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TACKLING ANOREXIA: CURRENT TRENDS AND INNOVATIONS IN TREATMENT STRATEGIES

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ABSTRACT

Anorexia nervosa is a severe psychiatric disorder characterized by persistent food restriction, distorted body image, and an intense fear of weight gain. It exhibits one of the highest mortality rates among mental illnesses, second only to opioid use disorder. This review synthesizes current evidence on the etiology, diagnosis, comorbidities, and treatment of anorexia nervosa. The multifactorial pathogenesis includes genetic, neurobiological, psychological, and sociocultural components. Diagnostic criteria according to ICD-11 emphasize low body weight and behavioral patterns of restrictive eating. anorexia nervosa frequently coexists with medical complications affecting cardiovascular, gastrointestinal, endocrine, and skeletal systems, which contribute to its high morbidity and mortality. The review evaluates established psychological treatments, and family-based therapy, and highlights the limited and effectiveness of pharmacotherapy, including antidepressants and antipsychotics. Emerging treatments ranging from intranasal oxytocin, cannabinoids, and ketamine to neuromodulatory methods like repetitive transcranial magnetic stimulation and virtual reality therapy show promise, but require further validation. The paper also explores inpatient care, alternative therapies (acupuncture, electroconvulsive therapy), and interventions targeting complications such as bone density loss. Despite significant advancements, relapse rates remain high, and recovery is often incomplete, underscoring the urgent need for individualized, multidisciplinary treatment approaches and further research into mechanism-based and integrative therapies.

KEYWORDS

Anorexia Nervosa, BMI, Eating Disorders, Psychiatric Disorders, Food Restriction

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1. Introduction

Anorexia nervosa (AN) is a medical syndrome involving deliberate restriction of food intake in order to lose weight and strive for a slim figure. According to 2011 meta-analysis done by Arcelus et al. [1], AN has the second highest death rate of any mental disorder right after opioid addiction. It is estimated that round 22% of children and adolescents worldwide show signs of eating disorders (EDs) [2]. As claimed by STRIPED, in collaboration with the Academy for Eating Disorders and Deloitte Access Economics [3], AN affects 0.16% of females and 0.09% of males within a one-year period in the United States. Anorexia takes an average of five or six years from diagnosis to recovery. Up to 30% of patients do not recover. This makes meaningful control interventions crucial but difficult [4].

2. Methodology

This review synthesized literature addressing AN, with an emphasis on current and emerging treatment strategies. The primary aim was to collate, evaluate, and interpret findings on various therapeutic approaches, including psychological, pharmacological, neuromodulatory, nutritional, and adjunctive interventions. Literature searches were conducted using reputable academic databases such as PubMed, Scopus, Web of Science, and Google Scholar. The search included publications from 2000 to 2025, with a focus on works published between 2019 and 2024 to ensure relevance and timeliness. Inclusion criteria comprised peer-reviewed articles, clinical trials, systematic reviews, meta-analyses, and established treatment guidelines written in English or with an English-language abstract. Studies were selected if they addressed AN-related topics including etiology, treatment efficacy, comorbidities, or long-term outcomes. Exclusion criteria included non-peer-reviewed sources (e.g., editorials, opinion pieces), studies not specific to AN, and case reports lacking generalizability.

3. Results

Ethology and risk factors of anorexia nervosa

The ethology of AN is complex, with many genetic, psychological, environmental, and social variables. A genetic predisposition is necessary but not sufficient for the development of the disorder. Twin and family studies, brain scans of affected and unaffected family members, and a current multicenter gene analysis support observations that AN is found in families with obsessive, perfectionist, and competitive traits, and autistic spectrum traits. Another study shows that patients who have a first-degree relative with mental AN have a 10-fold increased risk of developing the disease [5]. There are many factors that predispose to developing AN. Among the most common are personal factors including genetic factors, endocrine factors, or abnormal metabolism of neurotransmitters such as serotonin, norepinephrine, endogenous opioids. In addition, specific personality traits can also increase the likelihood of developing AN. These include obsessive-compulsive personality, histrionic personality, schizoid or schizotypal personality, elevated levels of anxiety and low self-esteem[6]. AN could be precipitated as a coping mechanism against, for instance, developmental challenges, transitions, family conflicts, and academic pressures. The onset of puberty and adolescence are particularly common precipitants, but anorexia is also found without apparent precipitants in otherwise well-functioning families[7].

