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Nursing Interventions needed in Preventing Refeeding Syndrome in Anorexia Nervosa Inpatients: Literature Review

Kebede, Yosabeth
Korhonen, Marjo

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Laurea University of Applied Sciences
Otaniemi

**Nursing Interventions needed in Preventing Refeeding Syndrome in
Anorexia Nervosa Inpatients: Literature Review**

Yosabeth Kebede
Marjo Korhonen
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Yosabeth Kebede, Marjo Korhonen

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Refeeding syndrome is a potentially preventable but poorly recognized and understood condition. The purpose of this thesis was to describe nursing interventions that are needed to prevent refeeding syndrome in anorexia nervosa inpatients.

The original articles for this systematic literature review were acquired through the electronic databases PubMed and Laurea Finna. The following set of predetermined inclusion and exclusion criteria were used: free, full-text, English language articles published between 2004 and 2015; after which a total of seven articles were selected for further review. An inductive content analysis was taken into use when reporting the findings. Deductions were then made from the findings to identify nursing interventions needed to prevent refeeding syndrome in anorexia nervosa inpatients.

The findings revealed four main categories for interventions: identifying individuals at risk, recognizing complications early, preventing the development of symptoms, and lessening symptoms or complications. Identifying individuals at risk entailed risk factors for refeeding syndrome and guidelines for identification. Recognizing complications early included daily patient monitoring and increasing awareness among healthcare professionals. Preventing the development of symptoms entailed guidelines for refeeding; macronutrient supplementation; electrolyte, vitamin, and trace element correction; balancing fluid and sodium; and supporting and guiding patients. Lessening of symptoms or complications included treating complications in early phase of treatment and alleviating discomfort.

Ethical aspects and trustworthiness of this thesis were extensively documented. Additional training for nurses, strong collaboration within multiprofessional teams, and further research were recommended.

Key words: preventing refeeding syndrome, anorexia nervosa inpatient, nursing intervention

Yosabeth Kebede, Marjo Korhonen

Hoitotyön toiminnot refeeding-oireyhtymän ehkäisemiseksi anoreksia nervosa-sairaalapotilailla

Vuosi 2016 Sivut 33

Refeeding-oireyhtymä on estettävissä oleva, mutta harvoin tunnistettu ja huonosti ymmärretty hengenvaarallinen tila. Tämän opinnäytetyön tarkoituksena oli kuvata hoitotyön toimintoja, joita tarvitaan estämään refeeding-oireyhtymä anorexia nervosa-potilailla.

Tässä kirjallisuuskatsauksessa käsitellyt julkaisut haettiin sähköisistä PubMed- ja Laurea Finna-tietokannoista. Käytössä oli seuraavat hakurajaukset: ilmaiset, kokonaiset, englanninkieliset julkaisut, jotka on julkaistu vuosina 2004-2015. Yhteensä seitsemän artikkelia valittiin tähän katsaukseen. Tutkimustulosten raportoinnissa käytettiin induktiivista sisällönanalyysia. Tutkimustuloksista tehtiin johtopäätöksiä sellaisten toimintojen tunnistamiseksi, joilla sairaanhoitajat voivat estää refeeding-oireyhtymän esiintymistä anorexia nervosa-potilailla.

Katsauksessa löytyi neljä pääkategoriaa: riskiryhmään kuuluvien henkilöiden tunnistaminen, komplikaatioiden varhainen tunnistaminen, oireiden kehittymisen estäminen ja oireiden lieventäminen. Riskiryhmän tunnistamiseen kuuluu riskitekijöiden löytäminen ja tunnistamisohjeiden hyödyntäminen. Komplikaatioiden varhainen tunnistaminen käsittää päivittäisen potilasseurannan ja terveydenhoitohenkilöstön lisäkouluttamisen. Oireiden kehittymisen estämiseen kuuluu potilaiden tukeminen ja ohjaaminen, sekä ohjeet lisäravitsemuksesta: makroravintoaineiden tasapainotus, varovainen nesteytys, sekä elektrolyyttien, vitamiinien ja hivenaineiden korjaaminen. Oireiden tai komplikaatioiden lieventämiseen kuuluu komplikaatioiden hoitaminen varhaisessa vaiheessa sekä epämukavan olon lievittäminen.

Tarkastelimme myös eettiset näkökulmat ja tämän opinnäytetyön luotettavuuden. Suosittelemme tiivistä yhteistyötä moniammatillisissa tiimeissä, lisäkoulutusta sairaanhoitajille, jotka työskentelevät riskiryhmään kuuluvien potilaiden parissa, sekä aiheen syvempää tutkimista.

Avainsanat: refeeding-oireyhtymän ehkäisy, anorexia nervosa-sairaalapotilas, hoitotyön toiminnot

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1. Introduction

Refeeding syndrome (RFS) is a life-threatening condition that manifests in severely undernourished patients undergoing refeeding whether orally, enterally or parenterally. Undernourished body is unable to tolerate excessive food intake too fast, which can lead to severe abnormalities in electrolyte, vitamin and fluid balance as well as in glucose metabolism (Crook, Hally & Panteli 2001). Patients with anorexia nervosa (AN) are at high risk for refeeding syndrome. These patients are often hypokalemic and hypovolemic, which makes refeeding and rehydration challenging (Boateng, Sriram, Meguid & Crook 2009).

Early accounts of refeeding syndrome were documented in the 1940s by Brozec and colleagues who witnessed cardiovascular failure when semi-starved patients were abruptly re-fed a normal diet (Brozec, Chapman & Keys 1948). Following World War II, Schnitker and colleagues observed that 21% of chronically starved Japanese prisoners, who were liberated after the war, died despite having been provided with normal diet that included vitamin supplements (Schnitker, Mattman & Bliss 1951).

In literature on anorexia nervosa, the focus is mainly on psychosocial therapy and means of preventing refeeding syndrome is seldom described (Hofer, Pozzi, Joray, Ott, Hähni, Leuenberger, von Känel & Stanga 2013). Refeeding syndrome is potentially preventable but relatively poorly recognized and understood. Therefore, more knowledge and understanding is needed among health care workers to prevent potentially lethal complications (Boateng et al. 2009).

Registered nurses play an essential role in recognizing the warning signs for refeeding syndrome as they work close to the patients and are often the first ones to notice changes in the patient's condition. The ultimate aim of recognizing refeeding syndrome and treating it in time is to save patients' lives.

2. Anorexia Nervosa inpatients

According to the ICD-10 classification of mental and behavioral disorders, clinical descriptions and diagnostic guidelines by World Health Organization (2010) " Anorexia nervosa is disorder characterized by deliberate weight loss, induced and sustained by the patient. It occurs most commonly in adolescent girls and young women, but adolescent boys and young men may also be affected, as may children approaching puberty and older women up to the menopause. The disorder is associated with a specific psychopathology whereby a dread of fatness and flabbiness of body contour persists as an intrusive overvalued idea, and the patients impose a

low weight threshold on themselves. There is usually undernutrition of varying severity with secondary endocrine and metabolic changes and disturbances of bodily function. The symptoms include restricted dietary choice, excessive exercise, induced vomiting and purgation, and use of appetite suppressants and diuretics. "

In the first nation wide outcome study of anorexia nervosa in Finland conducted by Keski-Rahkonen, Hoek, Susser, Linna, Sihvola, Raevuori, Bulik, Kaprio and Rissanen (2007) 2.2% of Finnish women suffer from severe AN and up to 5% suffer from milder forms of AN during their life time. Half of the severe AN cases were not detected through the health care system.

Anorexia nervosa is a lifelong illness with two distinctive subtypes: restrictive or binge eating and purging. It is also characterized by frequent relapses (Hofer et al. 2014). Symptoms of AN often manifest between the ages of 10 and 25, with the peak age of the illness generally lying between 15 and 19. Recovery from anorexia nervosa is a slow and gradual process. Nearly 25% of the subjects of the study by Keski-Rahkonen and colleagues recovered weight within a year, 33% recovered within two years and 67% within five years.

Certain medical complications such as ideal body weight (IBW)<70%, acute complications of malnutrition, bradycardia of <30 beats/minute, unstable vital signs and severe dehydration require inpatient treatment of AN patients (Hofer et al. 2014). The etiology and management of refeeding syndrome are often investigated using anorexia nervosa as a 'human model' because of its prevalence as a predisposing diagnosis for RFS (Crook 2014).

