

# Management of post-extubation anxiety in the intensive care unit

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## ABSTRACT

*Post-extubation anxiety causes significant distress in intensive care unit patients. This review provides treatment recommendations for managing anxiety during weaning and extubation from mechanical ventilation. Factors predisposing to anxiety include cerebral vascular disease, endocrine disorders, cardiopulmonary decompensation, disrupted sleep-wake cycles, and the stressful ICU environment. This review analyzed 21 articles sourced from Google Scholar and PubMed, focusing on case reports, case series, systematic reviews, and meta-analyses. These studies reported that dexmedetomidine effectively reduces extubation time and ICU length of stay through its anxiolytic properties. Antipsychotics, like quetiapine, showed potential in managing anxiety during ventilator weaning, but high-dose haloperidol posed risks. Benzodiazepines were linked to paradoxical agitation and respiratory suppression. Non-pharmacological treatments, such as aromatherapy, music therapy, and massage therapy, appeared to reduce anxiety and improve sleep quality. Caregiver approaches, including parental presence and psychological training, also reduced anxiety. In conclusion, non-pharmacological approaches should be prioritized, and pharmacological treatments considered when necessary. More research is essential to identify optimal treatments for post-extubation anxiety with minimal patient risk and effective symptom control.*

**Keywords:** Anxiety, ICU patients, critically ill patients, post-extubation

## INTRODUCTION

Post-extubation anxiety causes clinically significant distress in both intensive care unit (ICU) patients and family caregivers. Psychiatry is often consulted for recommendations in assisting the pulmonary-critical care team in the management of anxiety in patients who are mechanically ventilated, especially during the weaning process. This review provides treatment recommendations for managing anxiety during this process and will discuss the pathophysiology of anxiety in the ICU and evidence-based treatments currently available.

Potential factors that predispose patients to anxiety include cerebral vascular disease, endocrine disorders, cardiopulmonary decompensation, reduced brain and tissue perfusion, multiple medications, and disruption of sleep-wake cycles; the tense and stressful ICU environment also puts patients at risk. Panic attacks can be precipitated by stress-induced adrenergic hyperactivity, delirium that is marked by paranoid delusions, and visual or auditory hallucinations, which can be caused by dysregulated dopamine synthesis. It is important to recognize the underlying cause of anxiety in the ICU for effective treatment.<sup>1</sup> Study results have long indicated that the patients and their family members may have psychological symptoms, such as anxiety, depression, fear, guilt, helplessness, sadness, exhaustion, uncertainty, agitation, and even PTSD pre- and post-ICU admission.<sup>2,3,4</sup> These feelings include not only the fear of death but also concerns about potential disability in the future. These unhealthy conditions may lead to

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increased irritability, hypertension, tachycardia, cardiac ischemia, and psychological disruption in the patients.<sup>5</sup> Mental health is a key component of health-related quality of life (HRQoL) post-ICU admission, and HRQoL is lower in the survivors of critical illness than in the general population.<sup>6</sup>

Anxiety is a state characterized by apprehension, agitation, increased motor tension, autonomic arousal, and fear.<sup>7</sup> Patients receiving prolonged periods of mechanical ventilation report moderate to severe levels of anxiety despite receiving sedative and analgesic medications. Anxiety management is, therefore, a major treatment concern that should be considered as important as other components of disease management. Although there are suggested pathways to treat anxiety in outpatients, treatment guidelines for patients developing these conditions due to critical illness treated in ICUs are limited. Current studies support the fact that providing timely interventions that also meet the needs of family members are critical in reducing their anxiety. Despite this, studies in the literature on brief interventions that may treat stress and anxiety in patients treated for a critical illness are scarce. This review examines the utility of the various anxiety management techniques in patients treated in the ICU.