Diagnostic criteria

According to ICD-11 AN is the ED when the patients drastically reduce their food intake in order to achieve a low body weight, which is associated with a strong fear of gaining weight and a distorted perception of their own body. Visible symptoms include body weight below the lower limit for age and height – one of the criteria for the diagnosis of AN is a body mass index (BMI) of less than 18.5 kg/m2 in adults or a BMI < 5th percentile in children and adolescents. A consistent pattern of restrictive eating or other actions intended to achieve or maintain an unusually low body weight, often driven by an intense fear of gaining weight. Low body weight is overvalued and central to the person's self-evaluation, or the person's body weight or shape is inaccurately perceived to be normal or even excessive [8].

There are two subtypes of AN: the restrictive subtype haracterized by the patients who dramatically limit the amount and type of food they consume. The binge-purge subtype, when people restrict the amount and type of food they consume, but they may have binge-eating and purging episodes eating copious amounts of food in a brief time followed by vomiting or using laxatives or diuretics to get rid of what was consumed [9].

Diseases co-occurring with Anorexia nervosa

AN may be accompanied by changes in the structure and function of the heart, such as myocardial atrophy, mitral valve prolapse which is quite common in AN, pericardial effusion, sinus bradycardia, profound reversible sinus node dysfunction, and orthostatic hypotension [10]. Sudden cardiac death is often the cause of premature death in patients with AN [11].

AN unquestionably disrupts the functioning of the digestive system. As a direct result of weight loss and malnutrition, gastrointestinal transit time slows. Gastroparesis and constipation are quite common in patients with AN, especially as weight loss becomes more severe. Superior mesenteric artery syndrome-another disease which occurs in patients with AN as a result of weight loss-induced atrophy of the mesenteric fat pad. In early refeeding process due to small-bowel atrophy and a reduction in the absorptive area in patients with AN may be observed diarrhoea [12]. In addition, AN can result in several disorders of the body's functioning, including respiratory, hematopoietic, endocrine, nervous, or dermatological diseases.

Psychological treatment

Psychological treatment is the main treatment of AN indicated by guidelines. Three following methods are recommended as first line therapy in adult patients - Individual eating-disorder-focused cognitive behavioural therapy (CBT-ED), Maudsley Anorexia Nervosa Treatment for Adults (MANTRA) and specialist supportive clinical management (SSCM). If one of them cannot be used or is ineffective should be considered different of these three or eating-disorder-focused focal psychodynamic therapy (FPT) [13]. The results of the network meta-analysis do not fully confirm the guidelines for adult patients. There is no reliable evidence of a significant difference between the first-line therapy and treatment as usual (TAU) in outpatient adults with AN. This lack of difference pertains to symptoms, BMI, and dropout rates after up to 52 weeks post-randomization. Scientists suggest that there may be several reasons for these results. For example, TAU was carried out by experienced specialists who worked at, and were qualified by, the same institutions where the experimental treatments were implemented, some of which were also developed there. A further example is that this analysis focused solely on adult patients with AN, which may have flattened the effectiveness of different therapies, as adult patients with AN could have had a prolonged course of the disorder [14]. On the other hand, a recent meta-analysis revealed that the duration of an ED does not serve as a predictor for treatment outcomes [15]. In patients under 18 years of age family-based therapy is the main way. The second line are individual CBT-ED or adolescent-focused psychotherapy for anorexia nervosa (AFP-AN) [13]. Available evidence suggests that family-based therapy focused on EDs (FT-ED) may lead to more favorable weight outcomes than individual psychotherapy, particularly at the conclusion of treatment. However, this advantage appears to diminish over time, as no significant differences were observed at short or long-term follow-up periods. Interestingly, parent-only formats or those conducted separately for the adolescent and their caregivers tended to result in better weight outcomes at treatment completion compared to conjoint FT-ED. Nevertheless, insufficient follow-up data prevent firm conclusions about the durability of these effects, and preliminary findings imply that these differences may not persist in the long run [16]. Despite advancements in specialized treatment, currently available data do not allow for a definitive confirmation of the effectiveness of specific psychological interventions compared to other therapeutic strategies.