3. Refeeding syndrome

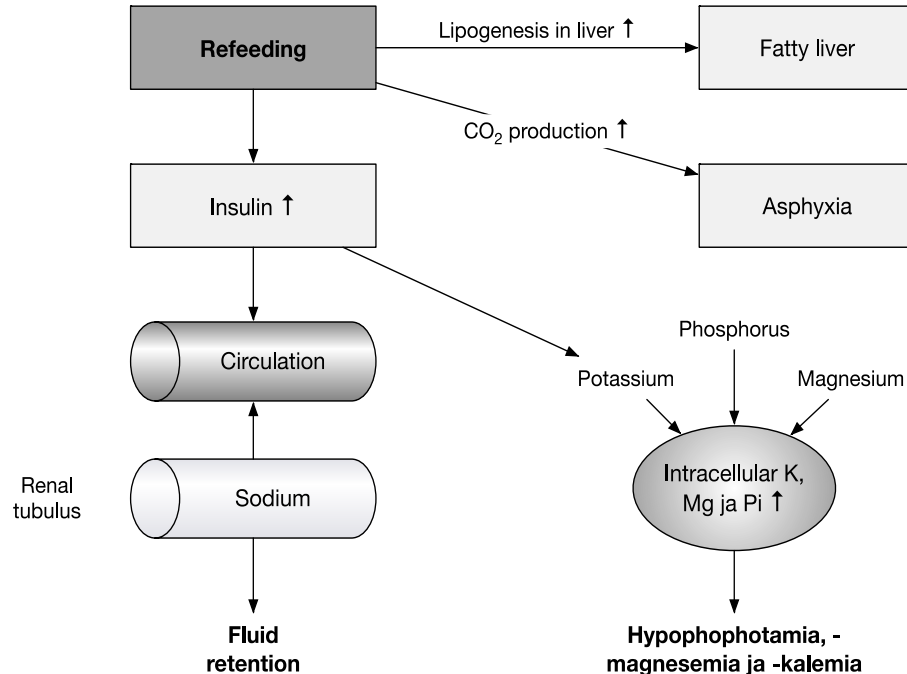
According to Crook (2014), refeeding syndrome is a life-threatening condition that can be seen in severely undernourished patients undergoing refeeding regardless of the route of nutrition administration. Refeeding itself is defined as a process of nutritional replenishment and weight restoration (Mehler, Winkelman, Andersen & Gaudiani 2010).

Refeeding syndrome reflects the body's transition from fat and protein catabolism to carbohydrate metabolism as explained by Tresley and Sheean (2008). Tresley and Sheean (2008) continue saying that this sudden change from catabolism to anabolism stimulates a disastrous increase in insulin production, which in turn leads to cellular uptake of glucose, phosphate, potassium, and magnesium. Sudden introduction of carbohydrate can also sometimes lead to fluid retention and thereby increase the extracellular fluid volume as explained by the same authors.

As Mehanna, Moledina, Travis (2008) and many others describe, refeeding syndrome is predominantly associated with hypophosphatemia, hypomagnesaemia, hypokalaemia, vitamin deficiency and fluid retention. However, Crook (2014) emphasises that even though hypophosphatemia is a major feature of refeeding syndrome, its presence alone in undernourished patients does not necessarily mean that RFS has occurred. Crook (2014) explains that there are many other causes of hypophosphatemia, hypomagnesaemia and hypokalaemia that are not necessarily related to RFS.

Furthermore, Crook (2014) brings out a fact that there is no universal agreement on the definition of refeeding syndrome. Precise definition of refeeding syndrome is difficult to find, as it is a complex syndrome and its symptoms may be non-specific (Mehanna et al. 2008). Therefore, there is lack of reliable information about the incidence of RFS. In a research conducted by Ornstein, Golden, Jacobson, Shenker (2003), hypophosphatemia, the most common manifestation of refeeding syndrome, appeared in 27,5% of the 69 anorexia nervosa inpatients that were studied.

Figure 1 Pathogenesis of refeeding syndrome. Excess carbohydrate administration triggers insulin surge, which results in fluid retention and electrolyte shifts. Fatty liver and asphyxia may also develop. (Ukkola 2007)



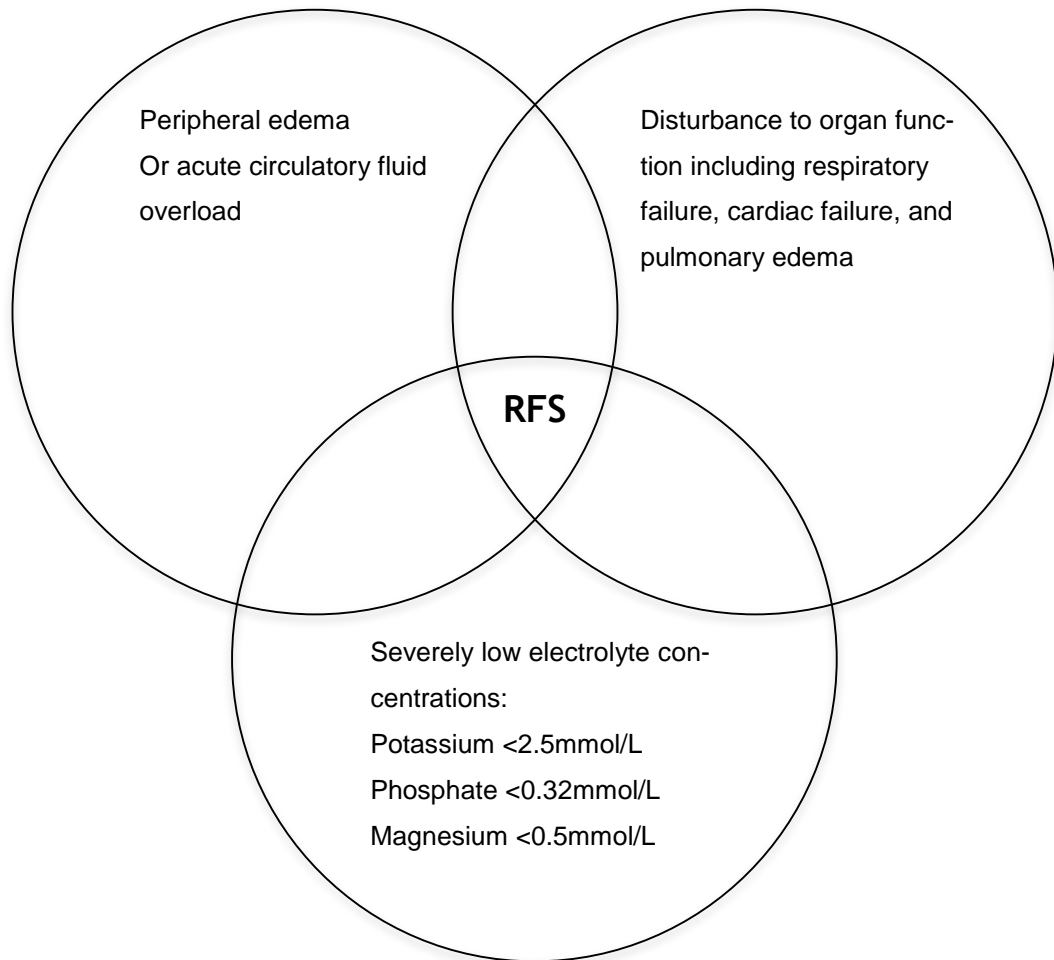
The British Association for Parental and Enteral Nutrition (BAPEN) describes that high-risk patients for refeeding syndrome are those with BMI less than 14kg/m² or those with prolonged poor intake for more than 15 days. According to Boateng et al. (2010), patient groups that are especially prone to developing RFS are anorexia nervosa patients, patients with malabsorptive states (e.g. celiac disease), cancer patients, elderly patients, patients with chronically uncontrolled diabetes mellitus, and chronic alcoholics.

