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Factors Associated With Success and Failure of Weaning Children From Prolonged Enteral Nutrition: A Retrospective Cohort Study

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ABSTRACT

Objectives: The aims of the present study were to assess the efficacy of a tube weaning program, and to identify factors associated with success and failure.

Methods: This was a retrospective cohort study including all pediatric patients on enteral nutrition (EN) for ≥ 6 months for whom at least 1 attempt of weaning was performed in a single tertiary referral center from 2012 to 2017, with a minimum follow-up of 6 months after EN discontinuation. Weaning program was individualized to each child. Weaning success was defined a priori. Factors associated with success were investigated using multivariate analysis.

Results: Ninety-four patients were enrolled, in whom a total of 114 attempts of weaning were performed at a median age of 51 ± 40 months. Success was achieved in 80 attempts (success rate of 70%). One hundred three (92%) weaning attempts were performed at home with a follow-up in the outpatient clinic, mostly (74%) by a progressive (>1 month) reduction of tube feeding. Patients who required psychological support during weaning had more failures than patients who did not (odds ratio = 5.7, 95% confidence interval [1.2–27.0], $P = 0.03$). The presence of impaired oral feeding skills at the time of EN discontinuation was also predictive of failure (odds ratio = 6.2, 95% confidence interval [0.05–0.5], $P = 0.005$).

Conclusions: Our progressive, mostly outpatient-based, patient-tailored program of weaning from EN is effective for tube-dependent children. Children who need psychological support during weaning and those who present impaired oral feeding skills represent a subgroup of at-risk patients for whom alternative weaning strategies may need to be considered.

Key Words: outcome, outpatient, pediatrics, tube feeding, weaning

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What Is Known

- Weaning children from prolonged enteral nutrition is a challenge for both parents and healthcare providers.
- Weaning practice widely varies worldwide, and predictive factors of success or failure are largely unknown.

What Is New

- A progressive, mostly outpatient-based weaning program is effective to wean children from prolonged enteral nutrition.
- The need for psychological support during weaning and the presence of impaired oral feeding skills may be predictive of weaning failure.

Enteral nutrition (EN) allows adequate nutritional intake and growth in children with chronic and/or severe diseases and in whom oral intake is impossible, insufficient, or unsafe (1). Most of the efforts have been devoted to provide safe and efficient EN, including the development of tube feeding products adapted to children, the use of percutaneous endoscopic gastrostomy, and home services (2). Once nutritional status is improved and oral feeding is medically possible, weaning from EN should be considered, but it may be difficult for many reasons. Therefore, some children continue to be tube fed for many years despite the disappearance of the initial indication for EN. Prolonged EN may negatively impact the development of normal oral feeding skills regardless of the underlying disease (3), because of the experience of negative oral stimuli (tube placement, gastroesophageal reflux, vomiting), the lack of tastes and textures, and the impairment of parent-child interactions at mealtimes (3–7). Side effects of long-term EN include decreased appetite, lack of interest in food or total refusal of oral feeding (8). In recent years, several weaning methods for tube-dependent children have been described, overall based on the rapid decline in caloric intake with the aim of provoking hunger and achieving weaning within a few weeks during a therapeutic hospitalization and under the supervision of a multidisciplinary team (9–15). Nonetheless, contrary to the management of EN (indications, contraindications, timing, and modalities), which have been addressed by international guidelines (16,17), no recommendations or agreement currently exist on weaning modalities, which are still based on individual,

