

Anorexia Nervosa: A Multi-Faceted Approach for Treatment

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ABSTRACT

Anorexia Nervosa is an eating disorder which involves self-restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory and physical health due to intense fear of gaining weight or of becoming fat. Effective and evidence based intervention in Anorexia Nervosa is quintessential due to the increasing prevalence, complications and mortality rate. This may include extensive therapy based on the need and medical status of the patient which may or may not require nutritional, pharmacological and psychosocial intervention. A critical review was undertaken on therapeutic treatment and complications of Anorexia Nervosa by understanding the underlying biochemical imbalances and psychosocial stressors. This review sheds light on evidence based research on nutrient intake for weight gain and maintenance along with careful management of refeeding syndrome and hormonal reactions. The outcomes of pharmacological treatments have been discussed. Modified and customized forms of psychological therapies including but not limited to family based therapy, enhanced cognitive therapy and psychodynamic therapy have been highlighted. Treatment methods in this manuscript have been widely used in various societies and yet require research and replicability. Vital access to treatment and recovery can also be hampered by a limited availability of care or lack of care in remote areas, by stigma, poor professional skills and poor understanding of the pathways to care. People with eating disorders can recover but they're at increased risk of relapse during periods of high stress or triggering situations. A holistic, longstanding and evidence based approach would prove to be effective in the treatment of the vulnerable population. Suggestions have been made for future research involving cultural perspectives, body perceptions according to gender and technological advancements.

Keywords: anorexia nervosa, nutritional therapy, psychological therapy, stress, nutrient deficiency, weight maintenance

INTRODUCTION

Disordered eating refers to a wide range of abnormal eating behaviors, many of which are shared with diagnosed eating disorders. Anorexia Nervosa is one such eating disorder which involves self-restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory and physical health. It involves intense fear of gaining

weight or of becoming fat, or persistent behavior that interferes with weight gain, even at a significantly low weight. There is disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Anorexia nervosa manifests in two forms vis the restricting type and binge

eating/purging type. People with restricting type of anorexia nervosa place severe restrictions on the quantity and type of food they consume. This could include counting calories, skipping meals, restricting certain foods such as carbohydrates and following obsessive rules, such as only eating foods of a particular color. These behaviors may be accompanied by excessive exercise. People with eating/purging type of anorexia also place restrictions on the food they eat but it is accompanied by binge eating or purging. Binge eating involves feeling out of control and eating a large amount of food. A person then 'compensates' for this eating by purging the food through vomiting, misusing laxatives, diuretics or enemas. These behaviors are unhealthy physically and mentally, and can even be life threatening.

The minimum level of severity is based, for adults, on current body mass index (BMI) or, for children and adolescents, on BMI percentile. The ranges below are derived from World Health Organization categories for thinness in adults whereas for children and adolescents, corresponding BMI percentiles should be used. The level of severity may be increased to reflect clinical symptoms, the degree of functional disability, and the need for supervision vis Mild: $BMI < 17 \text{ kg/m}^2$, Moderate: $BMI < 16-16.99 \text{ kg/m}^2$, Severe: $BMI < 15-15.99 \text{ kg/m}^2$ and Extreme: $BMI < 15 \text{ kg/m}^2$. The 12-month prevalence of anorexia nervosa among young females is approximately 0.4%. Less is known about prevalence among males, but anorexia nervosa is far less common in males than in females, with clinical populations generally reflecting approximately a 10:1 female-to-male ratio. Anorexia nervosa commonly begins during adolescence or young adulthood. It rarely begins before puberty or after age 40. The onset of this disorder is often associated with a stressful life event, such as leaving home for college (American Psychiatric Association, 2013). Hospitalization may be required to restore weight and to address medical complications. Most individuals with

anorexia nervosa experience remission within 5 years of presentation. Among individuals admitted to hospitals, overall remission rates may be lower.

The Crude Mortality Rate (CMR) for anorexia nervosa is approximately 5% per decade. Death most commonly results from medical complications associated with the disorder itself or from suicide. Suicide risk is elevated in anorexia nervosa, with rates reported as 12 per 100,000 per year. Comprehensive evaluation of individuals with anorexia nervosa should include assessment of suicide-related ideation and behaviors as well as other risk factors for suicide, including a history of suicide attempt(s). Individuals with anorexia nervosa may exhibit a range of functional limitations associated with the disorder. While some individuals remain active in social and professional functioning, others demonstrate significant social isolation and/or failure to fulfill academic or career potential.

