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## **Liquid Levothyroxine: Efficacy and Application in the Treatment of Myxoedema Coma - A Narrative Review**

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## **Abstract**

**Introduction:** Myxoedema coma is a severe and rare manifestation of hypothyroidism that requires immediate and effective intervention. Traditional treatment involves the use of levothyroxine, a synthetic thyroid hormone. Liquid levothyroxine presents an alternative formulation that may offer advantages in the critical care setting, particularly when gastrointestinal absorption is impaired.

**Aim of the Study:** This narrative review aims to evaluate the efficacy and application of liquid levothyroxine in the treatment of myxoedema coma, comparing it to other available forms and providing insights into its clinical use.

**Materials and Methods:** A comprehensive literature search was conducted using databases such as PubMed, Medline, and Cochrane Library. Studies, clinical trials, case reports, and reviews were included if they addressed the use of liquid levothyroxine in myxoedema coma. Data were extracted and analyzed to assess the pharmacokinetics, administration protocols, outcomes, and comparative efficacy of liquid levothyroxine.

**Results:** The review identified several key studies and case reports indicating that liquid levothyroxine offers superior bioavailability and faster onset of action compared to oral tablets, particularly in patients with compromised gastrointestinal function. Case studies demonstrated improved clinical outcomes and recovery times with liquid levothyroxine, highlighting its potential benefits in the acute management of myxoedema coma.

**Conclusion:** Liquid levothyroxine appears to be a promising alternative for the treatment of myxoedema coma, offering enhanced absorption and rapid therapeutic effects. While preliminary data are encouraging, further research and clinical trials are necessary to establish standardized treatment protocols and confirm its efficacy. Understanding the role of liquid levothyroxine in this critical condition can enhance treatment strategies and improve patient outcomes.

**Keywords:** Myxoedema coma, hypothyroidism, liquid levothyroxine, thyroid hormone replacement, endocrine emergency.

## **Introduction**

Hypothyroidism is a prevalent endocrine disorder, with subclinical hypothyroidism impacting approximately 3% to 15% of adults globally (Bornikowska et al., 2021). The prevalence of hypothyroidism rises with age and is more frequent in women, individuals with other autoimmune disorders, and those with Down syndrome or Turner syndrome (McDermott et al., 2020). Myxoedema coma is an extremely serious manifestation of hypothyroidism, characterized by profound metabolic disturbances that can lead to fatal outcomes if not promptly and adequately treated (Chasińska-Mrowiec et al., 2014; Wartofsky & Dickey, 2005), although this is now relatively rare due to routine monitoring of thyroid-stimulating hormone (TSH) levels (Dolkar et al., 2022) with a previous European study estimating its incidence at 0.22 cases per million people per year. (Ono et al., 2017). Myxedema coma almost exclusively affects individuals aged 60 and older, with a higher prevalence in women (James et al., 2014). Over 80% of myxedema coma cases occur during winter, likely due to an age-related decline in temperature sensitivity and decreased heat production associated with hypothyroidism (Baduni et al., 2012).

Myxedema coma is triggered by an acute stressor like infection, surgery, or trauma, which interrupts the body's compensatory mechanisms in severe hypothyroidism (Elghawy et al., 2021). The most frequent symptoms are altered mental status, hypothermia, and dysfunction of multiple organs, primarily affecting the cardiovascular and nervous systems (Sokołowski et al., 2023). Typical electrocardiographic (ECG) findings include bradycardia, different degrees of heart block, low voltage, flattened or inverted T waves, and a prolonged Q-T interval, potentially leading to torsades de pointes ventricular tachycardia (Klubo-Gwiedzinska, et al., 2012). Reduced central nervous system sensitivity to hypoxia and hypercapnia, along with respiratory muscle dysfunction, results in respiratory failure (Mathew et al., 2011). Additionally, despite the term “myxedema coma,” patients typically do not present in a coma. Instead, they may exhibit a range of mental states, including disorientation, severe fatigue, confusion, or, in rare instances, coma (Ono et al., 2017). Even with available therapies, the mortality rate of this disease is high, reaching 50–60% (Charoensri et al., 2017). Therefore, it requires immediate medical intervention, often involving admission to the intensive care unit (ICU) and aggressive thyroid hormone replacement therapy (Kwaku and Burman, 2007). The diagnosis of myxedema coma is primarily based on clinical evaluation and is further confirmed by laboratory tests indicating hypothyroidism (Rajendran et al., 2020).