Antidepressants

Selective serotonin reuptake inhibitors did not reveal weight gain but some of them may alleviate concomitant symptoms [17]. It has not been proven that fluoxetine causes weight gain in people with AN. Moreover, in higher doses it reduced the probability of weight gain [18]. It has also not been proven that fluoxetine affects the time of onset of relapse [19].

Based on neurobiological understanding of AN escitalopram could be efficient and safe pharmacological treatment because studies revealed reduced serotonergic and enhanced dopaminergic transmission in AN. This entails that perfect drug should decrease dopaminergic transmission and increase serotonergic, and this is the action demonstrated by escitalopram. There is a need for clinical studies confirming or reject these considerations [20].

Tricyclics are not recommended and studied today because of elevated risk of death in case of suicide attempt and greater chance to provoke lethal arrythmia especially in young and low weight patients. Monoamine oxydase inhibitors are no longer used due to both their ineffectiveness in promoting weight gain and their adverse side effects [17].

A retrospective study focused on outpatient treatment revealed interesting observations. One key finding is that pharmacotherapy is more effective than no treatment, especially with antidepressants such as fluoxetine, escitalopram, paroxetine, sertraline, and mirtazapine. In patients who switched medications, no increase in BMI was observed. The authors provided two possible explanations for this. Firstly, it may be related to medication adherence rather than the specific drug. Secondly, it's possible that this group was simply more resistant to treatment [21].

Antipsychotic drugs

Second-generation antipsychotic drugs are often prescribed to patients suffer from resistant AN even though their effectiveness has not been confirmed in studies. Olanzapine is the most common second-generation antipsychotic drug in research studies for the treatment of AN. The primary outcome measure in research has most often been body weight. However, in 5 of 7 randomized controlled trials considered in meta-analysis, there was no alteration in patients body mass [22].

Some studies indicate that olanzapine causes weight gain at the end of treatment in adult patients suffering from AN. However, there is no evidence that it has a positive effect on psychopathological features characteristic in this condition [23,24].

Case-control observational retrospective study conducted in Italy indicated that adolescents receiving low-dose olanzapine and control group treated without antipsychotics noticed greater reduction of depressive symptoms, than patients in group treated full-dose olanzapine. Regardless, low dose olanzapine had no influence on AN symptoms [25].

Nevertheless, antipsychotics can be helpful in exceptional cases. Olanzapine and aripiprazole may support the treatment of AN when it is accompanied by significant obsessiveness and invasive, fixed cognition. Quetiapine could be useful when severe anxiety and mood disorders bothering patient [22].

Only few studies have been conducted to test the impact of aripiprazole on AN treatment. More studies are needed, especially randomized controlled trials. Results of retrospective case study showed that besides BMI increase, arypiprazole can alleviate anorexia symptoms. Additionally, aripiprazole has lower risk of side effects. But, the size of this sample was small, so we cannot generalise this finding [26].

Due to the lack of evidence supporting the effectiveness of second-generation antipsychotics in the treatment of anorexia, they should not be used either as first-line therapy or as monotherapy [22].

Oxytocin

The number of studies linking oxytocin to AN psychopathology has been increasing. A meta-analysis focusing on the influence of intranasal oxytocin on attentional bias and emotion recognition in patients with AN found no significant effects. However, the authors highlighted that brain exposure to the hormone may have been insufficient [27]. In contrast, in patients undergoing refeeding who received 36 IU of intranasal oxytocin for 4–6 weeks, reductions in eating concern and cognitive rigidity were observed. Additionally, a decrease in salivary cortisol levels suggested a potential reduction in neuroendocrine stress responsiveness related to nutrition and eating behavior [28].

Cannabinoids

There is no high-level evidence supporting the use of cannabinoids in the treatment of AN. Dronabinol may promote weight gain; however, its effect on the ED Inventory-2 (EDI-2) score was also investigated, and no significant changes were observed (McKee et al., 2021). A meta-analysis indicates that weight gain is significant when dronabinol is compared with placebo, but not when compared with diazepam [30].