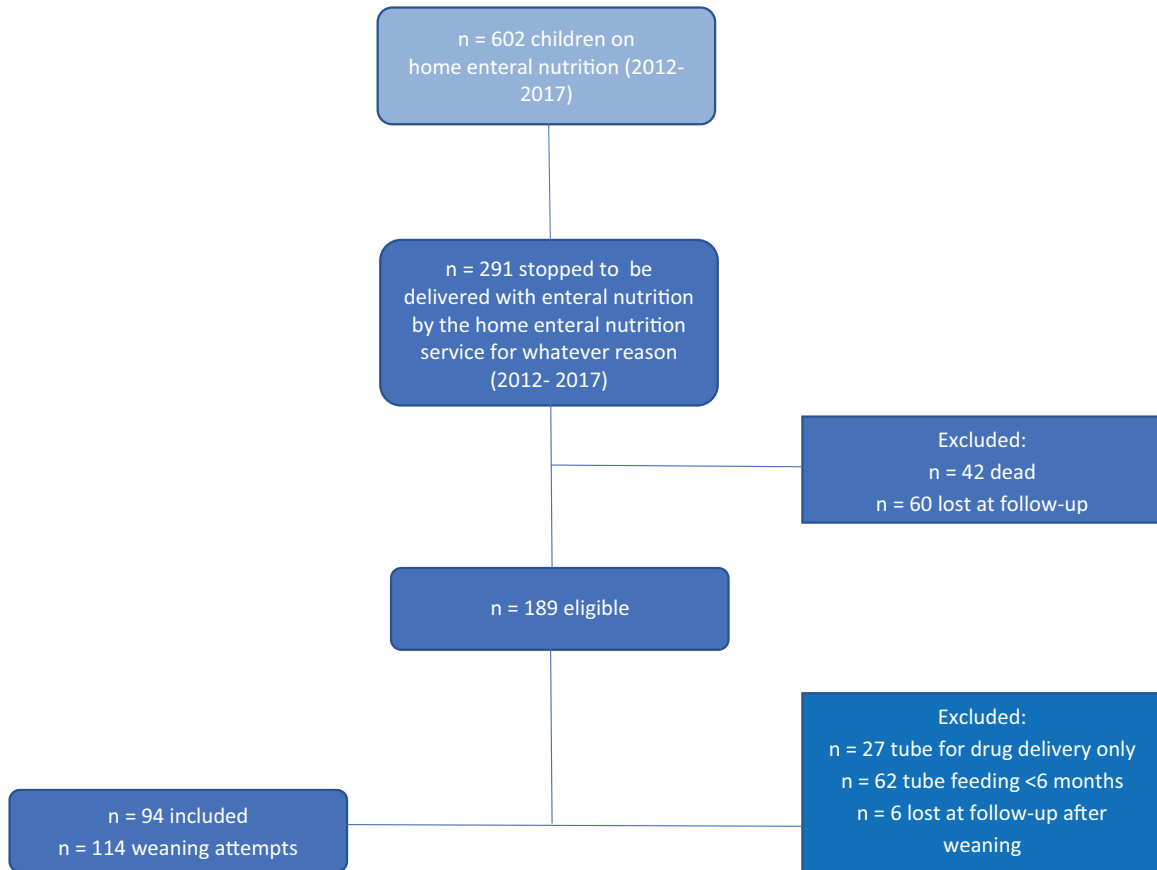


FIGURE 1. Study flow diagram.

nonstandardized experience or protocol. Moreover, the factors associated with success or failure of weaning have not been extensively addressed. The aims of our study were to assess the efficacy of a weaning program, and to identify factors associated with success and failure.

METHODS

Participants and Data Collection

This study was a retrospective, observational cohort study assessing all pediatric patients in whom an attempt of weaning from EN was performed in a single tertiary referral center from 2012 to 2017. Patients were selected from the electronic files of our home EN service. Children were eligible for inclusion when they had been on home EN (via nasogastric, gastrostomy, or jejunostomy tube) for at least 6 consecutive months, were aged 6 months to 18 years at the initiation of weaning, attempted to be weaned from EN at least once and had a minimum of 6 months follow-up after EN discontinuation (or 6 months of follow-up after resumption of EN in children who failed). Exclusion criteria were tube feeding for <6 months, tube placement as a route for drug delivery only, and discontinuation of EN for <6 months. Medical records were reviewed to assess sex, gestational age, birth weight, underlying disease, age at tube feeding introduction, tube feeding modalities, age at the time of weaning attempt, outcome, and duration of the weaning program. Multidisciplinary (dietician, psychologist, speech therapist) follow-up data were also collected. Nutritional outcome was studied by comparing the weight-for-age z score at the beginning of the weaning attempt and 6 months after the definitive discontinuation

of tube feeding, or 6 months after resumption of EN in children who failed to be weaned. In accordance with the French laws, as it was a retrospective observational study, neither formal informed consent from the patients nor ethical committee approval was required. All data were anonymized.

