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Nutritional Outcome Measures of Preadolescents and Adolescents Diagnosed with Anorexia Nervosa after Receiving Nasogastric Feedings versus Oral Diet upon Hospitalization

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Literature Review

Anorexia Nervosa Overview

Anorexia nervosa (AN) is a disease characterized by severe energy restriction due to an irrational fear of weight gain, thus resulting in weight loss and low body weight (Kelly, Shank, Bakalar, & Tanofsky-Kraff, 2014). Anorexia nervosa is also associated with potential life threatening consequences and has been linked to a substantially increased risk of death with a mortality rate due to all causes of death of approximately 5.0% per decade (Herzog et al., 2000) (Kelly et al., 2014). Although approximately one in five deaths associated with AN is a result of suicide (Arcelus, Mitchell, Wales, & Nielsen, 2011), 4% of individuals diagnosed with AN die from the medical complications of malnutrition (Crow et al., 2009) (Rylander, Brinton, Sabel, Mehler, & Gaudiani, 2017).

Diagnostic and Statistical Manual of Mental Disorders-5 Diagnostic Criteria for AN

In 2013, the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-4*) was updated to its fifth edition (*DSM-5*). The new *DSM-5* diagnostic criteria for AN includes the following: persistent restriction of calories, reported fear of weight gain or persistent behavior to prevent weight gain, and a disturbance in one's self-evaluation of body image (American Psychological Association, 2013). *DSM-5* also introduces body mass index (BMI) severity ratings (Mustelin, Silen, Raevouri, Hoek, Kaprio, & Keski-Rahkonen, 2016). The diagnostic BMI categories of AN are as follows: extreme (BMI < 15 kg/m^2), severe (BMI 15-15.99 kg/m^2), moderate (BMI 16-16.99 kg/m^2), and mild (BMI > 17 kg/m^2) (Kenny, Lichterman, & Abdelmonem, 2014). BMI percentiles are defined as thinness grade two (BMI < 3^{rd} percentile), thinness grade one (BMI 3^{rd} to 16^{th} percentile), normal weight (BMI 16^{th} to 85^{th}

percentile), overweight (BMI 85th to 95th percentile), and obese (BMI > 95th percentile) (Flament et al., 2015). As a result of the new diagnostic criteria, including the exclusion of amenorrhea, a Finnish longitudinal study found *DSM-5* is capable of capturing a 60% increase in lifetime prevalence of AN, from 2.2% to 3.6% (Mustelin et al., 2016). *DSM-5*'s new diagnostic criteria allows for more specific diagnoses in regards to severity of the disease and has the potential to diagnose those not presenting with amenorrhea.

Prevalence of Anorexia Nervosa

Retrospective data suggest AN typically begins in early adolescence (Nagl et al., 2016) and is most commonly diagnosed among female adolescents (Committee on Adolescence, 2003) (Smink, van Hoeken, Hoek, 2012). There is scarce research on the prevalence of AN among adolescents when *DSM-5'*s new AN diagnostic criterion is applied. Despite the little available research, a prospective longitudinal study found the 12-month prevalence of AN at baseline to be 0.4% and the cumulative lifetime incidence of AN to be 1.7% (Nagl et al., 2016). Similarly, a Dutch cohort study found the prevalence of AN to be 1.7% in adolescents when using the new *DSM-5* diagnostic criteria (Smink, van Hoeken, Oldehinkel, & Hoek, 2014). In contrast, data collected from the National Comorbidity Replication survey conducted in 2001-2003 revealed 0.9% of American women suffer from AN in their lifetime while 0.3% of American men suffer from AN in their lifetime based upon *DSM-4* criteria (Hudson, Hiripi, Pope, & Kessler, 2007).

Complications Associated with AN

Due to weight loss and malnutrition, AN affects multiple organs and physiological functions throughout the body of adolescents and preadolescents. Most medical complications

experienced by those with AN are treatable. However, some complications may result in permanent harm. The medical complications of AN secondary to malnutrition include electrolyte and volume status imbalances, cardiac function abnormalities, impaired gastrointestinal (GI) function, reduced bone mineral density, decreased liver function, abnormal reproductive function, endocrine abnormalities, and decreased musculoskeletal strength (Rylander et al., 2017). Patients suffering from AN are also at an increased risk of developing renal and respiratory issues along with dental problems, neurological impairments, and hematological abnormalities (Kelly et al., 2014). Patients with AN may also experience iron deficiency anemia, amenorrhea, and seizures as a result of restricting energy intake. Specific GI issues associated with caloric restriction include gastroparesis resulting in constipation, early satiety, and bloating, all of which are reversible with weight restoration (Westmoreland, Krantz, & Mehler, 2016). Renal issues observed in patients with AN include increased blood urea nitrogen, risk of kidney stones, and peripheral edema (Committee on Adolescence, 2003). While no organ is safe from the effects of AN, many of its associated medical complications are reversible with adequate weight gain; therefore, prompt and effective clinical interventions are necessary.