It's important to seek ongoing therapy and nutritional education for treatment of anorexia nervosa. This may include extensive therapy based on the need and medical status of the patient which may or may not require nutritional, pharmacological and psychosocial intervention.

TREATMENT: Nutritional Therapy

It is the position of the American Dietetic Association that "nutrition intervention, including nutritional counseling, by a registered dietitian (RD) is an essential component of the team treatment of patients with anorexia nervosa, bulimia nervosa and other eating disorders during assessment and treatment across the continuum of care" (American Dietetic Association, 2006). The role of the RD includes close monitoring and assistance in individualized meal planning and counseling to achieve successful weight restoration. In cases of refractory anorectic patients that require enteral and parenteral nutrition, the RD plays an important role in

determining and monitoring the regimen and nutrition goals for these patients. Daily caloric increases are a challenge for anorectic patients. Patients struggle with wanting to maintain control over their food choices and also find difficulty in making basic menu selections to meet their calorie goals. This requires a balance of patience, empathy and flexibility from the RD. It is imperative to acknowledge small successes and provide encouragement for these patients. Patients often exhibit self-defeating behaviors and habits, therefore requiring consistent guidance. For example, guidelines and limitations may need to be set for the amount of time spent with the RD, menu substitutions, meal times, and meal supervision. Along with encouragement and education regarding meal plans and general nutrition, the RD can help the patient achieve goals to incorporate nutrition practices to return to a normal healthy lifestyle.

Hormones and Anorexia Nervosa

Eating behavior is complex and multifaceted. Stress reactivity, both psychological and physiological, may distinguish over eater from under eater. Reactions to stress are associated with enhanced secretion of a number of hormones including cortisol, glucocorticoids, catecholamines, growth hormone and prolactin, the effect of which is to increase mobilization of energy sources and adapt the individual to eating disorders (Ranabir and Reetu, 2011). Cortisol is the main hormone involved in appetite regulation and energy balance by increasing available energy through gluconeogenesis and lipolysis (Rabasa and Dickson, 2016). In animals, glucocorticoid administration and corticosterone replacement led to hyperphagia and weight gain (Adam and Epel, 2016). Overeating of 'comfort foods' in humans may be stimulated by cortisol in response to stress, which can result in eating behavior (Gibson, 2006). Cortisol favors central fat deposition which causes a decrease in the adipostatic signal and an

increase in the orexigenic signal. As a result appetite and food intake increase. This phenomenon contributes to the current epidemic of obesity (Siervo et al, 2009).

Ghrelin is another hormone produced by ghrelinergic cells in the gastrointestinal tract, which functions as a neuropeptide in the central nervous system. Besides regulating appetite, ghrelin also plays a significant role in regulating the distribution and rate of use of energy (Lenard and Berthoud, 2008). When the stomach is empty, ghrelin is secreted. When the stomach is stretched, secretion stops. It acts on hypothalamic brain cells both to increase hunger, and to increase gastric acid secretion and gastrointestinal motility to prepare the body for food intake (Cummings and Overduin, 2007). Leptin another important hormone made by adipose cells helps to regulate energy balance by inhibiting hunger. It is opposed by the actions of ghrelin. Both Leptin and Ghrelin act on receptors in the arcuate nucleus of the hypothalamus to regulate appetite to achieve energy homeostasis. In Anorexia Nervosa, a decreased sensitivity to leptin occurs, resulting in an inability to detect satiety despite high energy stores (Coll et al, 2007). Alterations in brain serotonin (5-hydroxytryptamine [5-HT]) function are also thought to contribute to diverse aspects of eating disorders, including binge eating, perfectionism and impulsivity of eating. It also contributes to mood-regulation.