Procedure of Weaning

Weaning program was individualized to each child and no formal protocol was applied. Nonetheless, they may be recognized some common aspects and practical principles. The decision to start weaning was taken when: nutritional status was considered satisfactory according to the standard World Health Organization (WHO) growth reference charts (<https://www.who.int/child-growth/standards/en/>), and stable; underlying disease was nonprogressive; sensorimotor skills were improving, and swallowing functional and safe. Outpatient setting was preferred when possible, and was based on the progressive reduction of EN, which was obtained by daily volume reduction (usually—100 mL/day for 4 weeks, then further reduced based on clinical evolution) and/or consecutive discontinuation (1 day/wk for 1 month, then 2 days per week, etc), while encouraging oral intakes. In case of bolus regimen, it was also tried the reduction of bolus volume either daily or 1 every other day. Parental request was also taken into account. Weight was monitored monthly by parent reporting, whereas onsite outpatient visits were performed about once every 3 months. Inpatient weaning was usually considered as a second-level option, or based on the child medical situation and/or parental request. The

“NoTube” method (rapid, hunger provocation-based weaning method consisting in reducing EN >50% in less than a week, followed by a definitive discontinuation of tube feeding within few weeks during hospitalization) (12) was not considered an option in any case. Weaning was stopped if weight loss exceeded 10% compared to the weight at the beginning of the weaning attempt. Each program was designed and validated by a multidisciplinary team, made up of the referent pediatric gastroenterologist, a dietician, and other health professionals when clinically indicated, including a speech-language therapist and a psychologist. Overall, the approach to the child was multidisciplinary throughout the whole program.

Definitions

Patients were defined to be undernourished if weight-for-age z score was <-2 standard deviation (SD). An attempt of weaning was defined as the decision of starting to reduce tube feeding with the final aim of discontinuing it, i.e. the transition period toward an exclusive oral feeding. Weaning was defined as tube feeding discontinuation and resumption of an exclusive oral feeding. Weaning was a priori defined as a success when the patient was fully orally fed 6 months after discontinuation of EN, together with one of the following: <1 SD decline in weight for age z score, ≥ 1 SD decline in weight-for-age z score but weight-for-age z score still ≥ -2 SD, increase in weight-for-age z score over the 6 months follow-up after weaning. Conversely, weaning failure was defined as a decline in weight-for-age z score of >1 SD or a weight-for-age z score of <-2 SD 6 months after weaning (or tube feeding resumption for any reason in the first 6 months after discontinuation). Z score cut-off values used derived from the WHO Global Database on Child Growth and Malnutrition (<https://www.who.int/nut-growthdb/about/introduction/en/index5.html>). Impaired oral feeding skills meant the impairment of oral sensory functioning (hypo- or hypersensitivity), inhibiting acceptance and tolerance of liquids and food textures expected for age (18,19). Poor tolerance to EN

was defined by the occurrence of symptoms (vomiting, diarrhea, and/or abdominal pain) leading to the modification of EN regimen and/or formula (16,17). Diet was considered normal when balanced and age appropriate.

Statistical Analyses

Qualitative variables were expressed by frequencies and percentages. Continuous variables were expressed by mean and SD in case of normal distribution and by median and interquartile range otherwise. Two groups of patients were defined: success and failure. Differences between the 2 groups were analyzed using χ^2 or Fisher exact test, or Student or Wilcoxon t tests for nonparametric variables. Data were matched in case of multiple weaning attempts. Variables with a $P < 0.2$ in univariate analysis were introduced in multivariable logistic regression with a stepwise selection (results expressed with the odds ratio [OR] and its confidence interval). The significance level was set to $P < 0.05$. Statistical analyses were performed using Excel for Windows (2007).