Complications can also arise during the refeeding process of patients with severe malnutrition due to electrolyte imbalances (Gentile, 2012). Refeeding syndrome is a complication that can arise when increasing the caloric intake of severely malnourished patients, occurring in six to seven percent of patients diagnosed with AN (Golden, Keane-Miller, Sainani, & Kapphahn, 2013). Refeeding syndrome results from a large influx of calories causing a shift in electrolytes and fluids (Golden et al., 2013) and can lead to life-threatening cardiovascular, respiratory, and neurological complications (Mayr, Imgart, Skala, & Karwautz, 2015). Severe untreated hypophosphatemia has the potential to result in detrimental medical complications.

Hypophosphatemia can occur during the anabolic state induced by the reintroduction of calories. During periods of hypophosphatemia, the body uses its available stores of phosphorus, a major intracellular electrolyte, thus depleting blood levels of phosphate and other electrolytes and causing a shift in electrolytes from intracellular spaces (Sachs, Andersen, Sommer, Winkelman, & Mehler, 2015). The risk of refeeding syndrome is the greatest during the first two weeks of weight restoration; therefore, close monitoring for signs and symptoms of refeeding syndrome and supplementation of phosphorus should occur for prevention. Careful decisions must be made when choosing the mode of nutrition therapy and caloric prescriptions for severely malnourished patients.

Screening and Evaluation of Patients with AN

Due to the associated risks, mortality rates of AN are considerably higher than in other eating disorders and early detection is key (Fitcher & Quadflieg, 2016). Primary care physicians and pediatricians have the opportunity to screen patients for signs and symptoms of AN by reviewing anthropometric trends, examining eating patterns, and determining body satisfaction through surveys, such as the SCOFF questionnaire (Harrington, Jimerson, Haxton, & Jimerson, 2015). Primary care physicians have a unique opportunity to prevent severe AN due to their capability of early detection, evaluation, and prompt treatment (Committee on Adolescence, 2003). Yearly doctor's visits and sports physicals provide valuable opportunities to screen pre-adolescents and adolescents for signs of AN (Harrington et al., 2015).

The primary care physician or pediatrician should observe patients for amenorrhea, arrhythmia, bradycardia, brittle hair and nails, edema, hyperkeratosis, hypotension, hypothermia, lanugo, weight loss, and reduced bone mineral density (Harrington et al., 2015). Other signs of

AN include complaints of being "fat", restricting food intake to exclusively low calorie foods, skipping meals, developing eating rituals, participating in excessive exercise, and wearing baggy clothing (Harrington et al., 2015). Initially, the physician will identify emergency medical conditions if he or she suspects a patient of AN. Hydration status, the presence of ketones, and signs of kidney damage should be evaluated first. Anthropometric data and body temperature should also be obtained. Blood pressure should be recorded and electrocardiography studies should be conducted. Immediate lab testing should include a urinalysis, complete blood count and metabolic panel, electrolyte measurements, and thyroid function tests (Harrington et al., 2015).

The primary physician will diagnose a patient with AN and determine the severity of the disease based upon anthropometric and laboratory values. The severity of AN determines what kind of treatment facility is necessary and if hospitalization is required for stabilization. Cockfield and Philpot (2009) emphasize the importance of a multidisciplinary approach for the treatment and medical stabilization of AN, specifically the role of the dietitian in restoring normal weight, ensuring adequate dietary intake, and patient nutrition education. Psychotherapists or psychiatrists are also involved in the treatment of those diagnosed with AN (Harrington et al., 2015). Due to the multifactorial nature of this disease, a multidisciplinary team is needed for the treatment and management of AN.

