LA, Local anesthesia

[c] Fisher's exact test

Although the precise mechanisms behind the sustained effects of a single DEX infusion require further investigation, we hypothesize that its impact on the autonomic nervous system, pain pathways, and stress regulation could explain the observed lasting improvement in anxiety and depression.

The findings from our study have significant clinical implications. Chronic pain, especially when accompanied by anxiety and depression, presents a major challenge in both primary care and pain management settings [34–36]. Psychological comorbidities complicate the diagnosis and treatment of chronic pain, often resulting in poor therapy outcomes [37]. Our study suggests that DEX could be a valuable adjunct in managing chronic pain patients with co-occurring anxiety and depression. Given its effectiveness in improving multiple aspects of patient well-being, DEX may be considered as part of a comprehensive treatment plan addressing both the physical and psychological components of chronic pain.

From a clinical perspective, the ability to manage both chronic pain and comorbid psychiatric conditions with a single agent is highly valuable. Traditional approaches often involve a combination of analgesics, antidepressants, and anxiolytics, which can lead to side effects and polypharmacy [38].

Limitations

First, as a retrospective cohort study, there is an inherent risk of bias, particularly selection bias. The study focused on a specific patient population who received perioperative DEX regimens during interventional surgery, limiting the generalizability of the results to all chronic pain patients with comorbid psychiatric disorders. The lack of a randomized control group also limits the ability to draw definitive conclusions about causality.

Second, the one-month follow-up period is relatively short. While significant reductions in anxiety and depression scores were observed, it is unclear whether these benefits are sustained long-term. Given that chronic pain patients with comorbid psychological disorders often experience symptom fluctuations, further investigation is needed to assess the long-term efficacy of DEX in this population.

Thirdly, the lack of direct comparison with other commonly used anxiolytics or analgesics, which would help determine whether the observed improvements in anxiety, depression were specifically due to the anti-inflammatory properties of dexmedetomidine or the anxiolytic and analgesic properties of dexmedetomidine. Future research comparing dexmedetomidine with other pharmacologic interventions, such as alternative anxiolytics or analgesics, is needed to determine the unique contribution of dexmedetomidine and to better understand the mechanisms driving its effects on mental health.

Fourth, The study was conducted at a single center and involved a specific patient cohort (chronic pain with comorbid anxiety or depression), so the results may not be generalizable to all chronic pain patients, especially those without such comorbidities.

Future directions

The promising results of our study warrant further exploration of DEX efficacy in treating chronic pain patients with anxiety and depression. Future studies should include RCTs with larger sample sizes to confirm the DEX efficacy in reducing both pain and psychological distress. Additionally, studies with longer follow-up periods are needed to determine whether the benefits of DEX are sustained over time.

Exploring the neurobiological mechanisms underlying DEX's effects on pain and mood disorders would also be valuable. Research into how DEX modulates central pain processing pathways and affects brain regions involved in anxiety and depression could provide insights into its dual action and help optimize its use in chronic pain management.

Finally, studies examining the combination of DEX with other analgesics or antidepressants may help identify the most effective multimodal approach for managing patients with complex chronic pain and psychiatric comorbidities.

Conclusion

In conclusion, our study suggests that intraoperative DEX significantly improves anxiety and depression in patients with chronic pain. However, this treatment appears to be particularly beneficial for patients with comorbid anxiety or depression. DEX may serve as a promising adjunctive treatment for chronic pain patients, especially those with comorbid anxiety and depression. However, further prospective studies are needed to confirm these findings and explore the long-term effects and optimal dosing strategies for various patient populations.

Abbreviations

BPD	Bipolar disorder
DEX	Anorexia
GAD-7	7-item Generalized Anxiety Disorder scale
PHQ-9	9-item Patient Health Questionnaire

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Authors' contributions

Yiting Ren and Peng Huang wrote the main manuscript text and prepared figures. Xiaohong Jin reviewed the overall content of the articles. All authors reviewed the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request. Due to privacy and ethical restrictions, individual participant data cannot be made publicly available. However, aggregated data and summary statistics used in the analysis are available and can be shared with qualified researchers upon request.

Declarations

Ethics approval and consent to participate

The study was approved by The First Affiliated Hospital of Soochow University Ethics Committee(No.2024-678), and Written informed consent was obtained from all participants prior to the commence of the study. The study was conducted in accordance with the Declara- tion of Helsinki and its subsequent amendments.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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