RESULTS

Ninety-four patients were eligible for analysis based on inclusion criteria (Fig. 1). Demographics and tube feeding data are shown in Tables 1 and 2. The patients were classified according to medical and psychosocial comorbidities. A majority of patients had gastrointestinal ($n=30$, 32%) and genetic ($n=23$, 25%) underlying diseases. Other comorbidities were feeding disorder ($n=13$, 14%), diaphragmatic hernia ($n=10$, 11%), neurological disease ($n=6$, 6%), metabolic disease ($n=3$, 3%), malignancy ($n=3$, 3%), and others ($n=6$, 6%).

One hundred fourteen weaning attempts were performed over the study period (Table 3). Each patient underwent a median of 1 attempt (range: 1–4). Weaning was almost exclusively ($n=103$, 92%) carried out in the outpatient clinic. It was progressive (>1 month) in 65 (74%) cases, either by volume reduction or

TABLE 1. Baseline characteristics of study participants

Characteristics	n = 94
Sex, female (n, %)	48 (51)
Gestational age, wk (mean, SD)	37 \pm 3.9
Gestational age, wk (n, %)	
<28	3 (3)
28–31	9 (9)
32–36	24 (26)
≥ 37	58 (62)
IUGR (n, %)	23 (24)
Impaired oral feeding skills at EN beginning	67 (71)
Swallowing problems	20 (21)
Gastroesophageal reflux disease (n, %)*	41 (44)
Age at EN beginning, mo (median, IQR)*	4 (0–152)
Age at EN beginning, mo (n, %)*	
≤ 1	34 (37)
2–12	31 (33)
13–60	23 (25)
≥ 61	5 (5)
Oral feeding before EN (n, %)*	56 (61)
Undernutrition before EN (n, %)*	40 (44)

EN = enteral nutrition; IQR = interquartile range; IUGR = intrauterine growth retardation; SD = standard deviation.

* ≥ 1 missing data.

TABLE 2. Characteristics of tube feeding

Characteristics	n = 94
Enteral access (n, %)	
Gastrostomy	76 (81)
Nasogastric tube	11 (12)
Jejunostomy	7 (7)
Type of formula (n, %)*	
Polymeric hypercaloric	43 (49)
Polymeric isocaloric	31 (36)
Semielemental	11 (13)
Breast milk or infant formula	1 (1)
Special metabolic formula	1 (1)
Regimen (n, %)*	
Nocturnal continuous	70 (76)
Nocturnal continuous + ≥ 2 day-time boluses	7 (8)
Daily nap + nocturnal continuous	7 (8)
Bolus	6 (7)
24-h continuous	1 (1)
Poor tolerance to EN (n, %)*	6 (4)
Multidisciplinary follow-up (n, %)	
Dietician	94 (100)
Speech-therapist*	50 (59)
Psychologist	13 (16)

EN = enteral nutrition.

* ≥ 1 Missing data.

TABLE 3. Characteristics of weaning attempts

Characteristics	n = 114
Age at beginning, mo (mean, SD)	51 ± 40
Age at beginning, y (n, %)	
<1	10 (9)
1–5	79 (69)
6–10	14 (12)
>10	11 (10)
Duration of EN, mo (mean, SD)	39 ± 28
Undernutrition at beginning of weaning (n, %)*	12 (11)
Weight-for-age z score at beginning of weaning (median, IQR)*	−1 (−3 – +3)
Nutritional evaluation before weaning (n, %)	39 (34)
Oral/enteral energy intake ratio, % (median, IQR)	55 (2–75)
Impaired oral feeding skills at EN discontinuation (n, %)*	46 (40)
Weaning initiative (n, %)*	
Medical doctor	96 (86)
Parents	14 (13)
Child	2 (1)
Modality (n, %)*	
Outpatient	103 (92)
Inpatient	8 (7)
Day hospital	1 (1)
Multidisciplinary follow-up (n, %)*	
Dietician	114 (100)
Speech therapist	60 (53)
Psychologist	15 (13)
Others†	14 (12)
Rapid (≤1 mo) EN discontinuation (n, %)	29 (26)
Technique (n, %)*	
Daily volume reduction	45 (40)
Consecutive discontinuation	34 (30)
Combined or other	10 (10)

EN = enteral nutrition; IQR = interquartile range; SD = standard deviation.