Beside this, 5-HT anomalies in individuals with eating disorders are believed to have multiple determinants associated with secondary effects of their nutritional status, hereditary effects and long-term neurobiological sequelae of developmental stressors (Rask Andersen et al, 2010). Water soluble vitamins like vitamin B complex & vitamin C are more prone to washout from the body during stress as the brain utilizes more and more water soluble vitamins to produce energy. Therefore, body suffers from lack of these vitamins in stress conditions (Silverman et al, 2009). Several studies suggest that there

is little or no relation between vitamin A deficiency and eating disorder. It has been shown that eating disorder patients have higher plasma concentration of vitamins A and E. It is because in many eating disorder patients, especially women, the cholesterol concentration is found high compared to the normal individual. Therefore, fat soluble vitamins deposition is elevated. A significant correlation has also been observed between plasma cholesterol and both vitamin A and vitamin E concentrations (Rahman et al, 2016). Status of Vitamin B-6 gathers particular interest in patients with eating disorders. Vitamin B- is a coenzyme for 5-hydroxytryptophan decarboxylase, an enzyme involved in the serotonin biosynthetic pathway.

Serotonin appears to be involved in the control of appetite and it was suggested that drugs that increase central nervous system serotonergic activity are effective for treating eating disorders. It is possible that the chaotic eating of women with eating disorders may result from, or be worsened by, vitamin B-6 deficiency (Rahman et al, 2016). Several studies have observed that serum vitamin D levels are within the normal range among Anorexia Nervosa patients or it may even be higher when compared to controls. The reason for this is not fully understood. However, it may be a result of higher Vitamin D supplementation among patients with Anorexia Nervosa and/or changes in metabolic clearance and storage of this vitamin in adipose tissue (Holick, 2007).

The goals of nutritional rehabilitation for seriously underweight patients are to restore weight, normalize eating patterns, achieve normal perceptions of hunger and satiety, and correct biological and psychological sequelae of malnutrition (Marzola et al, 2013). A healthy goal weight for female patients is the weight at which normal menstruation and ovulation are restored and, for male patients, the weight at which normal testicular function is resumed.

Assessment and hospitalization

An assessment of eating disorder symptoms will assist the clinician in identifying target symptoms and behaviors that will be addressed in the treatment plan as well as in determining the diagnosis of eating disorder. A detailed report of food intake during a single day in the patient's life may be quite informative. A family history should be obtained regarding eating disorders and other psychiatric disorders, alcohol and other substance use disorders, obesity, family interactions in relation to the patient's disorder, and family attitudes toward eating, exercise, and appearance.

A detailed physical examination should be conducted by a physician familiar with common findings in patients with eating disorders. BMI, in conjunction with weight and height, has gained increasing attention in research and clinical settings as a tool for assessing eating disorder patients. Regular monitoring of BMI should be done. There are a host of other biochemical abnormalities to which attention has to be paid and those should be adequately treated.

Patients of eating disorders can be treated in intensive inpatient settings (in which subspecialty general medical consultation is readily available) to residential and partial hospitalization programs to varying levels of outpatient care. Patients who weigh less than approximately 85% of their individually estimated healthy weights have considerable difficulty gaining weight outside of a highly structured program. Healthy weight estimates for a given individual must be determined by that person's physicians on the basis of historical data (e.g., growth charts) and, for women, the weight at which healthy menstruation and ovulation resume, which may be higher than the weight at which menstruation and ovulation became impaired. In one study of 100 adolescent patients with anorexia nervosa, the resumption of menses occurred at a weight approximately 4.5 pounds greater than the weight at which menses was lost, at 90% of

healthy weight, 86% of patients resumed menses (Chakraborty and Basu, 2010).

Others factors which determine hospitalization include a rapid or persistent decline in oral intake; a decline in weight despite maximally intensive outpatient or partial hospitalization intervention; the presence of additional stressors, such as dental procedures, that may interfere with the patient's ability to eat; the weight at which the patient was medically unstable in the past; co-occurring psychiatric problems that merit hospitalization; and patient's denial and resistance to participate in his or her own care in less supervised settings (Yager and Powers, 2008).