According to Mehanna et al. (2008) the clinical features of refeeding syndrome occur as a result of the deficit of important electrolytes and the rapid change in basal metabolic rate. The symptoms of RFS can be seen in various organ systems including cardiovascular, gastrointestinal, musculoskeletal, respiratory, neurologic, metabolic and hematologic systems (Boateng et al. 2010). Boateng et al. (2010) describe refeeding syndrome as a cause for symptoms such as hypertension, arrhythmias, weakness, rhabdomyolysis, dyspnea, tremors, delirium, metabolic alkalosis, hyperglycemia, infections, hemolysis, anemia and acute tubular necrosis just to name a few. In the most severe cases, multisystem organ failure and death may occur (Boateng et al. 2010).

Since the definition of refeeding syndrome is problematic, it is probably not surprising that this condition sometimes remains undiagnosed (Crook 2014). Crook reminds that refeeding syndrome can be associated with high morbidity and mortality, especially when it is not diagnosed. Therefore, more knowledge of RFS is needed for its prevention and treatment.

In this thesis, refeeding syndrome is defined as severe disturbance in electrolyte and fluid shifts following the introduction of nutrients in undernourished patients. These shifts result from hormonal and metabolic changes and may cause life-threatening complications such as cardiac arrhythmias or congestive heart failure.

Figure 2 The three critical facets defining a manifest RFS (Rio, Whelan, Goff, Reidlinger & Smeeton 2013)



4. Nursing Interventions in preventing refeeding syndrome

Bulechek, Butcher, Docherman and Wagner (2013) define an intervention as *“any treatment, based upon clinical judgement and knowledge, that a nurse performs to enhance patient/client outcomes”*.

When nurses care for patients they follow the nursing process. According to Smeltzer, Bare, Hinkle and Cheever (2010) the traditional steps of the process are assessment, diagnosis, planning, implementation and evaluation. Nursing interventions are the actual treatments and actions that are performed to help the patient to reach the goals that are set for them. Nurses use their knowledge, experience, and critical thinking skills to decide which interventions will benefit the patient the most. During the implementation phase, the nurse continu-

ally assesses the patient's responses to the nursing interventions and the plan of care is modified as the patient's condition, problems and responses change (Smeltzer et al. 2010, 30-38).

The International Council of Nurses (ICN) Code of Ethics for Nurses has determined 'preventing illness' as one of the four fundamental responsibilities of the nurse. Fry and Johnstone (2008, 81-82) state that "*nurses are obliged to reduce the incidence and impact of otherwise preventable harm to people, including the preventable harms that might and do occur as a result of illness*". American Nurses Association (ANA) reminds that approaches to prevention should be comprehensive, including primary, secondary and tertiary levels of prevention. In the case of refeeding syndrome this would mean identification of patients at risk for RFS, prevent the development of severe symptoms if possible, or to lessen the symptoms if RFS has already manifested (Boateng et al. 2010).

Even though many nursing interventions are independent, others are interdependent requiring the participation of multiple members of the health care team (Smeltzer et al. 2010, 30-38). The NICE guidelines (2006) remind that healthcare professionals should ensure that anorexia nervosa inpatients receive coordinated care from a multidisciplinary team. A multidisciplinary team includes nurses, general practitioners or specialized physicians, dieticians, psychiatric nurses and doctors, and physiotherapists. Some patients may be more comfortable talking to pastors.

5. Purpose statement and research question

The aim of this thesis is to identify nursing interventions needed to prevent refeeding syndrome in anorexia nervosa inpatients by systematically reviewing relevant studies. The information provided in this thesis can benefit nursing students and nursing professionals, who are interested in improving their competency in caring for anorexia nervosa patients and enhance the quality of patient care.

The purpose of this thesis is to describe nursing interventions that are needed to prevent refeeding syndrome in anorexia nervosa inpatients. The choice of this topic was influenced by our desire to get better understanding of existing research.

The Research Question

What kinds of nursing interventions are needed to prevent refeeding syndrome in anorexia nervosa inpatients?

6. Research Methods

6.1 Principles of Literature Review

The research method used in this thesis is a literature review. This method seeks to review relevant literature in order to summarize the current knowledge about the topic in interest (Burns & Grove 2011, 188-223). In other words to say, literature review seeks to answer to a research question by systematically searching for and analyzing relevant literature (Aveyard 2010, 6). Aveyard (2010, 19) emphasizes that the systematic review process needs to be carefully documented by the authors so that the literature review can be accepted as a research methodology on its own right.

Literature review can be considered as an important research method in social and health care where up-to-date evidence-based knowledge is needed for the workers to fulfill their professional duty of continuously educate themselves. The volume of literature that exists in this field can be overwhelming. Through literature review nurses can provide a summary and an analysis of the existing relevant literature (Aveyard 2010, 6).

6.2 Data sources and electronic literature search

The data for this thesis was collected from three different databases: PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL) and Laurea Finna. The database searches were conducted in November 2015. The search words used in different combinations were nursing interventions, nursing, refeeding syndrome and anorexia nervosa.

As illustrated in Table 1, data searches were conducted in all three databases by using the same search words in the same combinations. When the search word combination *Nursing+ Refeeding syndrome+ Anorexia nervosa* was entered into the Laurea Finna database, the results shown were identical to that of search word combination *Nursing interventions+ Refeeding syndrome+ Anorexia nervosa*.

Table 1 Illustration of the electronic literature search process

Date	Database	Search words	Limitations	No. of hits	Articles selected by title	Relevant Articles
09.11.15	PubMed	Nursing interventions+ Refeeding syndrome+ Anorexia nervosa	Full text, English, 2005-2015	0	0	0
09.11.15	PubMed	Nursing+ Refeeding syndrome+ Ano- rexia nervosa	Full text, English, 2005-2015	0	0	0
09.11.15	PubMed	Refeeding syndrome+ Ano- rexia nervosa	Full text, English, 2005-2015	22	8	2
09.11.15	CINAHL	Nursing interventions+ Refeeding syndrome+ Anorexia nervosa	Full text, English, 2004-2014	0	0	0
09.11.15	CINAHL	Nursing+ Refeeding syndrome+ Ano- rexia nervosa	Full text, English, 2004-2014	23	3	1
10.11.15	CINAHL	Refeeding syndrome+ Ano- rexia nervosa	Full text, English, 2004-2014	3	2	0
10.11.15	Laurea Finna	Refeeding syndrome+ Ano- rexia Nervosa	Full text, English, 2005-2015	66	12	5
10.11.15	Laurea Finna	Nursing Interventions+ Refeeding syndrome+ Ano- rexia Nervosa	Full text, English, 2005-2015	6	1	0
Total				120	26	8