Inpatient Treatment for Anorexia Nervosa

Treatment of AN is dependent upon the nutritional status, compliance, and desires of the patient. Inpatient hospitalization may be necessary to achieve adequate weight restoration and medical stabilization in severe cases of AN when outpatient treatment options have failed

(Committee on Adolescence, 2003) (Golden et al., 2003). For a patient to be admitted to the hospital, he or she must be diagnosed with AN based upon *DSM-5* criteria and exhibit one or more of the following symptoms: severe malnutrition (<75% of average body weight for height and gender), extreme dehydration, electrolyte imbalances, or cardiac dysrhythmias (Committee on Adolescence, 2003). Patients diagnosed with AN may also require inpatient hospitalization if they show signs of physiological instability, such as bradycardia, low blood pressure, or hypothermia. Severe medical complications associated with AN, such as cardiac failure or seizures, also require inpatient hospitalization for clinical treatment (Committee on Adolescence, 2003).

The goals of inpatient hospitalization include weight restoration, correction of electrolyte imbalances, and reversal of medical complications secondary to malnutrition (Madden, Hay, & Touyz, 2015). Treatment guidelines for AN recommend inpatient weight gain rates between 0.5 to 1.4 kg/week; however, patients may be able to tolerate rates of weight gain as high as 2.0 kg/week (Redgrave et al., 2015). Initial calorie requirements for severely malnourished patients may be between 1,000-1,400 kcal/day (Golden & Meyer, 2004); however, the goal of caloric intake should be increased every 24-48 hours to achieve adequate weight restoration. The Academy of Nutrition and Dietetics recommends caloric prescriptions should be initiated at 1,200 kcals per day and increased based upon patient tolerance (Garber et al., 2013), but these recommendations vary by professional organization. Of the healthcare team, the registered dietitian plays a crucial role in determining the appropriate nutrition intervention to obtain metabolic recovery and promote sufficient weight gain in patients with AN while preventing refeeding syndrome (Golden & Meyer, 2004). Refeeding syndrome is a major concern when reinitiating calories to those suffering from severe malnutrition, but BMI percentile has been

proven to be a better predictor of refeeding syndrome than energy intake alone (Redgrave et al., 2015). Similarly, a randomized control trial conducted by O'Connor, Nicholls, Hudson, and Singhal (2016) found plasma phosphate levels in participants aged 10 to 16 years to be significantly associated with BMI percentile at the start of refeeding versus caloric intake; however, the patient must still be frequently monitored for tolerance when increasing caloric prescription.

Hospitals have developed protocols based upon available research to guide safe and efficient methods of refeeding patients diagnosed with AN; however current refeeding guidelines are inconsistent (Madden, Miskovic-Wheatley, Clarke, Touyz, Hay, & Kohn, 2015). The National Institute for Clinical Excellence, the Society of Adolescent Health and Medicine, and the American Psychiatric Association have published nutrition management guidelines for the treatment of AN. Current guidelines recommend caloric prescriptions less than that of resting energy expenditure, such as an initial refeeding rate between 10 to 40 kcal/kg/day or 20-80% of daily energy requirements (Madden et al., 2015). The Johns Hopkins Eating Disorder Protocol for adolescents and adults starts oral feedings at 1,200 to 1,500 kcal/day and advances as tolerated to 3,500 to 4,000 kcal/day to achieve rapid weight restoration (Redgrave et al., 2015). The protocol has additional treatment requirements for those diagnosed with extreme AN (BMI < 15 kg/m^2), including blood glucose testing, dextrose infusions, daily laboratory tests, electrolyte supplementation, and cardiac monitoring (Redgrave et al., 2015). In conclusion, treatment guidelines and protocols are commonly developed based upon "best practices" and "clinical judgement". Protocols tend to vary across treatment centers in regards to initial caloric prescriptions, advancement of caloric intake, and mode of nutrition therapy, but should all be developed based upon current guidelines and available empirical evidence.

Nutrition Treatment Options

Nutritional treatment options that have been researched for AN include an oral diet with food and high-calorie supplement drinks, NG tube feeding, and parenteral nutrition (PN) (Golden & Meyer, 2004). Previous research has shown the benefits and disadvantages to each mode of nutrition therapy (Hart, Franklin, Russell, & Abraham, 2013).

Oral Diet

Oral feeding, the least invasive treatment option and easiest to manage, has been proven to be beneficial in normalizing eating behaviors, but may result in fewer calories consumed from food when compared with NG feeding and PN (Hart et al., 2013). As mentioned earlier, the Johns Hopkins Eating Disorder Protocol starts oral feedings at 1,200 to 1,500 kcal/day and advances as tolerated to achieve rapid weight restoration (Redgrave et al., 2015). Consuming more than 1,500 kcal/day may be difficult for some patients initially and the clinical outcomes of consuming up to 3,500 to 4,000 kcal/day are under researched.

