BRIEF REPORT

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Characteristics and outcomes of avoidant/restrictive food intake disorder in Japanese elementary-school students on total parenteral nutrition

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ABSTRACT

The clinical outcomes of adolescents with avoidant/restrictive food intake disorder (ARFID) remain unclear. Furthermore, no report has compared the characteristics of ARFID and restricting-type anorexia nervosa (R-AN) in elementary-school students on total parenteral nutrition (TPN). This study retrospectively reviewed inpatients diagnosed with ARFID or R-AN between 2005 and 2019. Patients with ARFID (two boys and seven girls) and R-AN (13 girls) were hospitalized because of rapid physical deterioration, and nutrition therapy was continued without withdrawal. The ARFID group exhibited significantly lower body weights at admission than the R-AN group and gained an average of 6.5 kg during hospitalization; furthermore, the monthly weight gain during hospitalization was significantly higher, and no relapse was observed. Early physical improvement in ARFID resulted in good recovery. In conclusion, TPN can be easily introduced to patients with ARFID, in whom aversive eating is a concern, and is a suitable treatment for ARFID.

KEYWORDS

Adolescent, Anorexia nervosa, Avoidant/restrictive food intake disorder, Eating disorder, Total parenteral nutrition

INTRODUCTION

Eating disorders without a clear desire to lose weight are common among children. Children are more vulnerable to stress than adults and may experience severe anxiety regarding domestic or school stress, being forced to eat school lunch, and physical symptoms (vomiting associated with infection), which constitute triggers for eating disorders.[1]

In the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5),[2] the classification of eating disorders involved the replacement of feeding disorder of infancy or early childhood with a broader diagnostic term referred to as avoidant/restrictive food intake disorder (ARFID). Patients with ARFID typically want to gain weight but avoid eating for other reasons, such as the sensory characteristics of food, fear of potential consequences of eating (i.e., vomiting, reflux, choking), or lack of interest. However, patients with anorexia nervosa (AN) have an intense fear of gaining weight or becoming fat, although at a significantly low weight.[2] The DSM-5 suggests that eating or feeding disturbance may arise from an apparent lack of interest in eating or food, nutritional avoidance based on the sensory characteristics of food, or concerns about the aversive consequences of eating. In 2018, Norris et al classified patients with ARFID into three categories as follows: "ARFID-limited intake" subtype,

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"ARFID-limited variety" subtype, and "ARFID-aversive" subtype.[3] Compared with AN, ARFID is characterized by the absence of the fear of weight gain or perceptual disturbance of body shape.[4-6] Several studies have reported that adolescents with ARFID are younger and more likely to be male, experience longer hospital stays, and often require more enteral nutrition than adolescents with AN.[7-9] Compared with patients with other eating disorders, those with ARFID tend to remain untreated for a longer period, have a poor response to weight gain, and often withdraw from treatment.[7,10] Furthermore, some reports have indicated that long-term ARFID outcomes are comparable to AN outcomes;[11,12] however, one research group showed that ARFID outcomes were superior to AN outcomes.[13] Thus, a lack of consensus remains.

Alleviating malnutrition in adolescents with eating disorders is important; nevertheless, this is often difficult to achieve due to resistance to food intake and weight gain. A central venous line is traditionally inserted with a central venous catheter through the internal jugular or subclavian vein. However, central venous hyperalimentation with a peripherally inserted central catheter (PICC) is widely used in pediatric patients to reduce the risks of complications due to insertion. Although PICC nutrition therapy is expected to improve malnutrition early, catheter-related bloodstream infections can occur as a fatal complication. Therefore, careful management during hospitalization is required.[14,15]

In a previous study, we administered total parenteral nutrition (TPN) treatment for patients with refractory adolescent eating disorders who would typically not give consent for tube feeding and reported that early physical recovery with aggressive nutrition therapy led to improved prognoses.[16] In the present retrospective cohort study, we compared elementary-school students with ARFID on TPN with those with restricting-type AN (R-AN).

METHODS

Ethical approval

The present study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the ethical committee of the Clinical Research Center, Wakayama Medical University (No. 2844). All patients and their legal guardians provided full informed consent once the purpose and nature of this study had been explained.