Ketogenic diet and ketamine

A case report of a young woman with severe, long-standing AN who fully recovered after undergoing a novel therapeutic approach suggests a new direction in AN treatment. The first step of the intervention was the introduction of a ketogenic diet, which led to a 30–40% reduction in AN symptom severity. After two months, the patient received four ketamine infusions over a two-week period, resulting in complete remission. Six months later, she remained symptom-free while continuing the ketogenic diet [31].

Following this case report, pilot studies were conducted. The study involved five women who had achieved weight restoration but continued to experience persistent AN symptom. Participants followed a ketogenic diet for at least four weeks before receiving six ketamine infusions over 17 days. As in the initial case, patients experienced relief from AN symptom during the ketogenic phase, with further improvement

following ketamine treatment. Importantly, the intervention did not result in weight gain. One participant relapsed after four months, notably the only one who discontinued the ketogenic diet. The results suggest that this combined therapy may be both safe and promising. The authors also provided an update on the original case study patient, reporting that 28 months later, she remained in full remission, continued the ketogenic diet, and had gained weight [32].

Psylocibin

In the search for effective therapies for AN, an open-label feasibility study on psilocybin was conducted, in which psychological support accompanied the administration of the psychedelic. The results suggest that psilocybin treatment may be safe, well-tolerated, and acceptable. However, responses varied considerably between patients. Most participants found the therapy meaningful and beneficial. Four out of ten patients showed a significant reduction in ED symptoms at the three-month follow-up, although no significant effect on body weight was observed [33]. In animal models of activity-based anorexia (ABA), psilocybin supported the maintenance of body mass and enhanced cognitive flexibility. The study demonstrated that this cognitive effect depended on binding to the 5-HT1A receptor (5-HT1AR), as co-administration of psilocybin with a 5-HT1AR antagonist abolished the effect [34].

Low-dose testosterone

A reverse association has been observed between androgen levels and depression severity in females suffering from AN[35]. [23] Women with AN and relative androgen deficiency participated in a 24-week treatment with low-dose testosterone. The results showed that, compared to the placebo group, women receiving low-dose testosterone gained less weight and did not achieve sustained improvements in symptoms of EDs, depression, or anxiety [36].

Omega-3

Supplementation with omega-3 polyunsaturated fatty acids (PUFAs) does not appear to impact AN psychopathology or co-occurring conditions such as anxiety, depression, or obsessive-compulsive disorder. The only consistently reported benefit is nutritional restoration [37,38]. However, omega-3 PUFAs may enhance autonomic function in adolescent females with AN, particularly in cases of acute AN [39].

TNF-α and IL-6

A meta-analysis revealed that blood concentrations of TNF-α and IL-6 are elevated in patients with AN relative to individuals without the disorder[40]. Another meta-analysis demonstrated that inhibitors of the IL-6 pathway, such as tocilizumab, can lead to increases in body weight and body mass index (BMI). These findings suggest that inflammatory pathways may represent a potential therapeutic target for individuals with AN [41].

Caffeine

Caffeine metabolism depends primarily on the cytochrome P450 enzyme CYP1A2, whose activity varies significantly among individuals due to genetic factors [42]. It has been suggested that chronically elevated plasma caffeine levels may be associated with an increased risk of AN. Further research is needed to determine whether caffeine supplementation or restriction could have therapeutic or preventive effects in the context of AN [43].

Estrogen

Oligo-amenorrheic athletes with normal body weight exhibit increased expression of ED symptoms such as drive for thinness, cognitive rigidity, and greater body dissatisfaction (compared to non-athletes and eumenorrheic athletes). Among oligo-amenorrheic athletes who had not received estrogen therapy for 12 months, ED symptoms intensified, whereas no such increase was observed in those who received estrogen supplementation over the same period. These findings highlight the need for further studies to explore the role of estrogen in ED pathology and its potential therapeutic effect in patients with AN [44].

Dehydroepiandrosterone

A meta-analysis revealed that women with AN exhibit higher serum level of dehydroepiandrosterone (DHEA) and cortisol, but lower levels of dehydroepiandrosterone sulfate, compared to healthy controls. Monotherapy with DHEA does not improve bone mineral density (BMD), whereas combined treatment with DHEA and conjugated oral contraceptives has been shown to enhance BMD and reduce bone loss, but only in individuals with closed growth plates (physes) [45]. One study even reported a detrimental effect on BMD in adolescent patients with open physes [46]. The authors emphasize that, based on current evidence, DHEA supplementation is not a supported intervention for improving bone health in patients with AN [45].