Weight gain and maintenance

Refeeding programs should be implemented in nurturing emotional contexts. Nursing supervised oral refeeding of normal food in appropriate amounts and composition is preferred. Clinical consensus suggests that realistic targets are 2-3 lb/week for hospitalized patients and 0.5-1 lb/week for individuals in outpatient programs, although an intensive partial hospitalization, stepped-down program has reported gains of up to 2 lb/week. Occasionally, some patients may gain as much as 4-5 lb/week, but these individuals must be carefully monitored for refeeding syndrome and fluid retention. Intake levels should usually start at 30-40 kcal/kg per day (approximately 1,000-1,600 kcal/day). During the weight gain phase, intake may have to be advanced progressively to as high as 70-100 kcal/kg per day for some patients; many male patients require a very large number of calories to gain weight (Chakraborty and Basu, 2010).

For weight maintenance, it was found that weight-restored patients with anorexia nervosa often require 200-400 calories more than sex-, age-, weight-, and height-matched control subjects to maintain weight (Kaye et al, 1991). In a study, the weight, height, eating disorder symptoms, and severity of depressive and anxiety symptoms were assessed in 22 women with

anorexia nervosa at hospital admission and at follow-up occurring a mean of 29 months after patient discharge (Baran et al, 1995). The patients who were discharged while severely underweight reported significantly higher rates of re-hospitalization and endorsed more symptoms than those who had achieved normal weight before discharge. In another study, patients admitted to an inpatient service over a seven-year period, patients who were admitted involuntarily showed the same short-term rates of weight gain as those who were admitted voluntarily (Watson et al, 2000). Moreover, most of those who were involuntarily treated later affirmed the need for and exhibited a better attitude toward the treatment process.

Nutrient Intake

The other issue, aside from the amount of food needed for nutritional restoration is the question as to what types of foods are best and/or acceptable to those with Anorexia Nervosa. Surprisingly, there has been very little research on this issue, despite the fact that nutritional rehabilitation is a core focus of most Anorexia Nervosa programs. From a nutrition standpoint, the chances of replenishing macro and micronutrient needs are enhanced by increasing the variety of foods that are prescribed for the patient with Anorexia Nervosa (Marzol et al, 2013). In reality, this represents a great difficulty for patients as resistance to eating a variety of foods is a core element of their symptomatology. An important clinical issue is that no specific recommendations for macronutrient distribution in people with eating disorder have been developed. It should be noted that the daily macronutrient required (in adolescents and adults) to maintain weight (not gain), as defined by the Institute of Medicine, are 110-140 grams of carbohydrates, 15-20 grams of essential fatty acids and 1 gram of proteins per kilogram of body weight (Otten et al, 2006). Recommended Daily Allowances (RDA's) for vitamins and minerals vary by age and

gender, but can be met by intake of a multivitamin/multimineral tablet or liquid. Placing the emphasis on nutrient requirements, achieved through food intake, as opposed to caloric intake, may help to lessen the anxiety and resistance to refeeding observed in Anorexia Nervosa patients.

It has been suggested that the Anorexia Nervosa patient should be eating calorie dense food to replenish the necessary nutrients (Lutter and Rivera, 2003). Daily intake of foods containing protein of high biological value, such as whey and casein, and egg whites, that contain a high concentration of essential amino acids per gram and calorie density, should be recommended. Consuming small amounts of protein of high biological value, in conjunction with the protein source foods that are perceived as less challenging by Anorexia Nervosa patients (usually of a vegetable source), can help assure a faster restoration of nutrient status even in a continued state of reduced body weight. Additionally, a variety of protein food sources including fleshy fish and poultry should be encouraged.

Fat intake is a critical issue during Anorexia Nervosa refeeding. It is well known in scientific literature and in everyday clinical practice that Anorexia Nervosa individuals tend to avoid consuming fats resulting in lipid depletion and alterations (Misra et al, 2006). Importantly, neuronal walls and wiring between brain regions is highly dependent on lipid function. It is particularly important that Anorexia Nervosa patients replenish these stores by eating lipids-rich foods during treatment. Many fatty acids can be produced endogenously, but linolenic acid, an omega-3 polyunsaturated fatty acid, and linoleic acid, an omega-6 polyunsaturated fatty acid, are essential fatty acids that must be provided in the diet. These essential fatty acids are crucial for cellular membrane function and gene regulation (Rossell et al, 2005). Eicosapentaenoic acid (EPA) is the precursor for eicosanoids and the