## **METHODS**

A systematic review of publications was undertaken by two independent researchers using Google Scholar and PubMed. The focus was restricted to case reports, case series systematic reviews, and meta-analyses. The articles were searched using the keywords "Anxiety," "ICU patients," "critically ill patients," and "post-extubation." The articles with supporting words like "PTSD," "dementia," "delirium," and "depression" were also included. The search was supplemented by reviewing all references of relevant articles and conducting thorough abstract reviews. The final selection included 21 articles; 2 dealt with managing anxiety in the family caregivers of ICU patients, 7 described anxiety and its management in ICU patients, 4 studied the effect of music therapy on anxiety management, 3 dealt with the use of antipsychotics. The use of dexmedetomidine, benzodiazepines, massage therapy, hypnosis and

virtual reality, and aromatherapy was described in 1 article each. Article exclusion criteria included: 1) management of anxiety in a community setting; 2) articles not published in English; 3) articles that required institutional access; 4) articles published before 1980.

## **DISCUSSION**

Anxiety is one of the most common and most difficult psychiatric symptoms to manage in patients in the ICU. Although delirium receives significant attention, inadequate anxiety management can negatively impact the mental, psychological, psychosocial, and physiological health of critically ill patients. Hence, it is critical to understand the treatment options available for treating anxiety in the ICU setting. The evidence supporting certain pharmacological and non-pharmacological treatment options for this purpose is summarized in the following paragraphs and in Table 1.

### **DEXMEDETOMIDINE**

One study described the effectiveness of dexmedetomidine in decreasing time to extubation by indirectly reducing anxiety.<sup>8</sup> Dexmedetomidine reduced time-to-extubation and ICU length of stay in difficult-to-wean patients. This drug is a selective alpha-2 receptor agonist, which produces light sedation and light analgesia with opioid-sparing effects and blunts stress response through its sympatholytic properties. It also blunts the usual withdrawal from sedatives and opiates; it reduces ventilator asynchrony and provides a faster and safer extubation.

### **ANTIPSYCHOTICS**

Loxapine has not produced positive clinical outcomes in managing anxiety in critically ill patients.<sup>9</sup> Although there are reports of quetiapine successfully treating delirium in ICU patients, there is not enough literature specifically discussing the use of quetiapine in reducing anxiety in the ICU patients while weaning ventilation. A case study by Messina et al. reported that quetiapine was effective in managing anxiety during ventilator weaning in ICU patients.<sup>10</sup> Therefore, this

**Table 1. Summary of Studies**

Authors and Publication Year	Study Type	Study Participants	Results/Conclusions
Crippen et al, <sup>1</sup> 1995	Review article	Not applicable	Stress-induced noradrenergic hyperactivity can precipitate panic attacks and dopaminergic hyperactivity can lead to delirium.
Chiang et al, <sup>2</sup> 2016	Pragmatic quasi-experimental study	45 participants (treatment group: 24; control group: 21)	The practicality of Brief Cognitive Behavioral Psycho Education Program makes it a requirement to manage the stress and anxiety of main family caregivers
Hakak et al, <sup>3</sup> 2022	Cross-sectional study	68 patients	Patients admitted to ICU showed symptoms of anxiety.
McKinley et al, <sup>4</sup> 2008	Original research	100 patients	The Faces Anxiety Scale has the potential to be a useful instrument for the assessment of state anxiety by clinicians and for research into the reduction of anxiety in this vulnerable population.
Szokol et al, <sup>5</sup> 2001	Review article	Not applicable	The use of suitable protocols for the proper titration of sedation of mechanically ventilated patients and monitoring of the level of sedation in ventilated patients may decrease the amount of time that patients are ventilated and may alleviate some of the anxiety of recall of uncomfortable events.
Hatch et al, <sup>6</sup> 2020	Multi-center prospective cohort sub-study	21,633 ICU patients	More than half of those who responded to a postal questionnaire following treatment in the ICU in the UK reported significant symptoms of anxiety, depression, or PTSD.
Chlan et al, <sup>7</sup> 2011	Randomized controlled trial	57 mechanically ventilated patients	Visual Assessment Scale-Anxiety declined slowly over time, $-.53$ points per day ( $p = .09$ )
Dupuis et al, <sup>8</sup> 2019	Systematic review	10,860 studies	Low-quality evidence suggests the use of dexmedetomidine in patients deemed difficult to wean due to agitation, delirium, or anxiety.
Gaudry et al, <sup>9</sup> 2017	Randomized control trial	102 patients	Prematurely stopped the trial. Loxapine did not significantly shorten weaning from MV. However, loxapine reduced the need for resuming sedation.
Messina et al, <sup>10</sup> 2023	Case report	Not applicable	Administration of low-dose quetiapine led to eventual independence from mechanical ventilation and subsequent decannulation, by effectively managing the anxiety.
Rosenthal et al, <sup>11</sup> 2007	Case report	Not applicable	A second-generation anxiolytic was successfully used to facilitate weaning in a very anxious patient.
Reade et al, <sup>12</sup> 2009	Randomized trial	Twenty patients	Dexmedetomidine is a potential therapy for ICU-related delirious patients.
Kok et al, <sup>13</sup> 2018	Systematic review	Not applicable	Benzodiazepine use in the ICU is associated with delirium, symptoms of posttraumatic stress disorder, anxiety, depression, and cognitive dysfunction.