Study design and subject selection

In this retrospective study, we examined the clinical course of 22 elementary-school children who were admitted for eating disorders at the Department of Pediatrics in Wakayama Medical University between January 2005 and December 2019 and who received TPN treatment. Patients with ARFID (two boys and seven girls) and R-AN (13 girls) were retrospectively identified based on the DSM-5 criteria. Diagnosis was established after discussing the clinical course with three pediatricians who had extensive experience in treating pediatric psychiatric disorders. The indications for TPN treatment included cases of severe malnutrition, dehydration, electrolyte disorders, hypoglycemia, and heart failure; however, it was difficult to obtain consent for tube feeding from these patients.

Nutritional protocol under cognitive therapy for pediatric eating disorders

Patients were instructed on the importance of nutritional intake using cognitive behavioral therapy, and oral intake and infusion calories were determined in consultation with the physician in charge. None of the patients refused treatment, and they were eventually discharged if there was no need to force-feed them during hospitalization.

The inpatient medical team was organized by pediatricians, nursing staff, childcare staff, in-hospital class staff, and catheter management staff. The TPN energy intake on hospital admission started at 2090 kJ per day for the first week and was increased every week to ensure acceptable weight gain with oral feeding and TPN. Nasogastric (NG) tube feeding was started when oral intake did not improve for several months on TPN, and liver damage worsened (alanine aminotransferase of >100 U/L; normal range, 10–42 U/L). If NG tube insertion triggered the start of oral intake, tube feeding was promptly stopped. After confirming that normal dietary patterns were restored and that weight gain could be maintained even if TPN treatment was stopped, overnight stays were initiated. If repeated overnight stays did not affect food intake, the patient was discharged from the hospital and treated as an outpatient. After discharge, we followed up for a year of relapse of appetite.

Investigation and analysis

We retrospectively examined the patients' clinical data via a chart review. Information on age, sex, weight, height, body mass index (BMI), time from onset to admission, and gonadotropin levels was collected at admission. The information collected relative to the hospitalization period included the length of hospital stays, duration of TPN treatment, weight increase, BMI increase, medication, and use of NG feeding. To evaluate prognosis, the presence or absence of appetite loss relapse within one year after discharge was investigated.

The mean (standard deviation) age, height, weight, BMI, time from onset to hospitalization, length of hospital stay, and duration of TPN treatment in the ARFID and R-AN groups were evaluated and compared using Student's *t*-test. The two groups (ARFID vs. R-AN) were compared with respect to sex, medication, enteral nutrition, and rehospitalization using Fisher's exact test. The BMI

TABLE 1 Characteristics of patients with ARFID and R-AN

Case	Sex	Age[†]	Menarche	Subtype[‡]	Event for onset	Medication	FSH (at admission, mIU/mL)	LH (at admission, mIU/mL)	FSH (at discharge, mIU/mL)	LH (at discharge, mIU/mL)	Prognosis[§]
Patients with ARFID (n = 9)											
1	F	10y1m	Pre	Aversive	Gastroenteritis	Laxative	<1.0	<0.5	5.9	1.6	Recovery
2	F	10y3m	Pre	Aversive	Gastroenteritis	–	<1.0	<0.5	2.8	0.5	Recovery
3	M	10y4m	/	Intake	Family discord	–	1.5	<0.5	2.5	<0.5	Recovery
4	F	11y8m	Pre	Aversive	Gastroenteritis	Laxative	<1.0	<0.5	1.1	<0.5	Recovery
5	F	11y10m	Pre	Aversive	Orthodontics	–	<1.0	<0.5	11.7	5.9	Recovery
6	M	11y10m	/	Aversive	Forced to eat school lunch	–	<1.0	<0.5	8.0	3.1	Recovery
7	F	12y0m	Pre	Aversive	Food allergy	–	7.1	<0.5	7.1	7.9	Recovery
8	F	12y8m	Pre	Aversive	Junior high school exam	–	1.2	<0.5	7.1	5.7	Recovery
9	F	12y9m	Post	Aversive	Family discord	Laxative	<1.0	<0.5	7.0	<0.5	Recovery
Patients with R-AN (n = 13)											
1	F	9y3m	Pre	R-AN	Forced to eat school lunch	–	<1.0	<0.5	3.5	<0.5	Recovery
2	F	10y11m	Pre	R-AN	Desire for thinness	Anti-psychotic anxiolytic	<1.0	<0.5	3.5	<0.5	Relapse Feed tube
3	F	11y2m	Pre	R-AN	Unknown	Anti-psychotic SSRI	<1.0	<0.5	2.0	0.6	Relapse Feed tube
4	F	11y7m	Post	R-AN	Desire for thinness	Laxative	10.1	<0.5	14.0	15.4	Relapse
5	F	11y8m	Post	R-AN	Desire for thinness	–	<1.0	<0.5	9.0	0.5	Recovery
6	F	11y9m	Post	R-AN	Junior high school exam	Laxative	5.8	<0.5	9.5	3.6	Relapse
7	F	11y11m	Pre	R-AN	Desire for thinness	–	<1.0	<0.5	17.0	2.2	Recovery
8	F	12y0m	Post	R-AN	Family discord	Laxative	10.2	<0.5	4.1	5.2	Relapse
9	F	12y1m	Pre	R-AN	Family discord	Laxative	<1.0	<0.5	17.5	2.8	Recovery
10	F	12y2m	Pre	R-AN	Unknown	Laxative	2.2	<0.5	3.0	0.7	Relapse
11	F	12y6m	Post	R-AN	Family discord	Laxative	8.8	1.9	10.5	1.3	Relapse
12	F	12y7m	Pre	R-AN	Desire for thinness	Anti-psychotic SSRI	1.2	<0.5	4.3	0.5	Recovery
13	F	12y7m	Post	R-AN	Desire for thinness	Sleeping aid	<1.0	<0.5	5.5	1.1	Relapse