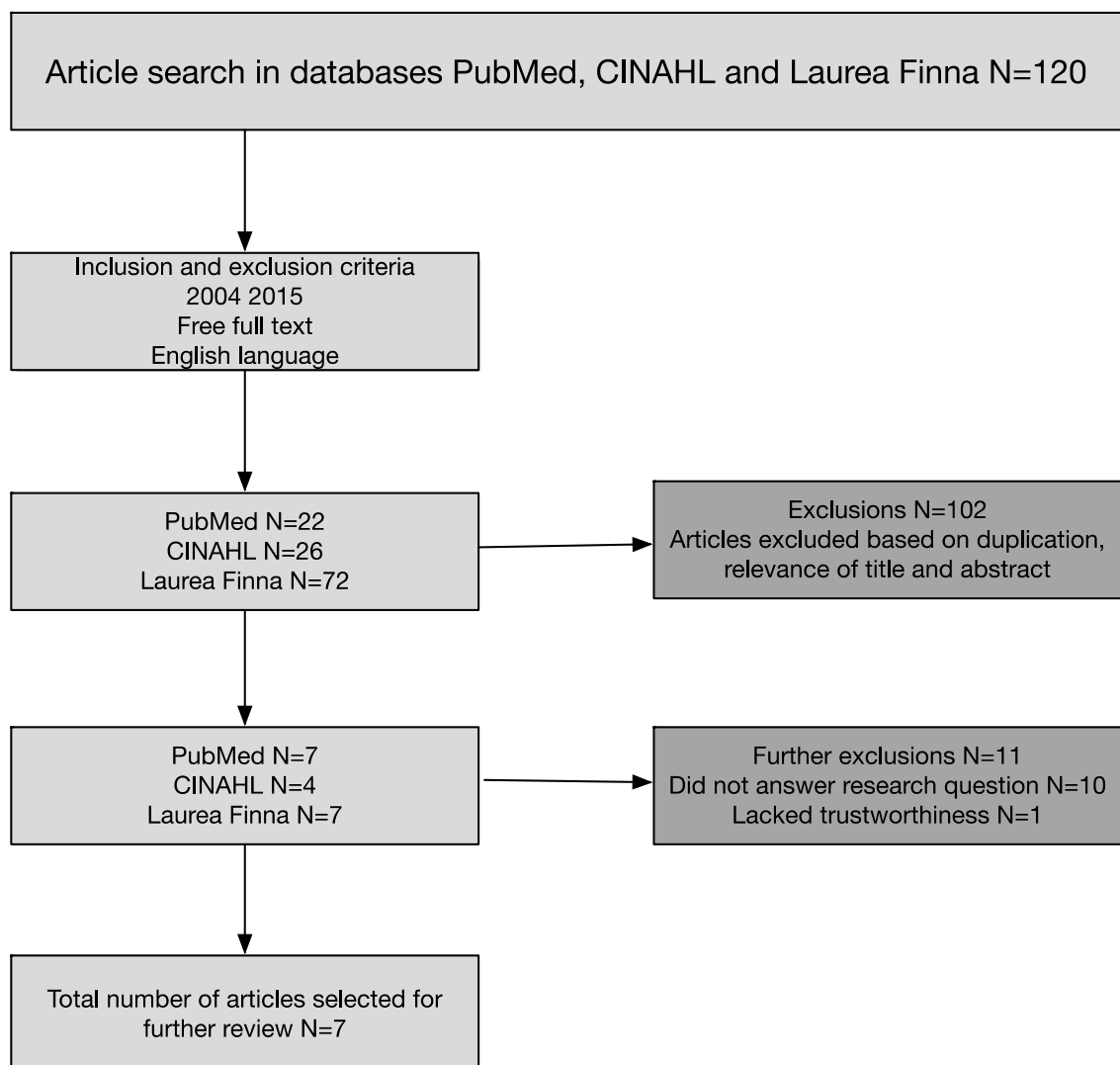
6.3 Inclusion and exclusion criteria for article selection

A set of inclusion and exclusion criteria were determined during the literature search and article selection phase to ensure that only high-quality articles that are relevant to our research question are included. The article search was limited to full text English language literature and to articles published between the years 2005-2015. When using CINAHL database

we had to limit our search to articles published between 2004-2014 because of technical issues. However, the oldest article used in this review was published in 2008. Other exclusion criteria for the literature search were paid articles and credibility of the articles.

The initial selection of the articles was conducted based on the relevance of their titles and significance of the abstracts. The titles and abstracts of the articles selected in this phase contained two or more of the search words. The final selection was done after reading through the whole text to ensure that the articles answered the research question. In total, seven articles were selected for this literature review: two articles from PubMed and five from Laurea Finna.

Figure 3 Illustration of the literature search and article selection process based on the inclusion and exclusion criteria



6.4 Data extraction

Data extraction is the process of collecting suitable data from the primary articles, which answer the research question (Elo, Kääriäinen, Kanste, Pölkki, Utriainen & Kyngäs 2014). To standardize the process of data extraction and maintain the validity of the results, it is important to use an extraction form (Bettany-Saltikov 2012). Data extraction needs to be done accurately and the authors should not attempt to slant the findings in any particular direction (Wager & Wiffen 2011).

Guided by the research question, the authors collected suitable raw data from all the seven primary articles. This was done on an article-by-article basis by both authors independently. An extraction form was taken into use to improve the trustworthiness of the process. The final decision on which data to include was made in the presence of both authors by giving due consideration to the purpose of the thesis. Cases of overlapping content were settled by choosing one from the most recent source. All final data were agreed upon by both authors with all discrepancies resolved.

6.5 Data analysis

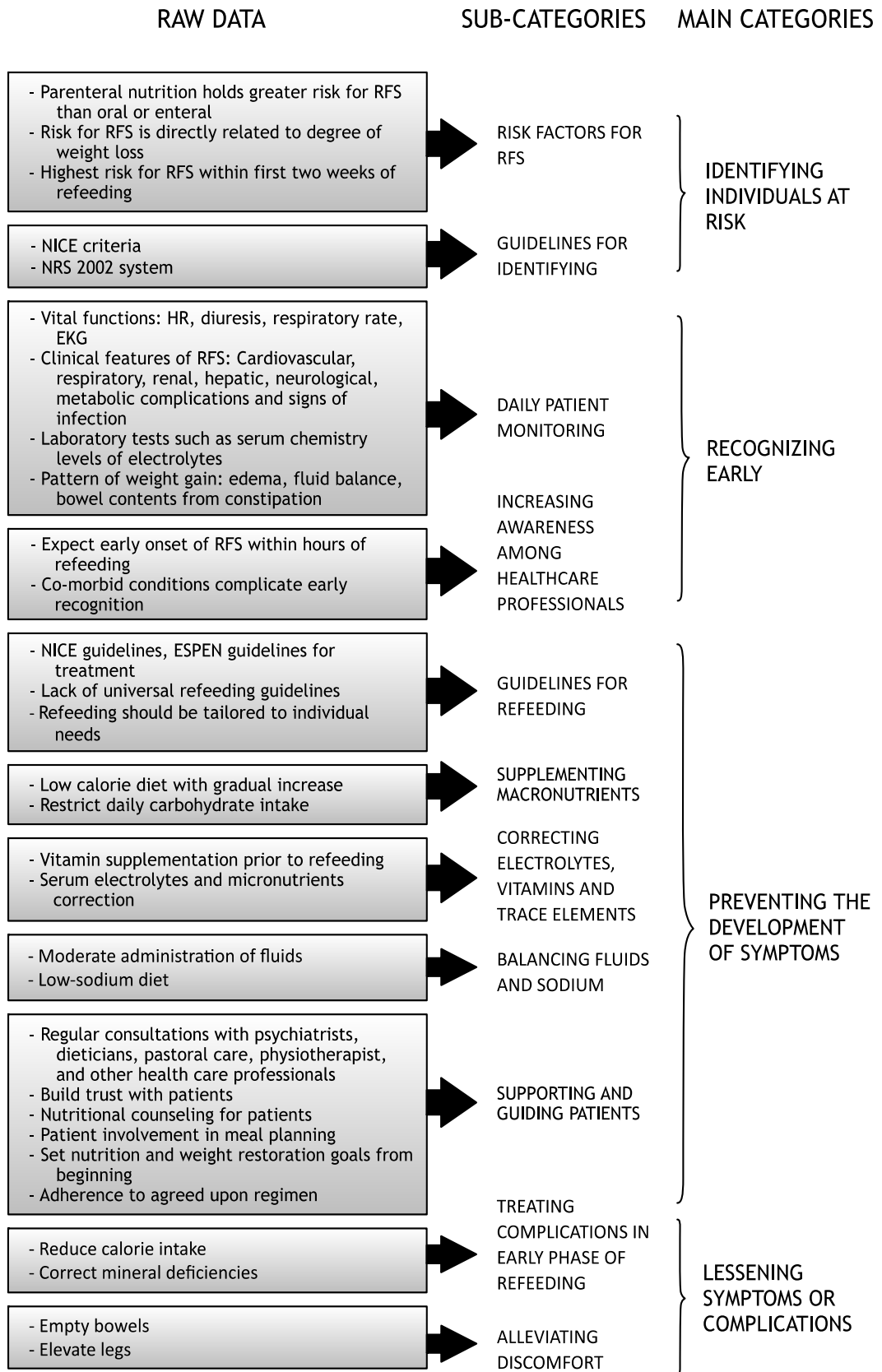
Inductive content analysis is used as the method of data analysis in this paper to report the findings. Polit, Hungler and Beck (2001, 459) describe content analysis as the process of organizing and integrating qualitative information according to emerging themes and concepts. Inductive approach is used when there is not enough knowledge about the topic or when the knowledge is fragmented (Lauri & Kyngäs 2005, 61). Inductive approach moves from the specific to the general level as explained by Burns and Grove (2011, 18).

