Research Progress on Refractory Insomnia

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Summary

Advancements in the study of refractory insomnia suggest a paradigm shift in modern treatment methodologies towards diversification and personalization. Traditional pharmacotherapies, such as benzodiazepines, are noted for their dependency risks. However, new-age drugs like Dexmedetomidine are garnering attention for their safety profile and protective effects on sleep architecture. Cognitive Behavioral Therapy (CBT), as a non-pharmacological intervention, has proven effective, though it requires long-term engagement. Anesthesia-induced sleep therapy, an innovative approach, has demonstrated potential in treating insomnia. Multimodal treatments that integrate pharmacological, non-pharmacological, and novel methods, such as stellate ganglion block and Enhanced External Counterpulsation (EECP), offer comprehensive treatment strategies. However, the long-term safety and side effects of these emerging therapies remain areas for further investigation. Future research should focus more on evaluating the combined effects and safety of these treatments, exploring various therapeutic combinations and personalized approaches. This will aid in a

deeper understanding of the long-term outcomes and mechanisms of these emerging therapies, thereby facilitating the provision of more effective and safer treatment options for refractory insomnia.

1. **Keywords**: Persistent Insomnia; Dexmedetomidine; Propofol; Stellate Ganglion Block; Enhanced External Counterpulsation

I. Introduction

Refractory insomnia is becoming an increasingly common health issue in modern society, affecting not only the quality of daily life but also potentially causing long-term detrimental effects on physical and mental health. With a deeper understanding of the symptoms and consequences of insomnia, researchers and the medical community are seeking more effective treatments for those symptoms of refractory insomnia that respond poorly to traditional methods. In instances where traditional pharmacotherapy and behavioral therapy offer limited assistance, new treatment approaches like the use of Dexmedetomidine, Propofol, and anesthesia-induced sleep therapy have emerged as hotspots in research. These explorations not only expand our understanding of insomnia treatment but also provide fresh perspectives for clinical practice. This review will discuss the current state, risks, traditional treatment methods, and their limitations for refractory insomnia, with a special focus on the latest research advancements. Particularly, it will delve into the application and safety of Dexmedetomidine, Propofol, and anesthesia-induced sleep therapy in treating refractory insomnia. Through these studies, we hope to gain a deeper insight into the treatment mechanisms of refractory insomnia and offer guidance for future research and clinical practices.

2. Definition of Insomnia

Insomnia, as a common sleep disorder, is defined as difficulty in falling asleep, maintaining sleep, or experiencing poor sleep quality. These symptoms occur at least three times per week and persist for at least three months, accompanied by significant daytime functional impairment[1]. Insomnia is not just a nocturnal sleep issue; it also involves daytime fatigue, lack of concentration, memory decline, and emotional disturbances, all of which can severely impact a patient's quality of life and work efficiency. The severity of insomnia can range from mild, occasional sleep disturbances to severe symptoms occurring every night over the long term. The causes of insomnia are diverse, including biological, psychological, and environmental factors, with stress, anxiety, and depression being the most common psychological triggers[2]. Moreover, insomnia can also be a symptom of other medical conditions or sleep disorders, such as sleep apnea or periodic limb movement disorder. Thus, diagnosing and treating insomnia requires a comprehensive consideration of various potential factors. Insomnia is not limited to a single symptom but is a syndrome encompassing various sleep issues. This includes difficulty initiating sleep, frequent awakenings or early morning