ARFID, avoidant/restrictive food intake disorder; FSH, follicle-stimulating hormone (the normal range for males is 2.0–8.3 mIU/mL, and the normal range for females in the follicular phase is 3.0–14.7 mIU/mL); LH, luteinizing hormone (the normal range for males is 0.8–5.7 mIU/mL and the normal range for females in the follicular phase is 1.8–10.2 mIU/mL); R-AN, restricting-type anorexia nervosa; SSRI, selective serotonin reuptake inhibitor; TPN, total parenteral nutrition treatment; /, not applicable. [†] Years and months at admission. [‡] Aversive, ARFID aversive subtype; Intake, ARFID intake subtype. [§] Prognosis, the presence or absence of appetite loss relapse within one year and with or without feeding tube during hospitalization.

TABLE 2 Comparison of patients in the ARFID and R-AN groups at admission

Variables	ARFID Group (n = 9)	R-AN Group (n = 13)	P-value	Cohen's d [95% CI]	Odds ratio[95% CI]
Age at admission (years)	11.5 ± 1.0	11.7 ± 0.9	0.608[†]	0.23 [−0.62, 1.08]	
Sex (boy/girl)	2/7	0/13	0.156[‡]		9.00[§][0.38, 213.18]
Menarche (pre/post)	6/1	7/6	0.329[‡]		5.14 [0.48, 55.64]
Height at admission (cm)	140.0 ± 4.9[¶]	147.0 ± 10.8	0.123[†]	0.76 [−0.19, 1.71]	
Weight at admission (kg)	23.8 ± 3.2[¶]	31.3 ± 6.0	0.007[†]	1.43 [0.40, 2.46]	
BMI at admission (kg/m^2)	12.1 ± 1.3[¶]	14.3 ± 1.2	0.001[†]	1.78 [0.69, 2.87]	
BMI Z-score at admission	−2.2 ± 0.6	−1.6 ± 0.3	0.008[†]	1.35 [0.40, 2.30]	
Onset to admission (months)	5.0 ± 2.9	4.3 ± 3.3	0.615[†]	0.22 [−0.63, 1.07]	

Data are shown as the mean ± standard deviation or number of cases. ARFID, avoidant/restrictive food intake disorder; BMI, body mass index; *CI*, confidence interval; R-AN, restricting-type anorexia nervosa. [†]Student-t test. [‡]Fisher's exact test. [§]Corrected odds ratio. [¶]Calculated for seven girls.

Z-score was calculated from the age and sex-adjusted BMI of Japanese children.[17] Differences with $P < 0.05$ were considered statistically significant. Cohen's d was used to calculate the effect size of difference for two independent groups, and odds ratios were used to calculate the effect size for binary variables. All statistical analyses were performed using JMP Pro 14 (SAS Institute Inc., Tokyo, Japan).