IGF-1 and risedronate

A randomized controlled trial was conducted to assess the effects of six months of treatment with recombinant human insulin-like growth factor 1 (IGF-1), followed by six months of risedronate therapy, on BMD in women with AN. The study demonstrated that this sequential therapy, compared to risedronate alone or placebo, significantly increased areal BMD in the lateral lumbar spine. However, no significant improvements were observed at other skeletal sites [47].

Denosumab

Influence of denosumab on the spine bone density was also examined. After 12 months of treatment increased areal bone mineral density of lumbar spine in women that taking denosumab in comparison to women receiving placebo [48].

Estrogen and rhIGF-1

The addition of recombinant human IGF-1 (rhIGF-1) to transdermal 17-β estradiol therapy in young women with AN did not result in measurable improvements in bone outcomes. Interestingly, lumbar areal bone mineral density increased to a greater extent in the group that did not receive rhIGF-1, likely because of weight gain. The authors suggest that the absence of a detectable effect of rhIGF-1 may be attributed to the fact that participants receiving this treatment were in poorer health at baseline compared to those receiving estradiol alone [49].

GH

The effects of growth hormone therapy in children with AN and growth failure have been investigated. The study included only girls with a bone age below 12 years and boys with a bone age below 14 years. Findings suggest that growth hormone therapy is safe and may be effective in increasing growth velocity. However, due to the small sample size, lack of long-term follow-up, and other study limitations, further research is needed to confirm its efficacy and safety [50].

Ghrelin

A four-week treatment with relamorelin, a ghrelin receptor agonist, was found to improve gastric motility in women with AN. Additionally, it may support body weight gain. However, three participants randomized to relamorelin discontinued the medication due to increased hunger, and two of them withdrew from the study entirely [51].

Lactobacillus reuteri DSM17938

The impact of *Lactobacillus reuteri* DSM 17938 on bowel movements and nutritional recovery was analyzed in female pediatric patients with AN and comorbid constipation. Participants received either *L. reuteri* or placebo for three months, alongside nutritional therapy. No significant differences between the groups were observed at the end of the treatment period. However, three months later, differences in constipation relief and BMI increase became statistically significant [52].

Alternative Interventions and Novel Therapeutic Modalities in Anorexia Treatment

In the realm of AN treatment, while pharmacotherapy and psychotherapy are foundational pillars, a burgeoning interest in alternative and adjunctive treatments has appeared. These innovative approaches aim to address the multifaceted nature of anorexia by integrating physical, psychological, and neurobiological strategies to facilitate recovery.

Emerging therapeutic interventions, such as repetitive transcranial magnetic stimulation (rTMS) and virtual reality (VR) therapies, are gaining attention for their potential to treat AN. rTMS, a non-invasive brain stimulation technique, has shown promise in modulating neural activity related to eating behaviours and body image disturbances in AN.

The Potential of rTMS in treating Anorexia Nervosa

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive technique used to modulate neural activity, offering insights into the neurobiological underpinnings of psychiatric disorders, and providing a therapeutic intervention for conditions such as major depressive disorder (MDD) [53,54]. Given its FDA approval for MDD and emerging evidence of efficacy in AN, rTMS represents a novel, mechanism-based therapy that warrants exploration in AN and bulimia nervosa.

The use of high-frequency rTMS (HF-rTMS) targeting the right dorsolateral prefrontal cortex (DLPFC) has been associated with changes in food selection among individuals with AN, indicating a reduction in fat avoidance and a potential modulation of restrictive food choice behaviour (Study Procedures; Preliminary Experimental Test of Hypothesized Neural Mechanisms). These findings suggest that the DLPFC, a region implicated in decision-making, impulse control, and reward processing, plays a critical role in the pathophysiology of EDs.