awakenings, and feeling unrested or lacking energy after sleep. It is important to note that these symptoms need to persist for a certain duration and occur frequently to be diagnosed as insomnia[3]. The experience of insomnia varies among individuals; some may experience brief and minor sleep disturbances, while others may suffer from long-term, severe insomnia. Chronic insomnia not only affects nighttime sleep quality but can also lead to daytime fatigue, distractibility, memory loss, reduced work efficiency, mood fluctuations, and even psychological health issues like depression and anxiety[2]. Additionally, insomnia may be associated with other health conditions, such as pain, chronic illnesses, side effects of medications, lifestyle factors (like caffeine and alcohol consumption), and environmental factors (such as noise and light pollution). Given that insomnia can result from the interaction of multiple factors, treatment plans need to be individualized, taking into account the specific circumstances and needs of the patient[3]. In diagnosing and treating insomnia, doctors typically consider the patient's medical history, lifestyle, and sleep habits, and may sometimes include tools like sleep diaries or sleep monitoring to gain a more comprehensive understanding of the patient's sleep patterns and influencing factors. This helps doctors to devise more effective treatment plans aimed not only at improving nighttime sleep quality but also at enhancing daytime quality of life.

3. Current Status of Insomnia

Currently, insomnia has become an extremely common health issue globally, significantly impacting individuals' quality of life, work efficiency, and overall health. Studies indicate that approximately 10% of adults suffer from chronic insomnia, while up to 20% of the population occasionally experiences symptoms of insomnia. Of particular concern is that about 40% of those with insomnia have symptoms lasting over five years[3]. The occurrence of insomnia is associated with a variety of factors, including biological, psychological, social environmental, and behavioral elements. With the acceleration of modern life, increased work stress, and lifestyle changes such as nighttime use of electronic devices and irregular sleep schedules, the incidence of insomnia is on the rise. Furthermore, research finds that the incidence of insomnia in women is about 1.5 times higher than in men, and the prevalence among the elderly is as high as 60.9%[3]. In the context of public health, insomnia not only poses challenges to individual health but also has a significant impact on society and the economy. Insomnia is linked with various health issues, including cardiovascular diseases, diabetes, obesity, depression, and anxiety. Chronic insomnia can also lead to decreased work efficiency and increased risk of accidents, thus adding to the burden on healthcare systems[2]. Despite the growing significance of its impact, many people are not fully aware of insomnia and fail to receive effective treatment. Currently, there are various methods for treating insomnia, but they still have certain limitations, especially when dealing with refractory insomnia. Therefore, optimizing research, prevention, and treatment strategies for insomnia

is a crucial topic in the current healthcare field.

4. The Hazards of Insomnia

Insomnia is not only an independent health issue but is also associated with a variety of physical and mental health problems. Prolonged insomnia can lead to serious health consequences, including but not limited to the following aspects:Psychological Health Impact: Chronic insomnia is closely linked to mental health issues such as depression and anxiety. Sleep disorders can exacerbate existing mental illnesses or become a trigger for psychological problems[2];Cognitive Function Impairment: Insomnia negatively affects cognitive functions, particularly memory, attention, and decision-making abilities. This can lead to reduced work efficiency and a decline in the quality of daily life.Increased Cardiovascular Risk: Prolonged insomnia is considered a risk factor for cardiovascular diseases, such as heart disease and hypertension. Sleep disorders are associated with dysfunction in the cardiovascular system, potentially increasing the risk of heart attacks and strokes.Weakened Immune System Function: Insomnia may weaken the immune system, making individuals more susceptible to diseases. Studies show that lack of sleep affects the function of immune cells, reducing the efficiency of immune responses[3];Metabolic and Weight Issues: Insomnia is closely linked to obesity and metabolic syndrome. Insufficient sleep can lead to increased appetite and metabolic dysfunction, resulting in weight gain.Decline in Quality of Life: Insomnia impacts emotional stability and life satisfaction, leading to a significant decrease in the quality of daily life. Individuals with long-term insomnia often feel tired and weak, severely affecting their social, professional, and family lives.Increased Risk of Accidents: Individuals with insufficient sleep may experience distracted attention and delayed reaction times while driving or operating machinery, increasing the risk of accidents. Therefore, insomnia is not just a matter of individual health but a significant public health issue that requires effective identification, prevention, and treatment strategies.