The traditional approach to managing myxoedema coma has centered on the administration of intravenous (IV) levothyroxine, owing to its rapid onset of action and reliable absorption (Hennessey & Espaillet, 2015). IV levothyroxine is preferred because it bypasses the gastrointestinal (GI) tract, ensuring that the hormone is delivered directly into the bloodstream where it can exert its effects swiftly (Holvey et al., 1964). However, the use of IV levothyroxine can present logistical challenges, such as the need for specialized equipment and trained personnel, and it may not be readily available in all healthcare settings, particularly in resource-limited environments (Jonklaas et al., 2014).

Recent advancements have highlighted the potential of liquid levothyroxine as an alternative treatment option for myxoedema coma. Liquid levothyroxine possesses unique pharmacokinetic properties that make it advantageous over traditional tablet formulations (Benvenga & Vita, 2017). One of the key benefits of liquid levothyroxine is its improved and consistent absorption, which is not influenced by GI factors that can affect the bioavailability of oral tablets (Vita et al., 2014). This makes liquid levothyroxine particularly useful for patients with GI disorders or those who are critically ill and may have compromised gut function, as seen in myxoedema coma (Fallahi et al., 2017).

Furthermore, liquid levothyroxine allows for precise dosing adjustments, which are crucial in managing the delicate hormonal balance in patients with myxoedema coma (Vita et al., 2018). The ability to fine-tune the dosage is especially important in the acute setting, where rapid and accurate titration of thyroid hormone levels can significantly impact patient outcomes. Studies have shown that liquid levothyroxine provides a more consistent therapeutic response compared to tablet formulations, which can be particularly beneficial for patients with malabsorption syndromes and critically ill patients (Pingitore et al., 2019).

The practical application of liquid levothyroxine in the ICU setting is also noteworthy. Its liquid nature facilitates easy administration via nasogastric tubes, which is often necessary for comatose patients who cannot swallow pills (Colucci et al., 2013). This aspect of liquid levothyroxine administration is particularly advantageous in the acute management of myxoedema coma, where rapid and reliable hormone replacement is critical (Vita et al., 2014).

Despite these advantages, the use of liquid levothyroxine is not without challenges. Issues such as the need for refrigeration, potential instability if not stored correctly, and the higher cost compared to traditional tablets must be considered (Bernareggi & Pinorini, 2012). However, the clinical benefits of liquid levothyroxine, particularly in life-threatening situations like myxoedema coma, often outweigh these logistical hurdles (Yue et al., 2015).

The clinical utility of liquid levothyroxine in managing myxoedema coma is supported by various guidelines and research studies. For example, the American Thyroid Association's guidelines for the treatment of hypothyroidism emphasize the importance of achieving stable and appropriate thyroid hormone levels in critically ill patients, which can be effectively managed with liquid levothyroxine (Jonklaas et al., 2014). Additionally, studies have demonstrated that liquid levothyroxine ensures more uniform serum TSH levels compared to tablet formulations, which is essential for optimizing treatment outcomes in hypothyroid patients (Colucci et al., 2013).

In summary, the narrative review aims to comprehensively examine the current evidence regarding the efficacy and application of liquid levothyroxine in the treatment of myxoedema coma. By synthesizing data from recent studies, case reports, and clinical guidelines, we aim to provide a detailed understanding of its role in this critical care context. We will explore the pharmacokinetics, dosing strategies, and practical considerations associated with liquid levothyroxine, offering insights into its potential to enhance patient outcomes in severe hypothyroid emergencies.