Bulimia nervosa, characterized by episodes of binge eating followed by compensatory behaviours, shares common neural circuitry disruptions with AN, particularly in frontostriatal pathways [55,56]. The efficacy of HF-rTMS in modulating these pathways in AN provides a rationale for its application in bulimia nervosa, where dysregulation of impulse control and reward processing could be targeted to ameliorate binge-purge cycles.

Implications for Treatment Development

The preliminary findings from rTMS studies in AN underscore the necessity of further research into the neural substrates of EDs and the potential for rTMS to alter disease-specific behaviours. In AN, where effective treatment options are limited and relapse rates are high, rTMS offers a novel therapeutic strategy that directly targets neural dysfunction.

Mechanism-based research using rTMS to probe neural circuits in AN can illuminate the neurobiological underpinnings of the disorder and guide the development of targeted interventions. Research has demonstrated that rTMS has the potential to modulate behaviour, which may contribute to reducing core symptoms and improving impulse control in individuals with AN. The growing evidence supporting the use of HF-rTMS in AN highlights its therapeutic potential and underscores the importance of further studies to better understand treatment mechanisms and efficacy [57][5].

Future research should focus on identifying the optimal targets within the neural circuitry of AN and bulimia nervosa, determining the most effective stimulation parameters, and evaluating the long-term outcomes of rTMS treatment. Such studies are crucial for advancing our understanding of AN and bulimia nervosa and for developing mechanism-based treatments that offer hope to those affected by this challenging disorder [58][6].

The Role of Virtual Reality in the Therapy of Anorexia Nervosa

The emergence of Virtual Reality (VR) as a therapeutic tool offers a novel avenue for enhancing treatment outcomes in AN therapy. Interactive VR environments, employing three-dimensional graphics through head-mounted displays, provide an immersive experience that enables patients to engage with stimuli representing real-life scenarios within a medically supervised setting. This innovative approach is particularly advantageous in the context of EDs, including AN, characterized by distorted body image, pathological eating habits, and a relentless pursuit of an ideal body shape [59]. The incorporation of VR-based exposure therapies, notably VR-CET (Cue-Exposure Therapy in Virtual Reality), has garnered empirical support for its efficacy, particularly in addressing bulimia nervosa and binge eating disorder, demonstrating its potential applicability to AN [60–63]. These VR-based interventions facilitate exposure to highly controlled environments that mimic real-life situations associated with ED triggers, thereby enabling the safe exploration and modification of maladaptive responses. Furthermore, VR's capability to simulate body exposure therapies offers unique opportunities for patients with body image disturbances (BID), a prevalent issue in AN, by allowing them to confront and reevaluate their perceptions in a supportive and controlled manner [64–67].

The continuous evolution of VR technology, coupled with its increasing accessibility, underscores the potential for expanding and diversifying therapeutic options for EDs, suggesting a promising direction for future research and clinical practice. As the VR market advances, the scope for its application in AN treatment is expected to broaden, potentially introducing new alternative forms of existing therapies and contributing to the enhancement of treatment efficacy and patient engagement [68].

The Role of Acupuncture in the Treatment of Anorexia Nervosa

The integration of complementary medicine, particularly acupuncture, into the treatment regime for AN represents an emerging field of interest within both clinical and research contexts. Despite established allopathic medical guidelines for the management of EDs, including AN, there exists a notable gap in comprehensive guidelines for the implementation of complementary modalities like acupuncture. This gap underscores a critical need for structured guidance to optimize the adjunctive use of acupuncture in treating AN, drawing upon both evidence-based practices and established codes of conduct [69].

Acupuncture, utilized as an adjunctive therapy, has demonstrated potential in addressing various symptoms and co-morbid conditions associated with AN, such as anxiety, digestive issues, and sleep disturbances [70–72].

The emerging guidelines propose a multifaceted approach to the application of acupuncture in AN treatment, emphasizing diligent care and professional behaviour, collaboration with other healthcare professionals, and ensuring the practitioner's well-being, alongside specific clinical practice recommendations. The guidelines draw heavily on principles established by the Australian Health Practitioner Regulation Agency (AHPRA) and the National Health and Medical Research Council (NHMRC) [73,74] adapting these frameworks to suit the unique context of acupuncture in AN treatment.