**Table 1. Summary of Studies (Continued)**

Authors and Publication Year	Study Type	Study Participants	Results/Conclusions
Gong et al, <sup>14</sup> 2020	Meta-analysis of randomized controlled trials	Not applicable	Aromatherapy with different essential oils could decrease anxiety significantly.
Umbrello et al, <sup>15</sup> 2019	Systematic review	Eleven studies (10 RCTs and one quasi-experimental design), 959 patients (range 17–373)	Music therapy is consistently associated with a reduction in anxiety and stress in critically ill patients.
Haas et al, <sup>16</sup> 1986	Experimental study	10 musically trained and 10 untrained subjects	Musical rhythm can be a pacemaker, with its ability to entrain respiration dependent on the strength of its signal relative to spurious signals from the higher neural centers that introduce noise into the central pattern generator.
Chlan et al, <sup>17</sup> 2013	A randomized clinical trial	10 RCTs with a total of 1061 participants	Music interventions are effective in reducing anxiety for adult burn patients.
Sabeti et al, <sup>18</sup> 2021	A qualitative descriptive study	Thirteen nurses and five physicians in the pediatric intensive care unit.	Open presence of parents, using innovative methods to communicate with children, and training and psychological support for nurses and parents, help manage pain and anxiety in Pediatric ICU units.
Monsalve-Duarte et al, <sup>19</sup> 2022	A systematic review and meta-analysis	10 RCTs with a total of 1061 participants	Preliminary evidence for the effectiveness of music interventions for adult burn patients.
Boitor et al, <sup>20</sup> 2018	A randomized controlled trial	83 patients	A 20-minute hand massage in addition to routine postoperative pain management can concomitantly reduce anxiety by two points on average on a 0–10 scale
Rousseaux et al, <sup>21</sup> 2022	A prospective randomized trial	One hundred patients	In all groups, anxiety decreased, and pain increased from baseline to the postoperative day.

case report describes a possible option to help patients with difficulty weaning from ventilation due to anxiety. Rosenthal et al. highlighted the anxiolytic effect of second-generation antipsychotics by successfully weaning a very anxious patient with a second-generation antipsychotic. Quetiapine was initiated for treating severe anxiety that was unresponsive to sedative-hypnotics. Once a therapeutic dose of quetiapine was reached, ventilator support was removed within 24 hours.<sup>11</sup>

Despite widespread use and incorporation into hospital guidelines, there is no significant evidence from

placebo-controlled trials that support the use of haloperidol or any antipsychotics in the management of ICU-associated delirium or anxiety related to extubation. The use of high-dose haloperidol, especially given intravenously, presents the risk of QTc interval prolongation. At least one study has suggested that dexmedetomidine provides a safer alternative option in comparison with haloperidol. It effectively reduced the time to extubation and ICU length of stay, facilitated liberation from mechanical support, reduced the need for supplementary sedation, reduced the risk of QTc interval prolongation, and decreased the need for tracheostomy.<sup>12</sup>

## **BENZODIAZEPINES**

According to Kok and colleagues, the use of benzodiazepine in the ICU is associated with anxiety, delirium, and symptoms of PTSD.<sup>13</sup> Benzodiazepine use can often cause paradoxical agitation and combination with opiates can lead to significant respiratory suppression.