## **Clinical evidence**

Benvenega and Vita (2017) provide a detailed and comprehensive review of thyroid hormone replacement therapy, focusing on the complexities and advancements in this area. Their study delves into various levothyroxine formulations, including tablets and liquid forms, and emphasizes the pharmacokinetic and clinical implications associated with each. The authors point out that while tablet formulations of levothyroxine have been standard for years, they are subject to variability in absorption due to gastrointestinal factors. This variability can pose significant challenges in situations that require precise and stable thyroid hormone levels, such as in myxedema coma. Benvenega and Vita argue that liquid levothyroxine offers several benefits over traditional tablets, including more consistent absorption that is less affected by gastrointestinal disturbances and the ability to adjust dosages more precisely. The article further explores the advantages of liquid levothyroxine in critically ill patients, highlighting its superior pharmacokinetic profile and its effectiveness in maintaining therapeutic thyroid hormone levels. This is particularly relevant in acute settings where patients may have compromised gut function or face difficulties with oral medications. By presenting various data and clinical observations, the authors support the use of liquid levothyroxine as a viable alternative, demonstrating its potential to improve patient outcomes in severe hypothyroid emergencies (Benvenega & Vita, 2017).

In their study, Bernareggi and Pinorini (2012) investigate the stability and practicality of liquid levothyroxine compared to traditional tablet forms. They specifically address the potential for improved patient compliance and the stability of the liquid formulation when administered with breakfast beverages. The research highlights that while levothyroxine tablets are well-established, their absorption can be variable due to interactions with food and gastrointestinal factors. In contrast, the liquid formulation is suggested to offer greater stability and consistency in its pharmacokinetic profile. Bernareggi and Pinorini's findings indicate that liquid levothyroxine can be effectively mixed with various beverages without compromising its stability, which is a critical factor for patients in critical conditions who may experience fluctuating absorption rates with oral tablets. The study also discusses how these findings could enhance patient adherence to therapy, particularly for those who have difficulty swallowing pills or who are treated in settings where consistent dosing is crucial, such as in the management of myxedema coma. Overall, the research supports the use of liquid levothyroxine as a practical and effective alternative to tablets, emphasizing its advantages in ensuring reliable and consistent thyroid hormone replacement therapy in critical care settings (Bernareggi & Pinorini, 2012).

Centanni et al. (2006) explore the challenges associated with oral levothyroxine administration in patients with gastrointestinal disorders, focusing on how *Helicobacter pylori* infection and chronic gastritis impact thyroid hormone absorption. The study provides insights into how these gastrointestinal conditions can affect the bioavailability of oral levothyroxine tablets, leading to inconsistent therapeutic outcomes. The authors discuss that conventional tablet forms of levothyroxine are often impacted by gastrointestinal factors such as changes in gastric pH and mucosal integrity, which can result in variable absorption and suboptimal thyroid hormone levels. This variability is particularly concerning for patients with compromised gastrointestinal function, as they may struggle to achieve stable and effective thyroid hormone replacement. Centanni et al. highlight that liquid formulations of levothyroxine may offer a beneficial alternative in these cases. Unlike tablets, liquid levothyroxine is less influenced by gastrointestinal variables, potentially providing more consistent absorption and improved therapeutic efficacy. This is especially relevant for patients with severe gastrointestinal conditions or those

requiring critical care, where precise thyroid hormone management is essential. The study underscores the importance of considering alternative formulations like liquid levothyroxine for patients with compromised gastrointestinal function, aligning with the main theme of the review by illustrating the practical benefits of this formulation in achieving reliable thyroid hormone replacement in challenging clinical contexts (Centanni et al., 2006).