Central to these guidelines is the endorsement of acupuncture as a complementary treatment, with evidence supporting its use in improving symptoms associated with AN, rather than as a primary treatment modality [70,71,75]. This distinction is crucial, aligning with the consensus that acupuncture serves best when integrated into a broader, multidisciplinary treatment strategy for AN. The inclusion of acupuncture in the treatment of AN, therefore, requires acupuncturists to adhere to a set of principles that ensures patient safety, fosters effective communication, and promotes collaborative care amongst healthcare providers.

Moreover, the guidelines acknowledge the importance of practitioner traits and qualities, such as empathy, respect, and professional boundaries, in fostering therapeutic relationships with AN patient [13,71,76,77]. Such relationships are pivotal to the success of treatment outcomes, particularly given the complex and sensitive nature of AN.

Electroconvulsive Therapy

Traditional treatment modalities for AN, including nutritional rehabilitation and psychological interventions such as cognitive-behavioural therapy and family-based therapy, often face limitations in the presence of severe depressive symptoms [78–80]. Electroconvulsive therapy (ECT) emerges as a potentially efficacious treatment for patients with AN who exhibit a severe comorbid depressive disorder and suicidal ideation, conditions where conventional treatments have not yielded adequate improvement [80,81].

Recent literature highlights the significantly heightened risk of suicidality in patients with AN, particularly in the context of comorbid mood disorders, making the effective treatment of depression within this population a priority [78,80]. However, the efficacy of antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), is often limited by gastrointestinal absorption issues due to prolonged abnormal eating patterns and potentially by the decreased availability of serotonin in severely underweight patients [81].

ECT, while traditionally reserved for severe, treatment-resistant depression, shows promising outcomes in terms of remission and response rates exceeding 60% and 70%, respectively [82], suggesting its utility in the context of AN with comorbid major depressive disorder (MDD). However, its application in patients with AN remains infrequent, even among those displaying severe depressive symptoms and suicidal behaviour [78–80,83]. This hesitancy may stem from concerns related to the general anaesthesia required for ECT and the potential for cognitive side effects, despite evidence suggesting its safety and efficacy in improving both depressive symptoms and BMI in this patient group [80].

A review of the existing literature, including retrospective studies and case reports, underscores the potential of ECT in facilitating not only an improvement in depressive symptoms but also in nutritional intake and weight restoration in patients with AN, without directly impacting disordered eating cognitions and body image distortions [80,83,84]. These findings suggest that ECT could serve as a crucial intervention for breaking

the cycle of severe depression and malnutrition in AN, thereby opening avenues for more effective engagement with nutritional and psychological treatments.

In conclusion, ECT represents a viable treatment option for patients with AN and severe comorbid depression, where traditional treatments fail to yield significant improvements. The integration of ECT with multidisciplinary care, encompassing medical treatment, psychotherapy, and nutritional support, is essential for addressing the complex needs of this patient population, promoting both psychological and physical recovery [79,80]. Further research is warranted to explore the long-term outcomes of ECT in AN, its impact on disordered eating cognitions, and the optimal protocols for its administration within this context.

Inpatient treatment

Due to the clinical guideline's outpatient care is recommended. However, higher levels of care, such as inpatient hospitalization provides an alternative to outpatient treatment for EDs. It is often recommended when the patient does not respond well to current treatment, is medically unstable, for example hypotension, bradycardia, arrythmia, hypothermia, dehydration, and refusal to drink, or is at elevated risk of harming themselves or others [85][86]. The risk of inpatient admission due to AN increased with the number of complications and prior diagnoses[86]. It is also noticeable that adolescents are more likely to being admitted to hospital than adults[86]. Due to the excessive costs of hospital treatment of patients, it is often short-term. Inpatient treatment offers multiple hours of treatment each day over a shorter period. Patients are monitored by an interdisciplinary team that monitors the patient's eating and prevents maladaptive compensatory behaviors [85]. Such a team should include a child and adolescent psychiatrist and/or pediatrician, a psychotherapist, a dietician, a physio- and/or occupational therapist and qualified nurses who can communicate with both the patient and their caregivers[86]. Once a patient's condition is stabilized enough in inpatient treatment, they can continue treatment at the lower levels of treatment [85]. It is noteworthy there are large discrepancies in admission rates and length of hospitalization between different countries in Europe. Nevertheless, there is international agreement on some of the medical and psychosocial indications for hospital admission[86].