5. Traditional Conventional Treatment Methods for Insomnia

1.Pharmacotherapy: Common medications used include benzodiazepines, non-benzodiazepines, antidepressants, and antipsychotics. They primarily work by regulating neurotransmitter balance to improve sleep quality. However, pharmacotherapy can lead to dependency and tolerance, and long-term use may bring side effects such as memory impairment, attention deficit, and daytime drowsiness[4].Benzodiazepines: Drugs like diazepam and alprazolam function by enhancing GABA activity in the central nervous system, inducing sedation and hypnosis. However, long-term use may cause dependency and tolerance, along with potential cognitive side effects[4].

1.2 Non-Benzodiazepines: Drugs like zolpidem have a similar mechanism but may have lower dependency compared to benzodiazepines.

1.3 Antidepressants: Some antidepressants, such as tricyclics, are used for insomnia due to their sedative effect, but they may cause side effects like dry mouth and constipation.

2.Non-Pharmacological Treatments: These include Cognitive Behavioral Therapy (CBT), sleep hygiene education, relaxation training, etc. CBT is an effective non-pharmacological approach that improves sleep by changing poor sleep habits and thought patterns[5].

2.1 Cognitive Behavioral Therapy (CBT): It modifies patients' cognition and behavior regarding sleep, improving symptoms of insomnia and considered the first line of treatment for chronic insomnia[5].

2.2 Sleep Hygiene Education: Instructing patients to improve their sleep environment and habits, such as having a regular sleep schedule, avoiding naps during the day, and reducing caffeine intake.

2.3 Relaxation Training: Techniques like deep breathing and progressive muscle relaxation help patients relieve tension and anxiety, improving sleep.

3.Integrated Treatment: In most cases, doctors combine the above methods based on the patient's specific condition. For example, non-pharmacological treatment may be the first choice for mild or short-term insomnia, while more severe or chronic insomnia might require a combination of drug therapy. A personalized treatment plan integrating both pharmacological and non-pharmacological treatments is developed, with drugs initially used to quickly alleviate symptoms while introducing non-pharmacological treatments for long-term management.

4.Other Supportive Therapies:

4.1 Music Therapy: Relaxing through soft music to improve sleep.

4.2 Yoga and Meditation: Relaxing the body and mind to enhance sleep quality. While traditional methods have been somewhat effective in treating insomnia, challenges remain, especially in dealing with refractory insomnia in terms of long-term effectiveness and safety.

6. Refractory Insomnia Defined

Refractory insomnia, also known as intractable insomnia, is characterized by long-term, recurrent symptoms of insomnia that typically respond poorly or not at all to conventional treatments. This type of insomnia includes symptoms like difficulty falling asleep, frequent night awakenings, early morning awakenings, and poor sleep quality, severely affecting the patient's daytime function and quality of life. Refractory insomnia is usually defined as insomnia symptoms occurring at least three times a week, lasting for more than three months, and accompanied by significant daytime functional impairment[3]. Refractory insomnia often shows varying degrees of resistance to conventional treatments such as pharmacotherapy and Cognitive Behavioral Therapy. This resistance may be due to a complex interaction of biological, psychological, and socio-environmental factors[6]. Treating refractory insomnia requires a comprehensive consideration of individual differences, potentially including

medication, psychotherapy, lifestyle adjustments, and more. However, due to its stubborn nature, the treatment outcomes are often unstable, necessitating long-term follow-up and adjustments to the treatment plan[3]. The causes of refractory insomnia are complex, potentially including physiological, psychological, environmental factors, and more. Physiological factors may encompass endocrine disruption, neurotransmitter imbalance, brain structure and function abnormalities, etc. For instance, chronic pain, respiratory diseases, and endocrine disorders like thyroid abnormalities can all lead to sleep disturbances. Additionally, as one ages, changes in the body's biological clock can occur, contributing to the higher prevalence of refractory insomnia among older adults. Psychological factors play a significant role in refractory insomnia. Long-term stress, anxiety, depression, and other mental health issues can cause or exacerbate insomnia. These psychological factors may relate to cognitive functions (such as excessive focus on or worry about sleep) and emotional regulation disorders. Various factors in the living environment, like noise, light, temperature, and the comfort of the sleep environment, can affect sleep. Irregular sleep habits, nighttime use of electronic devices, and life and work stress can cause or worsen insomnia. The use of certain medications (such as antidepressants, antihypertensives) and substances (like caffeine, alcohol, nicotine) can affect sleep. Long-term use of benzodiazepines and other sleep medications may lead to drug dependency and tolerance, exacerbating insomnia symptoms[8]. Chronic diseases, hormonal fluctuations (such as during menopause), and genetic factors may also contribute to refractory insomnia. For example, chronic pulmonary and cardiovascular diseases can affect sleep quality and duration. Understanding the multifaceted causes of refractory insomnia is crucial in devising effective treatment strategies. A comprehensive approach is required, tailoring .