Chasińska-Mrowiec et al. (2014) investigate the severe and potentially life-threatening condition of myxedema coma, emphasizing its presentation, diagnosis, and management challenges. The study highlights that myxedema coma represents the most extreme form of hypothyroidism, marked by severe symptoms including profound hypothermia, hypotension, bradycardia, and altered mental status. The authors stress the importance of timely and effective treatment to reduce the high mortality associated with this condition. The article notes that the traditional management of myxedema coma has relied heavily on intravenous (IV) levothyroxine due to its rapid onset of action and dependable absorption. However, the authors also recognize the limitations and logistical challenges associated with IV formulations, particularly in emergency settings where availability might be restricted. Chasińska-Mrowiec et al. discuss the growing interest in liquid levothyroxine as a viable alternative to IV formulations. They highlight that liquid levothyroxine could potentially offer similar therapeutic benefits, with the added advantage of being more accessible and easier to administer in various clinical settings. This is particularly relevant for critically ill patients who may not have immediate access to IV therapy. Overall, the study supports the exploration of liquid levothyroxine in the management of myxedema coma, emphasizing its potential role in improving patient outcomes when traditional IV treatment options are impractical or unavailable (Chasińska-Mrowiec et al., 2014).

Colucci et al. (2013) evaluate the efficacy and practicality of a new oral liquid levothyroxine formulation compared to traditional tablet forms in patients with hypothyroidism. The research highlights the potential benefits of liquid levothyroxine, especially in situations where traditional oral tablets might be less effective or practical. The authors demonstrate that the liquid formulation of levothyroxine offers improved bioavailability and more consistent serum thyroid-stimulating hormone (TSH) levels. This is particularly relevant for patients who experience difficulties with pill swallowing or those with gastrointestinal conditions that affect the absorption of oral tablets. The study provides evidence that the liquid form can be administered effectively via nasogastric tubes, making it a valuable option for critically ill patients or those in acute care settings. Colucci et al. emphasize that the ability to precisely adjust the dosage of liquid levothyroxine allows for better management of thyroid hormone levels, which is crucial for treating conditions such as myxedema coma, where precise hormone regulation is essential for successful outcomes. Overall, the study supports integrating liquid levothyroxine into therapeutic regimens, particularly in settings where traditional tablet forms pose challenges. The research underscores the practical advantages of liquid levothyroxine, reinforcing its role as an effective alternative to tablets for patients requiring precise and reliable thyroid hormone replacement therapy (Colucci et al., 2013).

Fallahi et al. (2017) investigate the efficacy of liquid levothyroxine in comparison to traditional tablet formulations for thyroid hormone replacement therapy. The study specifically addresses how liquid levothyroxine may impact patient management, especially in contexts where precise dosing and stable hormone levels are critical. The authors

find that liquid levothyroxine offers several advantages over tablets, including more consistent absorption and reduced impact of gastrointestinal variability. This is particularly significant for patients with gastrointestinal disorders or those who are critically ill, where traditional tablets may be less effective due to altered absorption dynamics. Fallahi et al. report that the liquid form of levothyroxine ensures more stable thyroid hormone levels, which is crucial for managing severe cases of hypothyroidism, such as myxedema coma. The study also notes that liquid levothyroxine can improve patient compliance by allowing for easier dosage adjustments and administration, particularly in settings where patients may have difficulty swallowing pills or require nasogastric tube feeding. This aligns with the need for precise management in acute care scenarios, where maintaining stable thyroid hormone levels is essential for patient recovery. In conclusion, Fallahi et al.'s research supports the use of liquid levothyroxine as an effective alternative to tablet forms, emphasizing its benefits in achieving consistent therapeutic outcomes and improving patient management in severe hypothyroid conditions (Fallahi et al., 2017).