As explained by Elo and Kyngäs (2007), inductive analysis process contains three phases: preparation, organizing and reporting. During the preparation phase the articles were re-read and the data was defined. In the organizing phase, the extracted data was coded and the results were pooled together according to emerging themes that answered the study question. These categories were grouped into four main categories and ten sub-categories. The coded content emerged from the findings and discussion sections of the primary articles.

When discussing the findings of this review, a deductive approach was used. In deductive analysis process, categories are developed based on the data that is reviewed for content and coded for correspondence to the identified categories (Elo & Kyngäs 2007). This method was chosen for discussing the findings of this review because the original articles did not directly refer to nursing interventions or the roles of nurses in preventing RFS in anorexia nervosa inpatients. The categories were created to accurately represent the findings of the review. The coded content for the discussion emerged from the findings of this paper where refer-

ences to the roles and actions of healthcare professionals in preventing RFS in anorexia nervosa patients were made by the original authors.

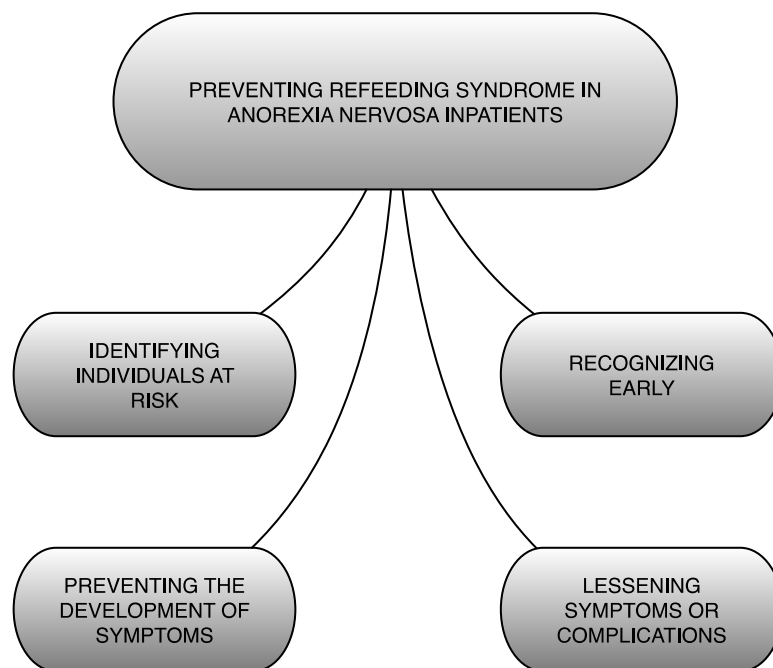
Figure 4 Illustration of the data extraction and categorization process



7. Findings

The findings of this literature review are presented in this section. Guided by the research question and purpose statement, seven articles were systematically reviewed. The articles comprised four literature reviews, one review article and two original research papers. Findings relating to the prevention of RFS in anorexia nervosa inpatients are presented here under four main categories.

Figure 5 Summary of the interventions needed in preventing refeeding syndrome in anorexia nervosa inpatients



7.1 Identifying individuals at risk

7.1.1 Risk factors for Refeeding syndrome

The most important factor in managing refeeding syndrome is prevention and therefore identification of individual who are at risk is essential. Individuals with weight loss of 10% within a period of three months or individuals who are less than 70% of their ideal body weight are at high risk for developing RFS (Tresley & Sheean 2008). Hofer et al. (2013) state that patients who receive aggressive nutritional support without adequate supplementation of micronutrients after chronically poor nutritional intake are most likely to exhibit the symptoms of RFS. According to Boateng et al. (2010) parental nutrition holds a greater risk for refeeding syndrome than oral or enteral, even though all routes of feeding can cause RFS. Furthermore,

Crook et al. (2014) state that intravenous glucose infusion before nutrition support in under-nourished patients is an important risk factor for developing RFS. In addition to that, Hofer et al. (2013) suggest that AN inpatients with phosphate levels <0.32 mmol/L during the refeeding phase are at higher risk for severe complications.

According to Mehler et al. (2010) the risk for refeeding syndrome is directly correlated with the extent of weight loss. Therefore, the same authors describe that patients' risk for RFS could be classified as mild, moderate, severe, or critical based on whether they are 10%, 20%, 30%, or more below their ideal body weight. Body mass index (BMI) could also be used in classifying patients (Mehler et al. 2010).

7.1.2 Guidelines for identification

Hofer et al. (2014) employed the internationally validated Nutritional Risk Screening System (NRS) 2002 to assess the nutritional risk of their inpatients, whereas Crook (2014) proposed the National Institute for Health and Care Excellence (NICE) clinical criteria for determination of patients at risk of developing refeeding problems (Crook 2014). Crook (2014), Hofer et al. (2014), Mehler et al. (2010) and Sachs et al. (2015) all encourage health care professionals to use the NICE criteria for determining patients at risk for RFS. Clinical Guidelines 32 (CG32), were designed as a guide to nutrition support in adults (NICE 2006). These criteria include Body Mass Index (BMI), recent weight loss, recent oral intake, drug history and baseline electrolyte levels (table 2).

Table 2 NICE criteria for determining patients at high risk of developing refeeding problems (NICE 2006)

<p>Patient has one or more of the following:</p> <ul style="list-style-type: none"> - BMI less than 16 kg/m² - Unintentional weight loss greater than 15% within the last 3-6 months - Little or no nutritional intake for more than 10 days - Low levels of potassium, phosphate or magnesium prior to feeding
<p>Or patient has two or more of the following:</p> <ul style="list-style-type: none"> - BMI less than 18.5 kg/m² - Unintentional weight loss greater than 10% within the last 3-6 months - Little or no nutritional intake for more than 5 days - History of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.

7.2 Recognizing complications early

7.2.1 Daily patient monitoring

Sachs et al. (2015) emphasise that careful monitoring of the AN inpatient during the first few weeks of refeeding for clinical and laboratory changes is of utmost importance since early recognition can reduce complications. The patient's vital signs such as blood pressure, heart rate and respiratory frequency should be measured few times per day (Sachs et al. 2015). Hofer et al. (2013) recommend that electrocardiogram should be monitored in the first week of refeeding.

Health care professionals need to be aware for the various clinical features of RFS to be able to watch for the early signs (Crook 2014). For example, low phosphorous levels can impair diaphragmatic contractility and lead to shortness of breath and impaired respiratory function (Sachs et al. 2015).

Close attention is essential especially to the anorexia nervosa patient's cardiovascular status until normalization of the heart mass has reverted towards normal with weight gain (Mehler et al. 2010). As Mehler et al. (2010) describe, anorectic individuals are normally bradycardic (heart rate less than 60 beats/minute) and therefore the presence of a more rapid heart rate, even if just in the 80-90 HR range, is an early sign of possible RFS.

Furthermore, peripheral edema and pulmonary edema are manifestations of heart failure and therefore clinical examination to detect the presence of edema in the ankle and shin areas is necessary during the early refeeding stages (Sachs et al. 2015). In addition to that, daily body weights and chart monitoring of fluid intake and output is important to optimize fluid balance and to prevent fluid overload (Hofer et al. 2013). According to Mehler et al. (2010) weight gain of more than 1.36kg in a week is usually not nutritionally sound and may be caused by fluid retention or retained bowel contents.

Health care professionals also need to be aware of the risk of hypoglycemia during the early course of refeeding and possible parental feed should be titrated down gradually to avoid the so called rebound hypoglycemia (Mehler et al. 2010). In anorexia nervosa, hypoglycemia is related to depleted hepatic glycogen reserves and gluconeogenesis substrates as explained by Mehler et al. (2010). The same authors continue saying that large glucose loads during aggressive refeeding stimulate significant amounts of insulin release from the pancreas, which cannot be offset by the depleted hepatic reserves of glycogen and these insulin surges cause hypoglycemia. In addition to that, AN patients often also have fasting hypoglycemia (Mehler et al. 2010).

Mehler et al. (2010) describe daily monitoring of the patient's plasma electrolytes and plasma glucose during the early phase of the refeeding process as an important method of preventing refeeding complications. Hypophosphatemia (<0.80 mmol/L) is a major feature of refeeding syndrome while hypomagnesemia (<0.70 mmol/L) and hypokalemia (<3.5 mmol/L) may be another metabolic predictors of developing RFS (Hofer et al. 2013). Hofer et al. (2013) advise that plasma glucose should be maintained between 100 and 150 mg/dL to prevent hypoglycemia and hyperglycemia.