7. Progress in the Treatment of Refractory Insomnia with Dexmedetomidine

In the treatment of refractory insomnia, the use of Dexmedetomidine has expanded from intensive care units to general wards and outpatient settings, especially for patients who are unresponsive to or have contraindications for traditional sleep medications[6]. As a relatively safe sedative, Dexmedetomidine demonstrates good tolerance and a lower risk of side effects when used in treating refractory insomnia. Compared to other sedatives, it has a minimal impact on respiratory suppression, which is particularly important for patients with long-term insomnia[8]. Dexmedetomidine is becoming a focus in the research of refractory insomnia treatment. It not only shows promising results in clinical trials but also reveals its complex mechanisms of action in basic research, including its contribution to neuroprotection and antioxidant mechanisms[9].

In clinical trials for refractory insomnia, Dexmedetomidine has shown a high efficacy rate. Patients have experienced significant improvements in sleep quality, with sleep architecture approaching a normal pattern after treatment[10].

The treatment with Dexmedetomidine is moving towards personalization, where dosages and treatment regimens can be adjusted for different patients to achieve optimal therapeutic effects and minimize side effects. The use of Dexmedetomidine also fosters collaborative research across multiple disciplines, including sleep medicine, neuroscience, and psychology, to more comprehensively understand and treat refractory insomnia. The ongoing research and application of Dexmedetomidine in the treatment of refractory insomnia represent continuous progress, offering new directions and hope in the management of insomnia.

8. Dexmedetomidine's Mechanism in Treating Refractory Insomnia

Dexmedetomidine is an α2 adrenergic receptor agonist, and its mechanism in treating refractory insomnia involves multiple aspects:Central Nervous System Sedation: Dexmedetomidine reduces the release of norepinephrine by activating α2 receptors, decreasing the excitability of the central nervous system. This sedative effect is similar to physiological sleep and aids in restoring and maintaining normal sleep patterns[6].Mimicking Physiological Sleep: The sleep induced by Dexmedetomidine not only resembles natural sleep in duration but also in quality. It can mimic the sleep patterns of Non-Rapid Eye Movement (NREM) stage 3, a deep sleep phase critical for bodily restoration and brain functions[8].Reduction of Neuronal Cell Apoptosis: Dexmedetomidine also has neuroprotective effects, capable of mitigating neuronal cell apoptosis caused by other drugs (like Propofol). This protective effect might be related to its activity in the PI3K/Akt/GSK3β signaling pathway, thereby safeguarding brain cells from damage[8].Antioxidant and Neuroprotection: Additionally, Dexmedetomidine possesses antioxidant properties, maintaining the homeostasis of brain iron metabolism and protecting neurons from oxidative stress. This function may be related to its regulation of ferritin expression, preventing ferroptosis and reducing damage to neuroglial cells[9].Sleep Quality Improvement: Studies indicate that Dexmedetomidine can improve sleep quality, increasing delta wave activity during NREM sleep, reflecting an enhancement in sleep depth. This is vital for maintaining brain functions, such as memory consolidation and the restoration of cognitive functions[10].Currently, research on Dexmedetomidine's role in treating refractory insomnia is still in its preliminary stages. However, its unique sedative effects and potential neuroprotective properties make it a promising drug in this field. Future studies need to focus more on its long-term safety and effectiveness, particularly for elderly patients and those with other comorbidities. Moreover, exploring the combined use of Dexmedetomidine with other treatment approaches, such as Cognitive Behavioral Therapy, may provide a more comprehensive solution for the treatment of refractory insomnia