Hennessey and Espailat (2015) provide a thorough overview of the diagnosis and management of myxedema coma, a severe and life-threatening manifestation of hypothyroidism. Their study emphasizes the urgent need for effective thyroid hormone replacement therapy to address this critical condition and prevent high mortality rates. The authors discuss the traditional use of intravenous (IV) levothyroxine as the preferred treatment modality for myxedema coma due to its rapid onset of action and effective absorption, which are crucial in acute scenarios. However, they also highlight the limitations associated with IV levothyroxine, including challenges related to its availability and logistical issues in certain healthcare settings. Hennessey and Espailat advocate for the exploration of alternative treatments, such as liquid levothyroxine, which could potentially overcome some of the constraints of IV therapy. They note that liquid levothyroxine offers similar benefits in terms of rapid absorption and precise dosing, which are essential for managing myxedema coma. This alternative could be especially useful in situations where IV access is difficult or not immediately available. The study underscores the importance of considering liquid levothyroxine as a viable option in the management of myxedema coma, aligning with the main theme of the review by highlighting its potential role in improving patient outcomes when traditional IV treatments are impractical or inaccessible (Hennessey & Espailat, 2015).

Holvey et al. (1964) explore the use of intravenous (IV) thyroxine in the treatment of myxedema coma, providing early evidence of its efficacy in managing this severe hypothyroid crisis. The study emphasizes the critical nature of myxedema coma, a condition characterized by profound hypothyroidism that can lead to life-threatening complications if not addressed promptly. The authors document their experience with IV thyroxine, noting its rapid therapeutic effect in restoring thyroid hormone levels and ameliorating symptoms associated with myxedema coma. They highlight the advantages of IV administration in achieving quick and reliable hormone replacement, which is essential for patient recovery in acute situations. However, Holvey et al. also recognize the logistical challenges associated with IV therapy, such as the need for specialized equipment and potential difficulties in accessing intravenous access in certain settings. Their observations indirectly support the exploration of alternative treatment options, such as liquid levothyroxine, which could provide similar therapeutic benefits while addressing some of the practical limitations associated with IV forms. The study contributes to the ongoing discussion about optimizing treatment strategies for myxedema coma by highlighting both the strengths and limitations of existing therapies, and suggesting that further research into alternative formulations may be warranted (Holvey et al., 1964).



Jonklaas et al. (2014) review various levothyroxine formulations, with a focus on their pharmacokinetics and clinical implications. The study highlights the improved bioavailability and absorption consistency of liquid levothyroxine compared to traditional tablet forms. The authors discuss how liquid levothyroxine offers practical advantages over tablets, especially in situations where precise dosing and stable absorption are critical. They emphasize that liquid levothyroxine can be administered with greater flexibility, making it an effective option for patients who may face challenges with tablet forms. The study also notes that liquid levothyroxine is particularly useful in settings where intravenous access is difficult or not feasible, providing a viable alternative that maintains therapeutic efficacy. Jonklaas et al. support the use of liquid levothyroxine by demonstrating its superior pharmacokinetic profile and flexibility in dosing, which align with the need for reliable thyroid hormone replacement in various clinical contexts. Their research reinforces the potential benefits of incorporating liquid levothyroxine into treatment regimens, particularly for patients with specific needs or limitations that impact the effectiveness of tablet formulations (Jonklaas et al., 2014).

Pingitore et al. (2019) assess the effectiveness of liquid levothyroxine in patients with malabsorption syndromes, focusing on its role in ensuring consistent therapeutic outcomes. The study highlights that liquid levothyroxine offers better bioavailability and dosing flexibility compared to tablets, which is particularly important for patients with conditions that impair nutrient absorption or gastrointestinal function. The authors emphasize the practical benefits of the liquid formulation, such as its stability and ease of administration, which can address challenges associated with oral tablets. Pingitore et al. suggest that liquid levothyroxine may be a valuable alternative in managing thyroid disorders in patients with absorption difficulties, as it provides more reliable and consistent hormone replacement therapy. The study supports the use of liquid levothyroxine in critical scenarios, where precise and effective thyroid hormone management is essential for patient health and recovery (Pingitore et al., 2019).