Moreover, Hofer et al. (2013) recommend monitoring plasma albumin, protein, calcium, and full blood count as well as serum ferritin, vitamin B12 and folate concentrations. The same authors also recommend that liver function tests (ALT/AST) should be monitored because hepatic dysfunction can occur in RFS. However, Mehler et al. (2010) mention that mild elevations of liver enzymes usually have little clinical significance and resolve with a slowing of the rate of the refeeding. On some occasion the elevations can be more obvious, in which case consultation with a dietician to reduce carbohydrate-dextrose calories is necessary (Mehler et al. 2010).

7.2.2 Increasing awareness among healthcare professionals

Tresley and Sheean (2008) emphasize the importance of educating health care professionals when they talk about preventing refeeding syndrome. According to Crook et al. (2014), the most important issue concerning RFS prevention is to be aware of the condition and anticipate problems. Anticipation is needed since the onset of refeeding syndrome can be very fast, even within hours of refeeding (Hofer et al. 2014). Health care professionals also need to appreciate the fact that risks for RFS apply regardless of the route of refeeding (Hofer et al. 2014).

Clinical characteristics unique to AN patients, such as bradycardia, gastroparesis and slowed colonic transit should be taken into account so that early symptoms of RFS can be detected and physical discomforts of weight restoration can be alleviated (Mehler et al. 2010).

7.3 Preventing the development of symptoms of refeeding syndrome

7.3.1 Guidelines for refeeding

There is no universal consensus on the optimal refeeding regimen for refeeding syndrome. Cook (2012) recommends the use of NICE guidelines, which advocate for slow, low energy refeeding to avoid RFS. Crook bases his recommendation of the current NICE guidelines on the lack of high quality evidence to propose a different course of action. Hofer and colleagues, on the other hand, developed their own guidelines for the prevention and management of RFS based on their long-term clinical experience and evidence-based literature. These guidelines recommend careful and gradual replenishment of energy, and were adopted by the European Society of Clinical Nutrition and Metabolism (ESPEN). Tresley et al. (2008), Mehler et al. (2010) and Sachs et al. (2015) also agree with a conservative approach to refeeding.

Madden, Miskovic-Wheatley, Clarke, Touyz, Hay and Kohn (2015) demonstrated the potential for more rapid refeeding protocol in a clinical cohort study of 78 adolescent, medically unstable, anorexia nervosa patients. The study demonstrated that the refeeding protocol resulted in immediate weight gain and was well tolerated with no indicators of RFS.

7.3.2 Supplementing macronutrients

The aim of nutritional rehabilitation in anorexia nervosa patients is to attain healthy ideal body weight (Mehler et al. 2010). Boateng et al. (2010) advice initiating energy replenishment at no more than 10kcal/kg/d for patients at risk, and as low as 5kcal/kg/d for the clinically unstable. They also recommend calorie increment of 15-20kcal/kg/d from days 4-10 and calorie advancement of 200-300kcal every 3-4 days. For enteral feeds infusion rates as low as 10ml/h are recommended. According to Tresley and Sheean (2008) feeding should be started at 10kcal/kg/d or about half of estimated needs with 1-1.5g/kg/d of proteins.

Crook (2014) argues that the composition of the feed is more significant than the energy content. He recommends that carbohydrate content should be limited to a maximum of 40% of the total energy intake and fat content should not exceed the maximum lipid elimination capacity of about 3.8g of lipid/kg/d. In line with NICE guidelines for treatment, Crook proposes weekly weight gain of 0.5-1kg where the initial energy intake is below daily average. Crook (2014) also warns about the dangers of overly cautious refeeding, which can result in underfeeding.

Conforming to the ESPEN guidelines, Hofer et al. (2014) suggest daily energy intake, regardless of the route of administration, of 10kcal/kg with slow increase to 15kcal/kg during the first three days of refeeding. This should be followed by energy supplementation of 15-20kcal/kg/d during days 4-6, and 20-30kcal/kg/d during days 7-10.

In the clinical trial conducted by Madden and colleagues (2015), patients were supplemented with 24 to 72 hours of continuous nasogastric feeds, which were discontinued with daytime clinical stability. Subsequently, energy intakes of 2400-3000kcal/day were supplemented with a combination of nocturnal and oral feeds. The proportion of energy sources in the nasogastric feeds was limited to $\leq 50\%$ from carbohydrates and about 30% from fats.

In agreement with previous recommendations, Mehler et al. (2010) state that calorie intake levels should begin at 600-1000kcal/day and increase 300-400kcal every three to four days. Further more, they advise complementing early nutritional rehabilitation with liquid supplements. Sachs et al. (2015) adhered to hospital protocol for refeeding with calorie intake of 1200-1400kcal/day and increased by 300kcal every third day. Their meal plan was comprised of about 45% of carbohydrates, 30% of proteins, and 25% or less of fat and foods lower in soluble fibers.

7.3.3 Correcting electrolytes, vitamins and trace elements

An effective means of preventing RFS is adequate supplementation of electrolyte, vitamin, and trace elements during initial refeeding (Boateng et al. 2010). Correction of electrolytes, soon after the initiation of refeeding, is important (Tresley & Sheean 2008). All the primary articles reviewed for this study emphasize the importance of correcting electrolyte abnormalities. However, Hofer et al. (2014) and Crook (2014) propose two conflicting approaches. Hofer et al. (2014) advocate for precautionary substitution of electrolytes prior to initiation of refeeding. In their clinical trial Hofer and colleagues prescribed phosphate supplements from the commencement of treatment. Crook (2014) disputes this by stating the irrelevance of electrolyte correction before refeeding. Instead he claims that this should be done alongside refeeding.

One of the significant contributors to the development of symptoms of RFS is vitamin deficiency caused by enzymatic activity after the onset of refeeding (Boateng et al. 2010). Thiamine supplementation should be initiated prior to and maintained along side refeeding because thiamine is a cofactor in glucose metabolism (Boateng et al. 2010; Crook 2014; Hofer et al. 2014).

Replenishing trace elements is crucial in the critically ill as they are depleted during the anabolic phase due to increased enzymatic activity (Boateng et al. 2010). Low concentrations of plasma selenium and copper have been demonstrated to occur in RFS (Crook 2014). According to Crook (2014), "loading" doses of trace element supplements, particularly zinc, selenium, manganese, and copper should be given when appropriate. This should be followed by maintenance doses given daily in the initial phase of refeeding. However, Hofer and colleagues discourage iron supplementation during the first week of refeeding (Hofer et al. 2014).

7.3.4 Balancing fluids and sodium

Sodium sparing, which is triggered by hyperglycemia and hyperinsulinemia during refeeding, results in fluid overload. Monitoring the changes in daily body weight and urine output helps assess fluid balance and prevent fluid overload, pulmonary edema, or congestive heart failure (Boateng et al. 2010). Boateng and colleagues recommend the administration of 20-30 mL/kg/d of normal saline for rehydration, and sodium repletion at less than 12mmol/L within a 24-hour period as needed. They also state that edema, elevated jugular venous pressure, and hepatomegaly are good indicators of fluid overload.

Low sodium diet (Crook 2014; Tresley & Sheean 2008) with fluid restriction of 1L/d (Tresley & Sheean 2008) may prevent fluid overload. Crook (2014) discourages the rapid correction of hyponatremia to avoid the risk for central pontine myelinolysis.

Hofer and colleagues adopted the ESPEN guidelines for treatment with the following recommendations for fluid and sodium balance: Days 1-3 restrict fluid intake to 20-30mL/kg/d and sodium intake <1mmol/kg/d; Days 4-6 fluid intake 25-30mL/kg/d; Days 7-10 fluid intake 30mL/kg/d. They also suggest further restrictions on sodium if edema develops. They claim that fluid and sodium restriction before the initiation of refeeding is crucial in minimizing the risk of developing edemas as a result of slow weight recovery (Hofer et al. 2014).

In their clinical trial Madden and colleagues restricted fluid administration to that provided by the nasogastric feeds and that prescribed in the oral menu, which was between 1540 and 1920mL/d. During the course of the study, none of their patients developed symptoms of fluid overload.