Patients may be admitted either voluntarily or compulsorily. Many reviews of the literature and meta-analysis indicate BMI at discharge and BMI difference after treatment between the compulsory and the voluntary groups were similar regardless of baseline BMI in AN patient. Such results demonstrate that compulsory treatments are neither superior nor inferior to voluntary ones in influencing weight gain [87]. Nevertheless, BMI is not the only indicator of full recovery because psychological, emotional, and social criteria should be considered[88].

Involuntary treatment is justified on legal and ethical grounds by the life-threatening implications of the starvation state and the consumer's impaired capacity for autonomy from severe mental illness. It is crucial to understand patient's point of view. Many of them perceive involuntary treatment as humiliating and punitive, which may disrupt the entire therapeutic treatment[89]. Even though it has been shown that attitudes toward involuntary treatment often change over time during or even after treatment, with involuntarily admitted patients retrospectively recognizing the need for treatment[89]. It should be noted that compulsory treatments are not an alternative form of therapy but rather a choice of care responding to different conditions: lack of insight, lack of compliance to therapy, psychopathological and medical severity [89].

To summarize the hospital treatment of patients with anorexia, it is worth noting that there are studies indicating that all diagnoses demonstrated significant improvements in weight, EDs psychopathology, and comorbid symptoms, with some exceptions for the AN binge/purge group. In exploratory analyses almost 50% of patients met criteria for full or partial remission at discharge and 37% at follow-up.

Dicussion and Conclusions

Anorexia nervosa remains one of the most challenging psychiatric disorders to treat, owing to its complex etiology, high mortality rate, and frequent resistance to standard therapeutic interventions. Its development involves a dynamic interplay of genetic, neurobiological, psychological, and sociocultural factors, which complicates diagnosis and demands a nuanced, multidisciplinary treatment approach. While established psychological interventions such as CBT-ED, MANTRA, SSCM, and family-based therapy form the foundation of care, evidence of their superiority over standard treatment is often inconclusive, particularly among adult patients. High dropout rates, poor long-term outcomes, and frequent relapses underscore the need for more personalized and enduring strategies.

Pharmacological approaches, including antidepressants and second-generation antipsychotics, generally show limited efficacy in directly addressing core AN symptoms, though they may assist in managing associated mood or anxiety disorders. Emerging pharmacotherapies, including intranasal oxytocin, psilocybin, ketamine, and agents targeting inflammatory pathways (e.g., IL-6 inhibitors), offer promising directions but lack robust clinical validation. Small-scale studies combining nutritional strategies (such as ketogenic diets) with neuroactive agents (e.g., ketamine) have shown potential, yet these approaches require replication in larger, long-term trials.

Innovative non-invasive interventions, particularly repetitive transcranial magnetic stimulation and virtual reality-based therapies, have gained attention for their ability to modulate dysfunctional neural circuits and improve cognitive flexibility and body image disturbances. Similarly, complementary therapies like acupuncture and ECT may serve as valuable adjuncts in complex or treatment-resistant cases, especially where comorbid depression or anxiety is prominent.

Inpatient treatment remains a critical resource for individuals at medical risk or those who do not respond to outpatient care. While both voluntary and involuntary admissions have shown comparable outcomes in terms of weight restoration, ethical concerns about patient autonomy and perceived coercion must be carefully considered. Importantly, successful treatment should be evaluated not only by changes in body mass index but also by psychological recovery, emotional stability, and social reintegration.

Looking ahead, future research must prioritize the identification of neurobiological markers and personalized predictors of treatment response. Investigating the long-term impact of emerging therapies, as well as their optimal integration into existing care models, will be essential. Furthermore, the use of digital tools including mobile apps and virtual monitoring, holds potential to support early detection of relapse and enhance patient engagement.

In conclusion, addressing the persistent challenges of AN will require a shift toward integrative, evidence-based, and patient-centered treatment models. Expanding the therapeutic toolkit through innovation, while ensuring ethical and individualized care, is vital to improving prognosis and long-term quality of life for individuals affected by this debilitating disorder.

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