*≥1 Missing data.

†Physiotherapist, psychomotor therapist.

consecutive discontinuation or both. In 29 (26%) cases weaning was rapid (tube feeding stopped within 1 month, within 1 week in 23 cases of them), based on a parents' request. The median duration of all the weaning attempts was 5 months (range: 0–68). Thirteen weaning attempts (11%) were precociously interrupted, and EN resumed, because of rapid weight loss (n = 10), infectious disease during the program (n = 2), or on child's request (n = 1). Finally, 80 attempts of weaning were successful, indicating a success rate of 70%. Notably, only 10 patients among those who failed resumed EN within 1 year (“nutritional” failures), of whom 7 remained undernourished at the last follow-up visit (median 34 + 16.7 months after weaning). At the end of the weaning program (when EN was definitively stopped), the median weight-for-age z score was significantly different between success group and failure group (−1 SD [−3 – +3] and −1.5 SD [−3–0], respectively; P = 0.025). At 6 months, the median weight-for-age z score was stable in the success group (−1 SD [−2.5 – +3]), while declined in the failure group (−2.1 SD [−2.5 – 1.5]; P = 0.001) (Figure, Supplemental Digital Content, <http://links.lww.com/MPG/B939>). A normal oral diet was reported in 72% of patients (missing data in 9 patients) when EN was discontinued, and in 78% of patients at 6 months.

Gastrostomy tubes were definitively removed after a median postweaning period of 5 months (range: 1–52). Stoma closure was spontaneous in 64% of cases. In the remaining cases a surgical closure was performed after a median of 4 months (range: 1–18).

Although older age and longer EN duration were found to be associated with weaning failure in univariate analysis, the associations were not confirmed in multivariate analysis (Table, Supplemental Digital Content, <http://links.lww.com/MPG/B940>; Table, Supplemental Digital Content, <http://links.lww.com/MPG/B941>). Patients for whom weaning was unsuccessful were more likely to require psychological support during weaning with an OR of >5 compared to patients who could be weaned (OR = 5.7, 95% confidence interval [1.2–27.0], P = 0.03). Impaired oral feeding skills at EN discontinuation had a >6-fold increase in the risk of weaning failure (OR = 6.2, 95% confidence interval [0.05–0.5], P = 0.005).

Overall, 93 out of 114 (82%) attempts of weaning led to a permanent cessation of EN, versus 18% resumption of EN. In the analysis of the subgroup of attempts at weaning who definitely led to EN discontinuation, the age at weaning and the duration of EN were not significantly associated to EN resumption (51 ± 43 vs 51 ± 40 months, P = 0.96; 38 ± 35 vs 43 ± 39 months, P = 0.67, respectively). Conversely, children who required a psychological support during weaning were more likely to come back to tube feeding in comparison to those who did not (n = 9, 10% vs n = 6, 30%; P = 0.016). All the children who resumed tube feeding had a gastrostomy (n = 21, 100% vs n = 74, 79%; P = 0.021).

DISCUSSION

This study shows that a progressive, mostly outpatient-settled, patient-tailored program of weaning from EN is effective for the majority of tube-dependent children. The need for a psychological support during weaning and the presence of impaired oral feeding skills at the time of tube feeding discontinuation are independently associated to the failure of weaning.

To our knowledge, this is the first time that the need for psychological support during weaning is found to be associated to the outcome of weaning itself. The risk of weaning failure was >5-fold higher among children who needed a psychological support during the weaning program. The reasons of psychological referral were variable, including disrupted parent-child interactions around meals and parental anxiety. It could be hypothesized that children/families who required a psychologist support were more likely to experiment difficulties in weaning because altered psychological factors may negatively affect the transition to an exclusive oral feeding. These children could be identified as a subgroup of patients at higher risk of failure, for whom it could be reasonable to adapt the therapeutic approach either delaying or addressing weaning to intensive inpatient strategies. The other factor which was found to be predictive of weaning failure was the presence of impaired oral feeding skills at EN discontinuation. It is easy to imagine that feeding skill factors play a crucial role while attempting to wean EN. Literature data stress the importance of oral stimulation techniques among the multidisciplinary management of weaning (9,20–22).