docosahexaenoic acid (DHA) is a fundamental structural component of grey matter and retina. EPA and DHA are two important long-chain omega-3 fatty acids that can be found in high amount in fish, meat, and eggs. These are food sources that Anorexia Nervosa patients tend to avoid, making the need to replenish EPA and DHA even more critical. It has been demonstrated that levels of plasma long-chain omega-3 fatty acids in vegetarian and vegan individuals are lower than in meat-eaters. In Anorexia Nervosa, enhancement of the biosynthesis of alternative fatty acids was found only partially compensated for the loss of polyunsaturated fatty acids. It is interesting to note that use of an EPA derivative (ethyl-eicosapentaenoate, Ethyl-EPA) administered as a daily supplement at 1 gram/day for a 3 month period, in a small sample of Anorexia Nervosa patients, resulted in positive outcomes in terms of weight restoration (Ayton et al, 2004).

A variety of carbohydrates can be offered, such as complex carbohydrates (bread, rice and potatoes) as well as fruits, fruit juices and vegetables. The choices made by the patient can be incorporated into the rest of the food ingredients. Vitamin and mineral RDA's can be achieved through use of supplements in liquid or tablet form, that can augment the vitamin and mineral content found in foods. The use of medical foods that are acceptable to the Anorexia Nervosa patient may also be considered when patients cannot eat a sufficient amount of food to achieve weight restoration or as a useful addition in case of unstable weight maintenance. Medical foods may reduce the stomach and gastrointestinal discomfort that refeeding with more caloric dense food may exaggerate. Moreover it has been showed that in Anorexia Nervosa patients, there is a delayed gastric emptying of solid but not of liquid meals, therefore liquid supplementations can be a well-tolerated intervention mostly at the beginning of refeeding treatment (Abell et al, 1987).

Refeeding Syndrome

Different types of gastric feeding and Total Parenteral Nutrition (TPN) may be indicated on a rare basis for more refractory cases of Anorexia Nervosa. TPN is a specialized procedure and should be undertaken only when medically necessary and by an experienced clinician, with the support of an experienced nursing and nutritional staff. Clinicians caring for these patients must be cognizant of the art of the refeeding process, given the multitude of potential clinical and biochemical caveats that can develop. The main tenet is to avoid overly aggressive refeeding protocols early in the refeeding process. Intake levels usually begin at approximately 600-1000 kcal/day and are increased by 300-400 kcal every three to four days. The treatment corollary of this is to individualize intake based on the rate of weight gain. Supplementing the diet with a liquid supplement in the early stages of refeeding to achieve the prescribed calorie goal is a very effective strategy to achieve weight gain. Liquid supplements can also be of value when added to achieve large caloric intake. Some programs recommend ultimately attaining an intake of 4000 to 5000 kcal per day, while others peak at 3000 to 3600 kcal per day. Even for normal weight adults, weight gain does not correlate exactly with the total excess calories ingested over basal requirements. In general, starved anorectics are metabolically inefficient, and may require more than the expected 3,500 kcal beyond maintenance caloric needs to restore a pound of body weight. The caloric requirement necessary to cause weight gain can vary between 1800 kcal/day and 4500 kcal/day.

Some simple general rules to follow are: (1) the Total Energy Expenditure (TEE) should never exceed twice the Basal Energy Expenditure (BEE), (2) caloric intake should rarely exceed 70 to 80 kcal per kilogram of body weight or 35 to 40 kcal/lb, (3) with the severely anorectic patient, begin a diet at 20 to 25 kcal per kilogram, (4) protein intake should not exceed 1.5 to 1.7 grams per kilograms of body weight, and is

generally in the 1 to 1.5 grams range, (5) if TPN or enteral feedings are being used, carbohydrate intake should not exceed 7 mg/kg/min, (6) weight gain should be in the two to three pounds per week range. Males generally peak at 4,000 kcal/day and females at 3,500 kcal/day. All approaches requires vigilant clinical and laboratory monitoring and individualization of a dietary plan depending on the rate of weight gain and the laboratory and clinical course of the patient. (Mehler, 2010).