## **AROMATHERAPY**

Aromatherapy, i.e., the use of plant essences for therapeutic purposes, might be effective in reducing anxiety and improving sleep quality.<sup>14</sup> It is considered a complimentary option to improve anxiety and sleep quality in intensive care patients since it is safe, cost-effective, and easy to use.

## **MUSIC THERAPY**

Umbrello et al. reviewed music therapy and its therapeutic effects in managing anxiety, as assessed by heart and respiratory rate and blood pressure in ICU patients.<sup>15</sup> Music therapy is defined as listening to music with the idea of a change in the emotional or physical state of health, and it has been specifically used for its effect in critically ill patients. Listening to music reduces anxiety through its intricate networks in the central nervous system and affects the neurohormonal pathways in the brain and autonomic system at several conscious and unconscious levels. It modifies the production of endorphins, cytokines, and endogenous opiates. This study also examined music's effects in reducing the need for sedation and analgesia during interventional procedures and reducing anxiety in critically ill mechanically-ventilated patients. Music intervention was associated with a significant reduction in self-reported magnitude of anxiety and reduced scales of respiratory rate, heart rate, and blood pressure. Physiologic studies have shown that heart rate and respiratory rate may synchronize with the characteristics of the music to which one listens, through the activation of the autonomic system.<sup>16</sup> A randomized control trial evaluated music as an alternative to sedative medications to alleviate the anxiety associated with the use of mechanical ventilation. Daily assessments of anxiety (on the 100-mm visual analog scale) and two aggregate

measures of sedative exposure (intensity and frequency) showed a greater reduction in anxiety compared with usual care. Patient-directed music intervention resulted in a greater reduction in sedation frequency compared with usual care and a greater reduction in sedation intensity compared with usual care, but not compared with noise canceling headphones.<sup>17</sup>

## **CAREGIVING APPROACH**

Another qualitative study by Sabeti et al. studied non-pharmacological pain and anxiety management and its barriers in the pediatric ICU. The study showed that increasing the open presence of parents, using communication based on the child's interests, and providing psychological training of nurses and parents can reduce anxiety.<sup>18</sup> Monsalve-Duarte and colleagues provided evidence for the therapeutic effectiveness of music interventions for managing pain and mental health in adult burn patients.<sup>19</sup> The effect of hand massage has also been studied on the pain and anxiety of the cardiac surgery critically ill patients. It has been suggested that hand massage can reduce intensity of anxiety by two points on average on a 0–10 scale and is a potent complement to other pharmacological treatments. Twenty minutes of moderate-pressure massage over the hands in calm uninterrupted surroundings is necessary for a significant reduction of pain and anxiety.<sup>20</sup> A randomized control trial by Rousseaux et al. compared and combined hypnosis and virtual reality effects on anxiety and pain in patients before and after cardiac surgery. After randomly assigning the patients to four arms (control, hypnosis, virtual reality, and virtual reality hypnosis) and having 20 minutes of one of the techniques the day before and the day after surgery, anxiety, pain, fatigue, relaxation, physiological parameters, and opioid use were evaluated before and after each session in this study.<sup>21</sup> This study that anxiety decreased even though pain still increased from baseline to the postoperative day and relaxation increased in both pre-and post-operative periods.

## **CONCLUSIONS**

In summary, anxiety during weaning off sedation presents a management dilemma for the ICU team



and family caregivers alike. Current evidence is limited on the use of medications for this purpose, and FDA-approved treatments are lacking. It is reasonable to employ non-pharmacological approaches initially, and when this fails, pharmacological treatment options can be considered. More research is needed to adequately identify post-extubation anxiety and provide guidance on choosing a single agent at a dose that presents the minimum risk to the patient while alleviating symptoms.

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