Previous studies reported older age at the beginning of weaning and longer time on tube feeding being associated with weaning failures (4,23,24). In our study, these associations were not confirmed by multivariate analysis, probably because they may be accounted for by confounding factors, such as psychological problems and impaired oral feeding skills. Moreover, in those studies the children were referred to the specialized teams as a second-step strategy because of weaning difficulties. Other studies suggested that younger age (<1 year) at tube feeding initiation and underlying neurological impairment could be risk factors for tube dependency and weaning failure (9,25,26). In our study there was no significant difference in weaning outcomes based on these variables. Interestingly, the number of children with an underlying neurological disease included was low (n = 6, 6%), compared to the total

number (n = 208, 35%) of patients with an underlying neurological disease on home EN in our center (26). This confirms that a low proportion of neurologically impaired children fulfill the criteria of weaning compared to the rest of the population.

The rate of success of our weaning program was high (70%) using a priori strict definition of weaning success. No consensus currently exists on the definition of weaning success. Ishizaki et al (23) and Mirete et al (25) considered successful an attempt of weaning leading to EN discontinuation or tube removal, respectively. For Hartdorff et al (11) success was defined by stopping EN and gaining weight at 3- and/or 6-month follow-up. For Marinschek et al (12) of the NoTube team, a successful weaning was represented by EN discontinuation with sufficient oral intake based on age/weight and overall weight loss <10%. Despite the variability in the definition of weaning success among studies, the success rate of our almost exclusively ambulatory weaning program was similar to previous studies. Wright et al (4) obtained a success rate of 78% with an outpatient weaning method based on progressive decrease of enteral feeds. A recent meta-analysis (6) exploring the management of tube-dependent children through both inpatient and outpatient weaning program found an overall success rate of 69.8%. The so-called "hunger provocation" weaning programs (11,12,14,15) had success rates of 80% to 90%. Considering that our success rate was similar to those reported for the hunger-based rapid inpatient weaning programs, we could consider that these more expensive (12) approaches could be indicated as a second-line strategy for more complex patients who had previous ambulatory weaning failures, or risk factors of failure as we identified here.

Children entered our weaning program regardless of their nutritional status. Indeed, about 10% of them were undernourished at the beginning of weaning. In the study by Gardiner et al (27) comparing the techniques of 6 Australian teams to 6 international teams carrying out weaning from EN, only 3 considered growth parameters as eligibility criteria for weaning. The only 2 commonly accepted eligibility criteria were clinical stability and swallowing safety. In addition, in our study undernutrition at the beginning of weaning was not a parameter associated with failure. We also found that most children who failed weaning were not reintroduced to EN despite persistently low weight-for-age z score. The decision to resume or not EN, however, could have been influenced by different factors, including the underlying medical condition, the tolerance to tube feeding, the age of the child, the experience of the practitioners, and the child's and family's wishes.

This study has limitations. First, since we considered weaning as EN discontinuation, we could have missed patients in whom weaning attempt was stopped before definitive EN interruption. Therefore, the number of weaning failures could have been underestimated. Second, a classification bias could have been caused by our definition of weaning success/failure. The criteria for successful weaning from EN, however, vary among different studies and we defined it a priori. Third, the study was retrospective and missing data were more likely to occur. For example, the definition of undernutrition could have been implemented by considering another nutritional parameter, such as weight-for-height ratio, but height measurements often lacked in the medical records. The strength of this study is being one of the few studies focused on a weaning program which was patient-tailored, mostly settled in outpatient clinic, and including one of the largest and most detailed cohort of tube-fed children who underwent attempt of weaning. Another strength is the fact that the efficacy of our weaning program was based on a priori definition of success considering not only the definitive discontinuation of EN, but also the impact of weaning on the nutritional status of children. Finally, follow-up data were

homogeneous, since all the children were followed up in the same medical center.

CONCLUSIONS

The findings of this study support the use of a progressive, patient-tailored, and almost exclusively outpatient weaning program in children with tube feeding dependency. Identifying risk factors for failure of weaning helps optimizing weaning strategies.

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