Forced nasogastric or parenteral feeding can each be accompanied by substantial dangers. When nasogastric feeding is necessary, clinical experience suggests that continuous feeding (i.e., over 24 hours) may be less likely than three to four bolus feedings a day to result in metabolic abnormalities or patient discomfort and may be better tolerated by patients (Steinhausen, 2002). As an alternative to nasogastric feeding, in very difficult situations where patients physically resist and constantly remove their nasogastric tubes, gastrostomy or jejunostomy tubes may be surgically inserted. Ten to fifteen per cent cases of Anorexia Nervosa require hospital based involuntary treatment. The general agreement is that children and adolescents who are severely malnourished and in grave medical danger should be refed, involuntarily if necessary, but that every effort should be made to gain their cooperation as cognitive function improves (Beumont et al, 2004).

PHARMACOLOGICAL TREATMENT

The etiology of anorexia nervosa appears to be multifactorial with genetic, neurobiological and psychological factors contributing to its development and maintenance (Miniati et al, 2016). Proposed contributing factors include serotonergic dysfunction, dopaminergic dysfunction and disturbances in the metabolism of norepinephrine (Bosanack et al, 2005). Indeed, what causes anorexia nervosa remains not fully understood. Proposed pharmacological treatment for anorexia

nervosa has been based on these biological theories, neurobiological research into the control of appetite and food intake, on clinical observations and uncontrolled studies (de Vos et al, 2014). Specifically, medications have been trialed to target maladaptive thought patterns, stimulate appetite, treat comorbid symptoms and prevent relapse after recovery. To date there is no established or recommended pharmacologic treatment for anorexia nervosa (Hebedrand, 2011).

Prior research has explored the potential applications of antidepressants, antipsychotics, nutritional supplements and hormonal treatments with mixed results (Crow et al, 2009). Historically, tricyclic antidepressants initially appeared promising but later randomized control trials did not support their routine use. As their use has also been associated with fatal cardiac arrhythmias in patients with low body weight, they are no longer recommended for clinical use in Anorexia Nervosa. Similarly, Lithium was reported to have benefit in weight restoration in early research but the electrolyte changes associated with starvation make its use medically dangerous. Early research on Selective Serotonin Reuptake Inhibitors also appeared promising but larger studies with longer follow-up reported no benefit in weight stabilization or relapse prevention (Flament et al, 2012).

Most recently, attention has turned to a potential role for antipsychotic medications in the treatment of Anorexia Nervosa. This work was predicated on an interpretation as Anorexia Nervosa patient's perceptions of their bodies as delusional. Second generation antipsychotics in particular were proposed as a way to treat serotonergic and dopaminergic dysfunction, to manage comorbid anxiety and depression and to induce weight gain (Kishi et al, 2012). Initial work on this hypothesis again seemed promising with several small studies reporting positive weight gain and decreased eating disorder psychopathology. However, most of these studies had small

sample sizes, unblinded participants and short periods of follow-up (McElroy et al, 2015). These studies have also been included in a two recent meta-analyses of randomized control trials of antipsychotics in anorexia nervosa that have reported no significant benefits in weight gain, eating disorder attitudes, anxiety or depressive symptoms in anorexia nervosa with second-generation antipsychotics when compared with placebo. The exception to this conclusion was very limited data suggesting that quetiapine can decrease comorbid anxiety and improve eating disorder attitudes based on one study that has not been replicated. Importantly, second-generation antipsychotic side effects including akathisia, drowsiness and elevated blood sugar have also been reported in several studies, further calling the potential balance between benefit and risk for into question (Kishi et al, 2012).

PSYCHOLOGICAL TREATMENT

Refeeding the anorectic patient is essential to achieving a successful treatment result by restoring body weight. Due to starvation-induced cognitive deficits in the patients, meaningful psychotherapy is possible only after concerted refeeding effort. However, weight restoration may be one of the most challenging and frustrating parts of the recovery process for many patients with anorexia nervosa. Traditionally, centers that treat patients who have moderate and severe degrees of anorexia nervosa have used a combination of behavioral techniques, cognitive restructuring, and a progressive structured program of oral caloric intake, to achieve the goal of weight restoration.

Perfectionism is well-known to co-occur with eating disorders (Shafran et al, 2002). Under these circumstances there is often an interaction between the two with the patients' perfectionist standards being applied to their attempts to control eating, shape, and weight, as well as to other aspects of their life. The original version of the cognitive behavioral theory recognized

that adverse mood states can disrupt dietary restraint and constitute a trigger of binge eating. It subsequently became clear that in some patients there is a more complex relationship between emotional states and binge eating (Waller, 2002). There can be no doubt that interpersonal processes contribute in a variety of ways to the maintenance of all forms of eating disorder (Cooper and Fairburn, 2011).