According to Mehler et al. (2010) assessing weight change during the first several weeks of hospitalization can be challenging. This is because with those medically compromised the most, even with careful initiation of refeeding, some patients who have gained edema weight will auto-diurese this weight as their true weight starts to rise whereas in others, they would have to lose all edema weight before they start gaining healthy weight.

Patients with anorexia nervosa are more prone to fluid overload and heart failure due to atrophy of the heart (Sachs et al. 2015). Sachs et al. (2015) suggest limiting fluid intake during early phase of refeeding. Regarding sodium restriction, they cite a study conducted by Aliti et al. (2013), which claims that salt restriction may result in activation of hormones which further increase sodium and water retention (Sachs et al. 2015).

7.3.5 Supporting and guiding patients

Nutritional counseling, helping with meal planning, and supporting the patient contribute to desirable outcome in the treatment of patients with refeeding syndrome (Sachs et al. 2015; Mehler et al. 2009). Mehler and colleagues underline the benefit of acknowledging small successes, providing encouragement and consistent guidance for patients. Educating the patient regarding meal plans and general nutrition can help the patient return to a healthy lifestyle (Mehler et al. 2009).

7.4 Lessening symptoms or complications

7.4.1 Treating complications in early phase of refeeding

If manifestations of refeeding syndrome are detected, the rate of feeding should be reduced and any electrolyte and mineral deficiencies that are present should be corrected (Sachs et al. 2015). Refeeding must then be continued slowly and increased gradually (Tresley & Sheean 2008). Sachs et al. (2015) remind that the patient's cardiovascular system and respiratory system should be closely monitored if manifestations of RFS occur.

7.4.2 Alleviating discomfort

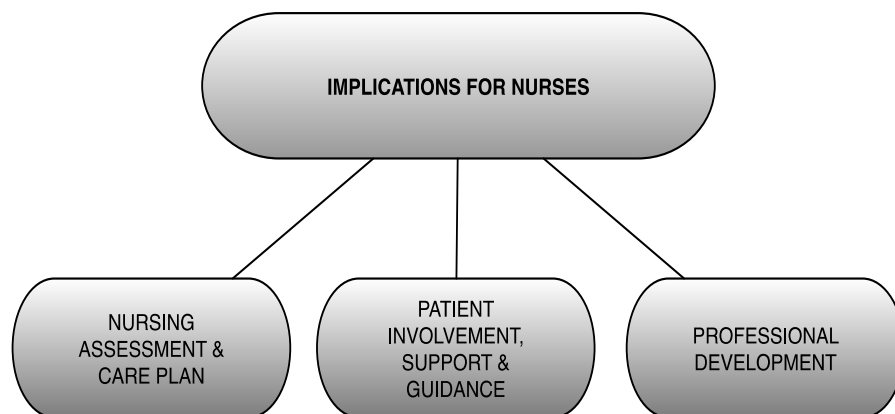
Mehler et al. (2010) explain that anorexia nervosa patients often complain of abdominal bloating and constipation because of the delayed stomach emptying and prolonged colonic transit time typical to this patient group. Mehler et al. (2010) suggest that a bowel regimen and adequate hydration may help alleviate these symptoms. For possible edema, Sachs et al. (2015) recommend concerted leg elevation during the day together with gentle reassurance.

8. Implications for nurses

This thesis aimed to identify nursing interventions for the prevention of RFS in anorexia nervosa inpatients. In the literature review, we uncovered several interventions by healthcare practitioners. However, these interventions were not specific to nursing practice. We deduced categories for nursing intervention based on references made to healthcare professionals in the findings.

These findings have great implication on nursing practice, as nurses are an integral part of the healthcare team. The findings will therefore be discussed within the context of nursing practice.

Figure 6 Main themes and categories for nursing interventions based on the findings of the literatures reviewed



8.1 Nursing assessment and care plan

The findings of our literature review emphasize the importance of recognizing patients at risk for refeeding syndrome. The use of NICE criteria is recommended for determining patients at risk. When taking care of anorexia nervosa inpatients who are at risk for refeeding syndrome, nurses need to anticipate problems since RFS can develop surprisingly quickly. In addition to that, nurses need to appreciate the fact that all routes of feeding can cause RFS.

Our findings show that careful patient monitoring and multi-disciplinary team management help to recognize the early symptoms of RFS and reduce morbidity and mortality. Therefore, nurses need to be aware of the various clinical features of RFS to be able to watch for early signs. Also knowledge about the clinical characteristics unique to AN patients is needed so that nurses are able to detect the early signs of RFS and alleviate the discomfort of the pa-

tients. Nursing interventions include monitoring the patient for clinical and laboratory changes and ask for a clinical review or consultation with the dietitian when needed.

A clear plan for the nursing care and what medical risk factors are present is needed and will assist to identify if restrictions need to be put in place. Collaborative approach of the care plan involving the patient and, if appropriate, the family will be most successful. The plan of care should be modified constantly as the patient's condition, problems and responses change. Also careful documenting is important to be able to follow up the weight pattern and development of the condition.

8.2 Patient involvement, support and guidance

Early phase of refeeding can be rather stressful for patients. Patients are often fearful of change in their routine and lose of control over their diet. They suffer from self-image issues and may have history of excessive exercising (The Phoenix Center Eating Disorders Service 2010).

In managing AN inpatients, it is important for the nurse to engage with the patient in a firm, non-judgmental and supportive manner. As mentioned in our findings, information may need to be communicated repeatedly because cognition in anorexia nervosa patients is diminished due to starvation. The nurse should handle all interactions patiently and compassionately.

Nurses should educate patients on appropriate eating behavior and fluid intake, and encourage them to commit to the refeeding plan. Food preference and weight goal are to be determined in collaboration with the patient and, when appropriate, his/her significant others. It is important to create understanding of the significance of the care plan with all parties involved, as families may feel sympathetic to the patient's appeal for alterations in the meal plan. A family-based intervention is of dire importance when treating children and adolescents (NICE Clinical Guidelines 2004).

It was evident in our findings that the nurse needs to restrict the availability of food to scheduled mealtime, pre-served meals and snacks. Mealtime supervision is essential to ensure adequate intake and after-mealtime supervision to prevent purging (Bulechek et al. 2013). The nurse should encourage the patient to take into use different relaxation, distraction, and encouragement techniques before, during and after meals to support the patient's eating.

In-ward treatment of anorexia nervosa patients requires a multidisciplinary approach, including nurses, that incorporates both the physical and psychological aspects. The physical man-

agement of AN patients includes nutritional intervention and psychopharmacological agents. The nurse has an important role in executing the nutrition plan, assessing the patient's needs, administering medications, monitoring and evaluating the patient's response to treatment.

The dietician, often, provides nutritional counseling to the patient. Psychological therapy is employed by psychotherapists and psychiatric nurses to address underlying behaviors and cognitions (NICE Clinical Guidelines 2004). This is even more crucial if the patient resists or does not comply with treatment (NSW Ministry of Health 2014). Nurses can also employ behavioral modification techniques to promote a healthy body image and reward patients for weight gained.

8.3 Professional development

Nurses need to possess sufficient skills to recognize and interpret the physiological and psychological signs, symptoms and complications of refeeding syndrome (Birmingham & Beumont 2004). Element 1 of ICN Code of Ethics for Nurses (2012) describes one of nurses' responsibilities as providing accurate, sufficient and timely information in a culturally appropriate manner to patients. Element 2 of the same code also states that the nurse carries a personal responsibility and accountability for nursing practice, and for maintaining professional competence through continual learning. In order to fulfill these challenging tasks nurses need theoretical and clinical training, support from management and administration, and collaboration with colleagues (Birmingham & Beumont 2004).

Given the fact that refeeding syndrome is, generally, poorly recognized and understood, providing nurses and other healthcare professionals with adequate training may prevent the development of RFS. If and when symptoms of RFS occur, well-trained nurses should be able to take appropriate measures.

9. Ethical Considerations

Systematic reviews are a form of research and as such they should be conducted in a responsible manner to ensure integrity and avoid misconduct (Wager & Wiffen 2011). Various organizations have produced publication ethics and guidelines. However, these requirements and conventions are scattered making it hard for researchers to get a whole picture of best practices. Wager and Wiffen (2011) encourage authors to consider the following practical and ethical issues when preparing and publishing a systematic review: list names of authors, avoid redundant (duplicate) publication, avoid plagiarism, be transparent by disclosing sources of funding and competing interests, and ensure accuracy.