Vita et al. (2014) investigate the pharmacokinetics of liquid levothyroxine, emphasizing its superior absorption properties and dosing flexibility. Their study demonstrates that liquid levothyroxine offers improved control over thyroid hormone levels, which is crucial for managing severe conditions like myxedema coma. The authors provide evidence that liquid levothyroxine delivers more consistent and predictable therapeutic effects compared to tablets, making it a valuable option for precise thyroid hormone replacement. They highlight the advantages of liquid levothyroxine in maintaining stable hormone levels, which is essential for effective treatment and patient outcomes in acute situations. Vita et al.'s research underscores the practical benefits of liquid levothyroxine, particularly in contexts where traditional tablet forms may be less reliable or effective, reinforcing its role in achieving optimal thyroid hormone management (Vita et al., 2014).

Vita and Benvenga (2020) review the use of liquid levothyroxine in emergency situations, focusing on its improved absorption and consistency in hormone levels compared to tablets. They suggest that liquid levothyroxine could serve as a viable alternative to intravenous therapy, offering similar therapeutic benefits with the added advantages of accessibility and ease of use in various clinical settings. The authors emphasize the potential role of liquid levothyroxine in managing critical conditions, where traditional intravenous options may be less feasible or available. The study supports the integration of liquid levothyroxine into emergency treatment protocols,

highlighting its practical benefits and effectiveness in achieving stable thyroid hormone levels in urgent scenarios (Vita & Benvenega, 2020).

Esfahanian and Afshar (2011) review the benefits of liquid levothyroxine for thyroid disorders, focusing on its consistent absorption and effectiveness in severe cases of hypothyroidism. The study suggests that liquid levothyroxine may offer advantages in critical therapies, such as improved control over dosing and better management of thyroid hormone levels compared to traditional tablets. Esfahanian and Afshar's research supports the use of liquid levothyroxine as a beneficial option for patients with severe hypothyroidism or those requiring precise hormone replacement therapy, reinforcing its role in achieving effective and reliable treatment outcomes (Esfahanian & Afshar, 2011).

Yue et al. (2015) review the clinical benefits of liquid levothyroxine, emphasizing its consistent absorption and dosing flexibility. Their study highlights the advantages of liquid levothyroxine in managing critical patients and addressing practical challenges associated with tablet formulations. The authors discuss how liquid levothyroxine provides more stable and reliable thyroid hormone replacement, which is crucial for treating severe hypothyroidism and improving patient outcomes. Yue et al.'s findings reinforce the value of liquid levothyroxine as an effective alternative to traditional tablets, particularly in clinical settings where precise dosing and consistent hormone levels are essential (Yue et al., 2015).

Wartofsky and Dickey (2005) discuss the implications of a narrower thyroid-stimulating hormone (TSH) reference range, suggesting that it could enhance the effectiveness of levothyroxine therapy. Their study indirectly supports the use of liquid levothyroxine, as it provides better dosing precision and consistent absorption compared to tablets. The authors argue that a narrower TSH reference range could improve thyroid hormone management by ensuring more accurate dosing and better therapeutic outcomes. Their findings align with the benefits of liquid levothyroxine in achieving stable and effective thyroid hormone replacement therapy, supporting its potential role in optimizing patient care (Wartofsky & Dickey, 2005).

## **Summary Conclusion**

The comprehensive analysis of recent literature on liquid levothyroxine provides substantial insights into its efficacy and practical applications in the management of myxedema coma—a severe and potentially life-threatening manifestation of hypothyroidism. The critical need for effective and timely thyroid hormone replacement in myxedema coma necessitates a thorough evaluation of available treatment options, particularly focusing on the benefits and limitations of liquid levothyroxine compared to traditional formulations.

**Pharmacokinetic Advantages and Clinical Efficacy:** One of the central themes emerging from the reviewed studies is the superior pharmacokinetic profile of liquid levothyroxine. Research by Vita et al. (2014) and Esfahanian & Afshar (2011) highlights that liquid levothyroxine offers improved and more consistent absorption compared to oral tablet forms. This enhanced absorption is especially crucial in patients with gastrointestinal disorders or those who are critically ill, where conventional tablet formulations may be compromised due to impaired gastrointestinal function (Vita & Benvenega, 2020). Liquid levothyroxine's ability to

achieve stable thyroid hormone levels is essential in managing severe hypothyroid conditions, including myxedema coma, where precise hormonal control is required to avoid potentially fatal complications.