Few studies have examined oral diet and the impact of greater caloric prescriptions on weight restoration, length of stay, and prevalence of refeeding syndrome; however, Golden et al. (2013) found an initial higher caloric prescription of 1,500 kcal per day resulted in shorter LOS ($p < 0.0001$) in patients 10 to 21 years of age diagnosed with AN. In a similar study conducted by Garber et al. (2013), higher calorie diets (1,400-2,400 kcal/day) in comparison with lower calorie diets (800-1,200 kcal/day) resulted in shorter LOS ($p < 0.001$), as well as greater weight gain ($p < 0.001$) in a population of hospitalized adolescents diagnosed with AN. Similarly, a study conducted by Smith et al. (2016) examined an accelerated refeeding protocol including only

orally fed patients aged 10 to 22 years with an initial caloric prescription of 1,500 kcal/day. This protocol resulted in an average weight gain of 1.4 kg/week, medical stabilization within 15 days, an increase in caloric intake of 164 kcal/day, and no diagnosed cases of refeeding syndrome (Smith et al., 2016). From these studies and the findings of Leclerc, Turrini, Sherwood, and Katzman (2013), it appears an initial oral diet prescription of 1500 kcal/day, progressed as tolerated, can yield effective results in adolescents and adults diagnosed with AN.

Enteral Feeding

Implementation of nasogastric (NG) tube feeding may be indicated if oral feeding does not yield sufficient weight restoration or if patient noncompliance is an issue (Committee on Adolescence, 2003). Hospital protocols may include supplemental nocturnal NG tube feedings, cyclic NG tube feedings, and continuous NG tube feedings. Although the use of NG tube feedings has yielded greater weight gain in patients diagnosed with AN in past studies, studies examining the effects of NG tube feeding on length of stay and other outcomes measures have been inconclusive.

In a study conducted by Agostino, Erdstein, and Di Meglio (2013) in a population of adolescents and young adults, length of stay was found to be significantly reduced ($p = 0.0002$) and the mean rate of weight gain to be significantly greater in the continuous NG-fed group versus the bolus-fed oral diet group. Similarly, a randomized controlled trial among adults found both weight gain and energy intake to be significantly greater in the cyclic NG-fed combined oral diet group versus the oral diet alone group (Rigaud, Brondel, Poupard, Talonneau, & Brun, 2007). Research by Gentile (2012) also found NG tube feedings, in coordination with electrolyte supplementation, to be a well-tolerated mode of nutrition therapy in a severely malnourished

population of both adolescents and young adults diagnosed with AN. In a systematic review of studies examining the outcomes associated with NG feedings in patients of all ages diagnosed with AN, Kells and Kelly-Weeder (2016) found greater short-term weight gain and correction of severe nutritional deficiencies in NG-fed patients; however, the study emphasizes the need for research to better understand the long-term effects of NG feeding. Despite evidence supporting greater weight gain in NG-fed patients, Robb et al. (2002) also argues the necessity for further investigation to better understand the effects of mode of nutrition therapy on length of stay and risk of refeeding syndrome. While NG feeding is more invasive than oral feedings and its results may not be sustainable post-discharge, it can be more effective at restoring patients to normal weight than oral diet alone.

Parenteral Nutrition

The effectiveness of PN on weight restoration in patients diagnosed with AN has been studied as well, but very little. A systematic review of approaches to refeeding adolescent and adult patients diagnosed with AN was conducted by Garber et al. (2016) and reported that PN is not recommended in patients with AN due to its associated complications. Diamanti et al. (2008) found weekly weight gain to be significantly greater in adolescent girls diagnosed with AN fed by PN at 40-60 kcal/kg daily versus those exclusively orally fed ($p < 0.0001$); however, the number of complications was also significantly higher in the PN group ($p = 0.004$) and the cost of PN was nearly twice that of oral treatment. It is also important to note that the patients within Diamanti et al.'s study were tapered off PN and an oral diet was initiated once they received 50 kcal/kg/day. Common problems associated with PN are infections, refeeding syndrome, and its costly expense (Hotta, Araki, Urano, & Ohwada, 2014). Due to its cost, potential complications,

and lack of evidence supporting its benefits in this population, PN is rarely used in the clinical setting to treat AN.

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