Family-based treatment is a three-phase treatment for adolescent patients with anorexia nervosa and their families over 16 1-hour sessions and a 9-month period (initially of 10 hours during 6 months). In the first phase, therapy is characterized by attempts to absolve the parents from the responsibility of causing the disorder and by complimenting them on the positive aspects of their parenting. Families are encouraged to work out for themselves how best to help restore the weight of their child with anorexia nervosa. In phase 2, parents are helped to transition eating and weight control back to the adolescent in an age-appropriate manner. The third phase focuses on establishing a healthy relationship between the adolescent and the parents. 24 1-hour sessions are provided over the 1-year period (Yager et al, 2014).

Specialist Supportive Clinical Management (SSCM) treatment should be delivered by therapists specialized in the treatment of eating disorders and should provide a standardized form of usual outpatient treatment. Patients with anorexia nervosa and a BMI of 15 kg/m² or lower receive up to 30 once-weekly individual therapy sessions and four monthly follow-up sessions. In those patients with a BMI >15kg/m² the number of sessions could be reduced to 20. It combines clinical management (i.e., giving information, advice and encouragement) with a supportive therapeutic style designed to build a positive therapeutic relationship and to foster change. Therapy content includes assessment, identification, and regular review of target symptoms, psychoeducation, monitoring of physical

status, establishment of a goal weight range, and nutritional education and advice. The aim is to help patients make a link between their clinical symptoms and their abnormal eating behavior and weight, and to support patients in a gradual return to normal eating behaviour and weight. Additional therapy content is determined by the patient (McIntosh et al, 2006).

Maudsley Model of Anorexia Treatment for Adults (MANTRA) is an empirically based cognitive-interpersonal treatment, which proposes that four broad factors, linked to underlying obsessional and anxious (or avoidant) personality traits, are central to the maintenance of anorexia nervosa. These are (1) a thinking style characterized by inflexibility, excessive attention to detail, and fear of making mistakes; (2) impairments in the socio-emotional domain (e.g., avoidance of emotional experience, regulation, and expression); (3) positive beliefs about how anorexia nervosa helps the person in their life; and (4) unhelpful responses of close others (e.g., over-involvement, criticism, accommodation to symptoms). These factors are targeted in treatment with the aim of improving weight, eating disorder and other symptoms, and psychosocial adjustment. The treatment style is motivational. Differences from other treatments include that the model was developed specifically for anorexia nervosa, it is based on biological and psychological research, and is tailored to characteristic temperamental traits in this disorder.

CBT-E is the abbreviation for “enhanced cognitive therapy”, and it refers to a “trans-diagnostic” personalized psychological treatment for eating disorders. It was developed as an outpatient treatment for adults but is an intensive version for day patient and inpatient settings, and a version for younger people. As an outpatient therapy treatment CBT-E has four stages and is available in a short (20 sessions) and longer version (40 sessions). In stage one, the focus is on gaining a mutual understanding of the person’s eating

problem and helping him or her modify and stabilize their pattern of eating. In the brief second stage progress is systematically reviewed and plans are made for the main body of treatment. Stage three focuses on the processes that are maintaining the person's eating problem (e.g., addressing concerns about shape and eating). In the last stage the emphasis shifts onto the future. There is a focus on dealing with setbacks and maintaining the changes that have been obtained (Fairburn, 2003).

Focal Psychotherapy (FPT) is an outpatient psychodynamic-oriented psychotherapy for moderately ill patients with anorexia nervosa (BMI >15 kg/m²). The first phase focuses mainly on therapeutic alliance, pro-anorectic behavior and ego-syntonic beliefs (attitudes and behavior viewed as acceptable), and self-esteem. In the second phase of treatment, main focus is placed on relevant relationships and the association between interpersonal relationships and eating (anorectic) behavior. The pertinent aspects of the final phase are the transfer to everyday life, anticipation of treatment termination, and parting. Before every treatment session the patient's weight is assessed and documented (Zipfel et al, 2014).