RESULTS

Characteristics of patients with ARFID

The characteristics of patients with ARFID and R-AN are summarized in Table 1. Among those with ARFID, eight patients presented with concerns about aversive eating (aversive subtype), whereas one patient showed an apparent lack of interest in eating (intake subtype). Previous events that might be associated with ARFID onset included gastroenteritis (n = 3), family discord (n = 2), orthodontics (n = 1), being forced to eat school lunch (n = 1), food allergy (n = 1), and junior high school examinations (n = 1). In the R-AN group, rather than the ARFID group (n = 0), the desire for thinness sometimes caused the onset (n = 6). All female patients with ARFID and R-AN had either amenorrhea or no menstruation, and gonadotropin levels were low at admission but improved at discharge.

Comparison between patients with ARFID and R-AN at admission

A comparison between patients with ARFID and R-AN at admission is shown in Table 2. There was no significant difference in age or time from onset to admission between the groups. Patients in the R-AN group were all girls. Height at admission tended to be higher in the R-AN group than in the ARFID group. Body weight and BMI Z-score at admission were significantly lower in the ARFID group than in the R-AN group.

Comparison between patients with ARFID and R-AN during the clinical course

A comparison between patients with ARFID and R-AN during hospitalization is presented in Table 3. No significant differences in the length of hospital stay and duration of TPN treatment were observed between the two groups. Growth during hospitalization tended to be higher in the ARFID group than in the R-AN group. There was no significant difference in weight gain during hospitalization; however, the ARFID group showed a significant increase in monthly weight gain (P = 0.044) and BMI Z-score gain (P = 0.025). In the ARFID group, laxatives were administered to three patients during hospitalization. In the R-AN group, laxatives were administered in six cases, selective serotonin reuptake inhibitors (SSRIs) and antipsychotics were prescribed in two cases, antipsychotics and anxiolytics were prescribed in one case, and sleeping aids were prescribed in one case. Two patients in the R-AN group underwent gastric tube nutrition therapy. At one year after discharge, there were significantly more patients in the R-AN group who were readmitted due to appetite loss recurrence (n = 8) than in the ARFID group (n = 0).

DISCUSSION

Comparisons of the ARFID and R-AN groups at admission showed no difference in age and time from onset to admission; however, weight and BMI Z-score were significantly lower in the ARFID group than in the R-AN group. Regarding the comparison of hospitalization progress, weight gain tended to be higher in the ARFID group, and monthly weight and BMI Z-score gains were also significantly higher. In the R-AN group, antipsychotics, SSRIs, and sleeping aids were administered. In addition, two patients in the R-AN group refused oral intake and required tube feeding. Compared with the ARFID group, the R-AN group often resisted nutritional treatment for a longer period, which was believed to have slowed the pace of weight gain.

The diagnosis of ARFID was established by three pediatric specialists. Eight patients with ARFID were classified as having an aversive subtype, and one patient was classified as having an intake subtype. Similar to previous reports,[3,18]

TABLE 3 Comparison between patients in the ARFID and R-AN groups during hospitalization