The topic of this thesis was chosen through a mutual agreement between the authors. Once the topic was approved, a thesis plan was formulated and forwarded to the supervisors. The thesis writing process progressed in stages, wherein versions of the thesis were submitted for approval.

This study was conducted through a literature review of 7 articles, which are presented in Appendix 1 of this paper. The original articles were acquired from databases PubMed and Laurea Finna. The articles from PubMed were free-access whereas the articles from Laurea Finna were accessed by using student credentials to log into the database. The process of literature search, article selection, and data analysis is clearly documented in section 6 of this paper to ensure accuracy.

This paper has been written in accordance with Laurea UAS's Guidelines for writing thesis (King 2013). Appropriate accreditation was given to the authors of the original literatures, by clear cross-referencing to author, work and pages. In addition to in-text references, a list of references was prepared acknowledging author and publisher rights.

According to Oliver (2010, 28-29), the principle of informed consent applies to researches involving human participants, social groups and organizations, businesses and corporate entities. Since this study, as a systematic literature review, had no direct interaction with human participants or any of the above mentioned bodies, there was no need for acquiring informed consent. The authors of this paper have not received any funding for the research and/or authorship of this paper nor have they other competing interests.

9.1 Trustworthiness

Trustworthiness of a qualitative study is an indicator of how much the findings of the inquiry are 'worth paying attention to' (Licolin & Guba 1985). Elo et al. (2011) recommend ascertaining the trustworthiness of content analysis study by reporting the process of qualitative content analysis accurately. This begins by demonstrating the trustworthiness of the data collection process.

Choosing the most appropriate method of data collection to answer the research question is crucial in ensuring the trustworthiness of content analysis (Elo et al. 2011). The large volume of collected data in qualitative analysis demands for data interpretation and coding in a valid and reliable manner (Moretti et al. 2011). The process of category formation should be explained to illustrate the trustworthiness of the study (Elo et al. 2011). Schreier (2012) rec-

ommends data analysis to be performed by more than one person to improve comprehensivity and outcome of data interpretation.

When reporting the findings of the study the main consideration is to ensure that the findings answer the aim and research question. Further more, meticulous description of the data analysis and the relationship between primary data and the findings is essential in assuring the readers of the trustworthiness of the study (Elo et al. 2011).

The data for this thesis was collected from three different databases: PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL) and Laurea Finna. The reason for using PubMed is that it contains an extensive amount of international journal citations and abstracts, offering reference to biomedical literature (U.S National Library of Medicine 2015). Aveyard (2010, 76) recommends CINAHL for those who seek information for a nursing-based literature review because it contains a large amount of international nursing literature. Laurea's Finna article search was used to acquire English language articles that students of Laurea UAS have free access to through the secure library database. The authors themselves conducted the article search in the above-mentioned databases, after which the process and outcome were approved by both thesis supervisors and Laurea UAS's librarian.

The authors equally participated in extracting raw data, coding the information, highlighting emerging themes, and finally grouping them categorically based on the similarities they exhibited. The findings were then reported, without bias, as stated by the original authors. The discussion was presented by addressing the research question, within the scope of nursing profession.

9.2 Limitations

This systematic review has identified nursing interventions needed in preventing RFS in anorexia nervosa inpatients. A major limitation of this study was the lack of literature written by nursing professionals that address our research question. The discussion section of this paper was, therefore, deduced from the evidence provided in the original literatures where references to healthcare professionals were made. Another important constraint was the authors' lack of experience in carrying out similar studies. Aveyard (2004) states that novice researchers may not be as thorough as more experienced researchers when identifying, critiquing, and binging together literature.

The criteria set for the literature search may have resulted in the exclusion of valuable literature. This study reviewed only literature published between the years 2004 and 2015. Older articles, regardless of their significance to this study, were discarded. Due to time and re-

source constraint, only free-access literatures from three electronic databases were selected for review. Excluding literature not written in the English language also meant excluding original research and clinical trials from other regions. Some of the guidelines for identification and treatment of RFS recommended by the literatures we reviewed, may only be applicable in the countries where the researches were published.

10. Further recommendations

Due to lack of research by nursing professionals, the original articles reviewed in this study were conducted by physicians and/or dieticians. All of the articles emphasized the significance of a multiprofessional team effort. It is, therefore, recommendable that all team members collaborate seamlessly for an optimal patient outcome. Nurses, as part of the healthcare team, play a significant role in facilitating the treatment of AN inpatients and preventing the development of RFS.

Moreover, we recommend nurses receive appropriate training to be able to identify individuals at risk for RFS, prevent the development of complications, recognize symptoms of RFS once they manifest, and lessen the gravity of symptoms. For future studies, we recommend further research on the nurse's role in preventing and managing patients with refeeding syndrome.

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Appendix 1

Reviewed articles

Article	Authors	Title	Type of study	Key concepts	Aim of the study	Main findings
1	Boateng, B.S., Sriram K. & Meguid, M.	Refeeding Syndrome: Treatment considerations based on collective anal- ysis of literature case reports	Systematic literature review	RFS, AN, Nutri- tional support, RFS complica- tions	To provide management recommendations for feed- ing the undernourished patients at risk for RFS	The most effective means of preventing or treating RFS are: recognizing pa- tients at risk; providing adequate electrolyte, vitamin and micronutri- ent supplementation; moderate fluid admin- istration; energy supple- mentation with low calo- rie diet and slow incre- ment; and monitoring of critical laboratory indi- ces.
2	Tresley, J. & She- aan P.M.	Refeeding Syndrome: Recognition Is the Key to Prevention and Manage- ment	Literature review/ Case example	RFS, AN, Pre- vention of RFS, Management of RFS	To find ways to improve the prevention and man- agement of RFS	Early recognition of risk factors for and symptoms of RFS is vital. Educating health care professionals is paramount to preven- tion of RFS.
3	Crook, M.A.	Refeeding syndrome: Problems with definition and management	Literature review	RFS, Nutrition	To evaluate current NICE guidelines for the diagnosis and management of RFS against other proposals	It is premature to rec- ommend a change to the existing NICE guidelines due to lack of random- ized controlled trials in existing research.

4	Hofer, M., Pozzi, A., Joray, M., Ott, R., Hähni, F., Leuenberger, M., Känel, R. & Stanga, Z.	Safe refeeding management of anorexia nervosa inpatients: an evidence based protocol	Retrospective observational case study	AN, RFS, refeeding, complications, mortality	To evaluate the effectiveness of ESPEN guidelines (2011), regarding complications and mortality.	RF management of AN inpatients by ESPEN guidelines is safe.
5	Madden, S., Mis-kovic-Wheatley, J., Clarke, S., Touyz, S., Hay, P. & Kohn, M.	Outcomes of a rapid refeeding protocol in Adolescent Anorexia Nervosa	Research article- clinical trial	AN, RFS, Rapid refeeding, Inpatient treatment	To demonstrate potential for safe, more rapid refeeding by using standardized refeeding regime.	Calorie prescription can safely exceed levels recommended by contemporary guidelines for refeeding.
6	Mehler, P.S., Winkelman, A.B., Andersen, D.M. & Gaudiani, J.L.	Nutritional Rehabilitation: Practical Guidelines for Refeeding the Anorectic Patient	Review Article	Refeeding, AN, Nutritional rehabilitation, RFS	To identify practical guidelines for refeeding the anorectic patient.	A well-balanced nutritional oral plan with slow initiation of caloric intake is the optimal approach for refeeding, but alternative modes also have limited roles.
7	Sachs, K., Andersen, D., Sommer, J., Winkelman, A. & Mehler, P.S.	Avoiding Medical Complications During the Refeeding of Patients With Anorexia Nervosa	Non-systematic literature review	Refeeding, AN, medical complications, nutritional rehabilitation	To review major complications that may arise during refeeding, how best to avoid them, and how to treat them.	Gradual increase of calories overtime is paramount to preventing RFS. Recent opinion, however, challenges the approach of low calorie start with slow and gradual increase. Further studies are needed to determine if more aggressive feeding protocols have universal safety and efficacy.