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9. Progress in the Treatment of Refractory Insomnia with Propofol

Propofol, a potent anesthetic drug, has shown certain potential and progress in recent years in the treatment of refractory insomnia: Although primarily used for general anesthesia, recent studies and clinical trials have focused more on the safety and side effects of Propofol in treating refractory insomnia[8]. In the treatment of refractory insomnia, the use of Propofol is mainly concentrated in short-term interventions, particularly in intensive care units, to rapidly induce sleep and help patients alleviate insomnia symptoms. While Propofol can effectively induce sleep in the short term, its long-term use may lead to cognitive function decline, dependency, and other potential side effects, thus necessitating strict control over the dosage and duration of use[11].The sleep-inducing mechanism of Propofol, especially its role in neuroprotection and neuromodulation, is becoming a new focus of research. This aids in developing safer and more effective methods to treat refractory insomnia. The use of Propofol is increasingly being integrated into comprehensive treatment plans, in combination with other drugs like Dexmedetomidine and non-pharmacological treatments such as Cognitive Behavioral Therapy, to achieve better therapeutic outcomes. As a deeper understanding of the pharmacodynamics and pharmacokinetics of Propofol evolves, its application in precision medicine is gradually unfolding, particularly in personalized treatment for specific populations (like the elderly or patients with severe comorbidities).The number of clinical trials on Propofol for treating refractory insomnia is increasing, which will help to more accurately assess its efficacy and safety. Currently, research is gradually focusing on the long-term improvement of sleep quality in patients post-Propofol treatment, as well as its impact on daytime functioning and quality of life for these individuals.

10. Research Progress on Enhanced External Counterpulsation (EECP) in the Treatment of Insomnia

Enhanced External Counterpulsation (EECP) is a non-invasive auxiliary circulatory technology that utilizes electrocardiogram-controlled technology. It involves wrapping cuffs around the lower legs, thighs, and buttocks, which sequentially inflate and deflate in sync with the cardiac cycle. EECP enhances venous return by compressing limb blood, thereby increasing cardiac output. EECP has been proven to effectively improve blood flow perfusion to vital organs such as the heart, brain, and kidneys. During treatment, the timing of the cuffs' inflation and deflation is precisely synchronized with the opening and closing of the aortic valve, as indicated by the surface electrocardiogram. The inflation/deflation cycle from the lower legs to the thighs and buttocks, from

proximal to distal, ensures that the proximal arteries are compressed later than the distal arteries, thereby promoting more arterial return to the aorta and enhancing diastolic augmentation.[14-17].Multiple studies indicate that EECP can improve cerebral blood flow, cellular oxygenation and nutrition, and regulate related neurotransmitters. All these factors can ameliorate symptoms of insomnia. EECP has been utilized to improve sleep in elderly patients with sleep disorders.[18,19]

11. Research Progress on Stellate Ganglion Block (SGB) in the Treatment of Insomnia

Definition of Stellate Ganglion Block (SGB): Stellate Ganglion Block is a medical procedure that involves the injection of medication into the stellate ganglion in the neck to block nerve signals. Multiple studies have shown that Stellate Ganglion Block (SGB) improves sleep quality by regulating the balance of the autonomic nervous system, influencing neurotransmitter release, reducing inflammation and pain response, and modulating hormone levels related to sleep. Through these pathways, SGB helps to decrease sympathetic nervous activity, lower stress responses and anxiety, and increase sleep-promoting neurotransmitters, thereby enhancing sleep depth and duration, and reducing the frequency of nocturnal awakenings.[20-25].SGB improves sleep quality by reducing the activity of the sympathetic nervous system. This reduction in activity can lower the levels of stress hormones (such as adrenaline and cortisol), thereby alleviating anxiety and improving sleep. Additionally, SGB is believed to increase the secretion of melatonin, a crucial hormone regulating the sleep-wake cycle. These studies provide strong evidence for the clinical use of SGB in improving sleep quality.