MEDICAL COMPLICATIONS

The semi-starvation of anorexia nervosa, and the purging behaviors sometimes associated with it, can result in significant and potentially life-threatening medical conditions. The nutritional compromise associated with this disorder affects most major organ systems and can produce a variety of disturbances. Physiological disturbances, including amenorrhea and vital sign abnormalities, are common. While most of the physiological disturbances associated with malnutrition are reversible with nutritional rehabilitation, some, including loss of bone mineral density, are often not completely reversible. Behaviors such as self-induced vomiting and misuse of laxatives, diuretics, and

enemas may cause a number of disturbances that lead to abnormal laboratory findings; however, some individuals with anorexia nervosa exhibit no laboratory abnormalities.

Leukopenia is common, with the loss of all cell types. Mild anemia can occur, as well as thrombocytopenia and, rarely, bleeding problems. Hematologic abnormalities, with trilinear deficiencies in red cells, white cells, and platelets, have been described in those with mild to moderate anorexia nervosa. Cell line abnormalities appear to be related to gelatinous transformation of the bone marrow, rather than to vitamin deficiency (Misra et al, 2006). Gelatinous marrow transformation is characterized by fat cell atrophy, loss of hematopoietic cells, and deposition of extracellular, gelatinous mucopolysaccharides, rich in hyaluronic acid. Additionally, patients with anorexia nervosa and hematologic deficiencies are inappropriately referred for bone marrow biopsy, with workups for malignancy that delay appropriate management of the eating disorder (Sabel et al, 2013). It is known that gelatinous marrow transformation resolves with adequate nutrition and weight restoration, as long as the underlying pathology is resolved or controlled.

Dehydration may be reflected by an elevated blood urea nitrogen level. Hypercholesterolemia is common. Hepatic enzyme levels may be elevated. Self-induced vomiting may lead to metabolic alkalosis (elevated serum bicarbonate), hypochloremia, and hypokalemia. Laxative abuse may cause a mild metabolic acidosis. Serum thyroxine (T4) levels are usually in the low-normal range, triiodothyronine (T3) levels are decreased, while reverse T3 levels are elevated. Females have low serum estrogen levels, whereas males have low levels of serum testosterone. Cardiac abnormalities, specifically cardiomyopathy are known in patients with Anorexia Nervosa and have been attributed to the deficiency of multitude of minerals, vitamins and electrolytes. It is important to recognize that patients with anorexia can

develop cardiac dysfunction and early nutrition along with medical optimization can lead to complete reversal of cardiac dysfunction.

Low bone mineral density, with specific areas of osteopenia or osteoporosis, is often seen. The risk of fracture is significantly elevated. Diffuse abnormalities, reflecting a metabolic encephalopathy, may result from significant fluid and electrolyte disturbances. There is often a significant reduction in resting energy expenditure. Many of the physical signs and symptoms of anorexia nervosa are attributable to starvation. Multi-disciplinary team approach involving cardiologist, metabolic support, internist, and psychiatrist is required for appropriate care of these patients. A multi-disciplinary team including cardiologist, nutritionist, social support, psychologist, psychiatrist and other medical specialists specific to cases is required for the management of anorexia nervosa.

CONCLUSION

Effective and evidence based intervention in Anorexia Nervosa is quintessential due to the increasing prevalence, complications and mortality rate. Treatment methods in this manuscript have been widely used in various societies and yet require research and replicability. Vital access to treatment and recovery can also be hampered by a limited availability of care or lack of care in remote areas, by stigma, poor professional skills and poor understanding of the pathways to care. Uncontrolled environmental factors such as impact of social media, cosmetic industries, bullying and body shaming are of importance in understanding the process of psychotherapy as well as nutrition habits. Psychological research can further be conducted in the cultural context of Eastern Countries where increase in eating disorders is still considered the by-product of "Westernization". As far as the scope of this review is concerned, there is a major barrier to treatment which is not seeing anorexia

nervosa as an illness but rather a lifestyle choice. People with eating disorders can recover but they're at increased risk of relapse during periods of high stress or triggering situations. Thus, a holistic, longstanding and evidence based approach would prove to be effective in the treatment of the vulnerable population.

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