Variables	ARFID Group (n = 9)	R-AN Group (n = 13)	P-value	Cohen's d [95% CI]	Odds ratio [95% CI]
Hospitalization (days)	182 ± 103	214 ± 131	0.542†	0.27 [−0.58, 1.12]	
Duration of TPN (days)	122 ± 77	118 ± 72	0.904†	0.05 [−0.80, 0.90]	
Height at discharge (cm)	141.3 ± 5.0¶	148.5 ± 10.1	0.080†	0.70 [−0.18, 1.58]	
Weight at discharge (kg)	31.0 ± 3.6¶	35.9 ± 6.4	0.094†	0.87 [−0.02, 1.76]	
BMI at discharge (kg/m^2)	15.6 ± 1.6¶	16.2 ± 1.7	0.433†	0.49 [−0.37, 1.35]	
BMI Z-score at discharge	−1.1 ± 0.6	−0.9 ± 0.5	0.543†	0.37 [−0.48, 1.23]	
Physical recovery during hospitalization					
Height growth (cm)	1.8 ± 2.3	1.5 ± 2.0	0.750†	0.14 [−0.71, 0.99]	
Monthly Height growth (cm)	0.20 ± 0.23	0.17 ± 0.19	0.684†	0.18 [−0.67, 1.03]	
Weight gain (kg)	6.5 ± 2.1	4.6 ± 4.6	0.278†	0.48 [−0.38, 1.34]	
Monthly weight gain (kg)	1.41 ± 0.86	0.74 ± 0.61	0.044†	0.93 [0.03, 1.83]	
BMI increase (kg/m^2)	2.9 ± 1.4	1.9 ± 1.9	0.167†	0.62 [−0.25, 1.49]	
Monthly BMI increase (kg/m^2)	0.67 ± 0.47	0.31 ± 0.27	0.032†	1.00 [0.10, 1.90]	
BMI Z-score increase	1.08 ± 0.53	0.66 ± 0.65	0.126†	0.69 [−0.19, 1.57]	
Monthly BMI Z-score increase	0.25 ± 0.18	0.11 ± 0.09	0.025†	1.05 [0.14, 1.96]	
Events in progress					
Medication	3	10	0.079‡		6.67 [1.00, 44.29]
Enteral nutrition	0	2	0.494‡		4.13§ [0.18, 96.94]
Rehospitalization	0	8	0.006‡		29.36§ [1.41, 613.49]

Data are shown as the mean ± standard deviation or number of cases. ARFID, avoidant/restrictive food intake disorder; BMI, body mass index; *CI*, confidence interval; R-AN, restricting-type anorexia nervosa; TPN, total parenteral nutrition treatment. †Student-*t* test. ‡Fisher's exact test. §Corrected odds ratio. ¶Calculated for seven girls.

the aversive type was the most common. Aversion to eating has been reported to be associated with a more severe and acute onset of ARFID.[18] Thus, we speculate that most patients with ARFID in the present study had an aversive subtype.

There have been a few reports on the long-term prognosis of eating disorders in young patients.[12,19-22] In a previous study on the association between height at presentation and outcomes,[21] five out of 23 patients with AN at follow-up (22%) had a height two standard deviations under the age-expected average; however, only one of these cases was short at baseline. In our study, aggressive nutrition therapy resulted in a height increase in both cases during hospitalization. There was no significant difference in growth between the ARFID and R-AN groups; however, the ARFID group tended to show a greater increase in weight, height, and BMI Z-score and had more premenarchal patients than the R-AN group. Consequently, the ARFID group had a greater physical recovery after TPN than the R-AN group, and patients with ARFID are expected to further improve in the long term.

Patients with ARFID had low resistance to treatment and were more receptive to inpatient treatment, but required a hospital stay of approximately six months until their dietary intake was completely stable. We previously reported that the gonadotropin levels and biochemical findings gradually improved several months after starting treatment in adolescents with eating disorders who received TPN treatment.[16] Therefore, it is considered that short-term nutritional treatment is insufficient for complete physical recovery. In our opinion, we speculated that ARFID, which is not associated with a desire to lose weight, still leads to rapid weight loss due to a loss of appetite. Specifically, patients with ARFID initially undergo a triggering event (although it may not be obvious, or it may involve inherent sensory sensitivities or avoidance of foods by type, texture, color, or smell, among others, such as children with autism) of refusal to eat, after which dietary intake is reduced followed by malnutrition leading to physical deterioration and further loss of appetite. Additionally, the gonadotropin levels at admission were low, which may have contributed to their physical deterioration; however, the treatment improved the gonadotropin levels in all cases. Therefore, patients with ARFID are expected to recover physically and improve their appetite if long-term nutritional management is successful. Similarly, this hypothesis is supported by the fact that the ARFID group did not relapse after nutritional recovery in this study. Improving physical deterioration due to malnutrition is considered a major strategy for improving appetite in patients with ARFID.

This retrospective cohort study is limited to severe patients requiring inpatient treatment and does not provide treatment guidelines for ARFID in general. In the future, a treatment guideline for ARFID should be established by examining the long-term therapeutic effects in a prospective study, including patients with mild symptoms.

In summary, despite the concern about aversive eating, TPN was not rejected by patients with ARFID. Thus, it can be easily introduced as a treatment to these patients and may be a suitable option during the growth period.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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