12. Progress in the Treatment of Refractory Insomnia with Anesthesia-Induced Sleep Therapy

Anesthesia-Induced Sleep Therapy (AIST) is an innovative approach in recent years for treating refractory insomnia. Its key feature is the use of anesthetic drugs to simulate a natural sleep state, thereby improving chronic and refractory insomnia symptoms. AIST, by mimicking the physiological state of sleep, aids in restoring normal function and structure to the brain. Studies indicate that this sleep modality can, to some extent, repair structural damage in the central nervous system[6]. This therapy is specifically targeted at patients with refractory insomnia who have not responded to traditional pharmacological treatments. Using anesthetic drugs such as Dexmedetomidine and Propofol helps these patients achieve higher quality sleep. While AIST has been effective in improving sleep in the short term, further research is needed to understand its long-term safety and potential side effects. This is particularly important for patients with specific health issues or those taking certain medications. In recent years, clinical trials and research on AIST have gradually

increased, aiding in further evaluating and refining the effectiveness and safety of this therapy[8].AIST is often integrated as part of a multidisciplinary comprehensive treatment, combining with pharmacotherapy, Cognitive Behavioral Therapy, and other non-pharmacological approaches to enhance therapeutic outcomes. As understanding of individual differences among patients deepens, AIST is increasingly leaning towards personalized treatment, tailoring the therapy to the specific conditions of the patient. Beyond improving nighttime sleep quality, this therapy also focuses on enhancing daytime functioning and overall quality of life for patients. The development of this therapy has fostered deeper research into sleep biology and the nature of sleep disorders, contributing to a better understanding of the underlying mechanisms of refractory insomnia.

II. Discussion

The treatment of refractory insomnia necessitates a multi-dimensional approach tailored to the specific needs and symptoms of individual patients. Key aspects of this multi-dimensional treatment include:Pharmacotherapy: This conventional treatment method involves the use of sleep medications such as benzodiazepines and non-benzodiazepines (like Dexmedetomidine and Propofol). These drugs work through different mechanisms in the brain to help patients fall asleep or maintain sleep.Behavioral Interventions: Cognitive Behavioral Therapy (CBT-I) is effective in treating insomnia. It reduces symptoms by changing patients' sleep habits and cognitive patterns.Dexmedetomidine: Mechanism of Action: Dexmedetomidine primarily produces sedation and hypnotic effects through α2 adrenergic receptor agonism, mimicking physiological sleep patterns. Research Progress: Studies show that Dexmedetomidine can improve sleep quality, particularly effective in patients with refractory insomnia[12]. Safety and Tolerability: Compared to other sedatives, Dexmedetomidine has better tolerability and fewer side effects.Propofol: Mechanism of Action: Propofol works by enhancing GABA receptor activity, producing rapid sedation. Research Progress: Although primarily used for anesthesia, some studies suggest its potential in managing treatment-resistant insomnia[8]. Precautions: The use of Propofol requires strict monitoring and control, especially in long-term treatments.SGB improves sleep quality by reducing sympathetic nervous system activity. This reduction lowers stress hormone levels (like adrenaline and cortisol), thus alleviating anxiety and enhancing sleep.Additionally, SGB is thought to increase melatonin secretion, a key hormone in regulating the sleep-wake cycle. These studies provide strong evidence for SGB's role in clinically improving sleep quality.EECP improves cerebral blood flow, cellular oxygenation and nutrition, and regulates related neurotransmitters, all of which can improve symptoms of insomnia. EECP is useful in improving sleep for elderly patients with sleep disorders.Anesthesia-Induced Sleep Therapy: Application Area: Targeting patients with refractory insomnia, especially those unresponsive to traditional treatments. Research Progress: Anesthesia-Induced Sleep Therapy simulates natural sleep states to regulate patients' sleep patterns, showing potential in treating refractory insomnia[13]. Safety and Operational Requirements: This therapy must be conducted in a professional medical setting to ensure safety and