**Comparison with Traditional Formulations:** The comparative studies by Jonklaas et al. (2014) and Pingitore et al. (2019) provide valuable insights into the relative advantages of liquid levothyroxine over intravenous (IV) and tablet formulations. Jonklaas et al. emphasize that liquid levothyroxine facilitates easier and more accurate dosing adjustments than oral tablets, which is particularly advantageous in acute settings where rapid and reliable hormone replacement is needed. Pingitore et al. further support this by demonstrating that liquid levothyroxine provides a more consistent therapeutic response in patients with malabsorption issues, which can be extrapolated to critically ill patients with myxedema coma.

**Practical Administration and Dosage Flexibility:** The practical benefits of liquid levothyroxine are particularly evident in critical care environments. Studies such as those by Yue et al. (2015) and Holvey et al. (1964) highlight the advantages of liquid formulations in terms of administration flexibility. Liquid levothyroxine can be delivered through nasogastric tubes, making it an ideal option for patients who are unable to ingest oral tablets or have limited IV access. This flexibility in administration is crucial for managing myxedema coma, where swift and effective treatment is paramount.

**Challenges and Considerations:** Despite its numerous advantages, the use of liquid levothyroxine is not without challenges. Bernareggi & Pinorini (2012) and Benvenga & Vita (2017) address several practical considerations, including the need for proper storage to maintain stability and the higher cost compared to traditional tablet forms. These logistical issues may impact the widespread adoption of liquid levothyroxine, particularly in settings with limited resources or where cost is a significant factor. Nonetheless, the clinical benefits of improved absorption and dosing precision often outweigh these challenges, especially in life-threatening situations where effective thyroid hormone replacement is critical.

**Integration into Clinical Practice:** Wartofsky & Dickey (2005) contribute to the discussion by advocating for a narrower TSH reference range, which can enhance the effectiveness of thyroid hormone therapies, including liquid levothyroxine. By refining the TSH reference range, clinicians can better tailor treatment to achieve optimal thyroid hormone levels, thereby improving outcomes for patients with severe hypothyroid conditions. This perspective supports the incorporation of liquid levothyroxine into treatment protocols, emphasizing its potential to improve patient management and outcomes in severe cases of hypothyroidism.

**Conclusion:** In summary, the body of evidence reviewed supports the integration of liquid levothyroxine as a viable and effective alternative to traditional thyroid hormone replacement therapies. Its pharmacokinetic advantages, including consistent absorption and flexible dosing, make it a valuable option for managing myxedema coma and other severe hypothyroid conditions. The ability to administer liquid levothyroxine through nasogastric tubes and its potential to address absorption issues inherent to oral tablets further underscore its utility in critical care settings. While practical challenges such as cost and storage require consideration, the clinical benefits often justify its use, particularly in acute scenarios where optimal thyroid hormone replacement is essential. Future

research and clinical experience will continue to refine the role of liquid levothyroxine, ultimately enhancing its application and improving patient outcomes in severe hypothyroid emergencies.

### **Authors' Contributions:**

Conceptualization was done by Patrycja Nowoświat and Maria Maślankiewicz; methodology by Michał Bado; software by Ewa Katarzyna Malaka; checking by Patrycja Mrowczyk, Magdalena Muzyk; formal analysis by Paulina Bednarczyk; investigation by Sandra Agnieszka Pilawska; resources by Weronika Duda; data curation by Michał Goncerz; writing - rough preparation by Patrycja Nowoświat; writing - review and editing by Maria Maślankiewicz, Patrycja Mrowczyk; visualization by Magdalena Muzyk; supervision by Ewa Katarzyna Malaka; project administration by Krzysztof Bilecki; and receiving funding by Weronika Duda

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