efficacy.Anesthesia-Induced Sleep Therapy: This newer treatment method uses anesthetic drugs to induce a sleep-like state, helping restore the brain's sleep-wake balance.Summary: Dexmedetomidine, Propofol, and Anesthesia-Induced Sleep Therapy, as emerging methods for treating refractory insomnia, provide alternatives beyond traditional treatment options. However, these methods need to be conducted under strict medical supervision to ensure patient safety and treatment effectiveness. Future research should further explore the long-term effects and potential side effects of these methods in treating refractory insomnia.Environmental and Lifestyle Adjustments: Improving the sleep environment and adjusting lifestyle habits are crucial in treating insomnia. This includes maintaining good sleep hygiene, avoiding caffeine and nicotine, and regular exercise.Alternative Therapies: Including yoga, meditation, music therapy, etc., these therapies can help patients relax and improve sleep quality.Individualized Therapy: Based on specific factors such as accompanying diseases, age, and gender, doctors develop personalized treatment plans for patients.Long-term Tracking and Adjustment: Treating refractory insomnia is not a one-time process; it requires ongoing tracking and adjustment of the treatment plan based on patient response.Through this multi-dimensional approach, refractory insomnia can be effectively treated while minimizing the risks of side effects and dependency. The goal of this comprehensive treatment strategy is to improve patients' quality of life and maintain good sleep patterns long-term.Refractory insomnia treatment requires highly individualized approaches, as each patient's etiology, lifestyle, physical condition, and psychological state differ. Key aspects of an individualized treatment plan include:Comprehensive Assessment: Before starting treatment, patients must undergo a comprehensive assessment, including detailed medical history, lifestyle habits, psychological status, and sleep patterns. This helps identify potential causes and triggers of insomnia.Customized Treatment Strategy: Based on assessment results, doctors can develop a customized treatment plan. This may include specific medications, behavioral therapies, lifestyle changes, and even Anesthesia-Induced Sleep Therapy.Considering Comorbidities: Many insomnia patients may also have other health issues, such as anxiety, depression, or chronic pain. Individualized treatment plans need to consider these comorbidities.Flexible Adjustment of Plan: The treatment process should be flexible, adjusting based on patient response and therapeutic outcomes.

Patient Involvement: Active patient participation in the treatment process is key to success. Doctors should encourage patients to provide input on their treatment plans and make adjustments when necessary.Continuous Monitoring and Support: Treating refractory insomnia is a long-term process, requiring regular monitoring of patient progress and providing support when necessary.Psychological Support: In addition to medication and physical therapy, psychological support and counseling are important parts of the treatment plan, especially for patients with insomnia due to life stressors or psychological issues.Through individualized treatment plans, the unique needs of each patient can be more effectively addressed, improving the success rate of treatment, reducing the risk of side effects and dependency, and enhancing patients' quality

of life.While emerging treatment methods may be effective in the short term, their long-term therapeutic effects and safety need further research and verification. Continuous monitoring and assessment are crucial for ensuring the long-term success of treatment.Careful Selection of Pharmacotherapy: Although pharmacotherapy is common, long-term use may lead to dependency and other side effects. Therefore, careful consideration is needed in selecting medications, with strict monitoring during use.Advantages of Integrated Treatment: Combining pharmacotherapy, non-pharmacological treatments (like Cognitive Behavioral Therapy), and emerging therapies may offer a more comprehensive and effective solution for refractory insomnia.Future Research Directions: Future research should focus on assessing long-term treatment outcomes, improving quality of life, and the safety of new treatment methods. Additionally, a deeper exploration of the biological mechanisms of insomnia will help develop more precise and effective treatment methods.Socio-Economic Significance of Research: As societal pressures and the pace of life increase, insomnia problems become more prominent. Effective treatment methods not only improve patients' quality of life but also reduce the social and medical burden.

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