Functional Recovery and Outcomes of Patients with Disorder of Consciousness Receiving Intermittent Bolus Feeding via PEG in a Sitting Position: A Case Series

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Abstract

Background: Literature regarding enteral feeding modalities in patients with Disorder of Consciousness (DOC) secondary to Acquired Brain Injury (ABI) is scant. Gastro-esophageal reflux and aspiration pneumonia are common in this patient population. Intermittent bolus feeding via Percutaneous Endoscopic Gastrostomy (PEG) and adoption of a more physiological posture during feeding may reduce morbidity and mortality. The primary study aim was to evaluate the incidence of lung infections in DOC patients treated with high-speed intermittent enteral nutrition in a verticalized position. Secondary aims were to assess the impact of this management on patient care, nutritional status, sleep-wake rhythm, and functional status.

Methods: Eight patients were monitored over 12 weeks and followed up 12 months after ABI. Enteral nutrition was administered starting from a speed of 64 ml/h and increased by 50 ml/h every 3 days. Collected data included: signs of infection, gastrointestinal tolerance, time in/out of bed, nutritional parameters, polysomnography, disability and cognitive scales.

Results: There were no gastrointestinal side-effects and no lung infections occurred. Nutritional status and sleep patterns improved. Time out of bed increased. Cognitive scale scores indicate an improvement in cognitive and disability profile.

Conclusion: Intermittent high-speed enteral nutrition via PEG did not increase infection risk and did not interfere with rehabilitation goals. Larger studies are needed to draw conclusive evidence on the management of enteral feeding and posture reconditioning in DOC patients.

Keywords: Brain injury • Disorder of consciousness • Rehabilitation • Enteral feeding • Aspiration pneumonia

Introduction

Acquired Brain Injury (ABI) includes a variety of traumatic or non-traumatic acute brain lesions characterized by the onset of a variably long-lasting state of coma (Glasgow Coma Scale ≤ 8) together with motor, sensory, cognitive and/or behavioral impairment. ABI can disrupt the brain's arousal and awareness systems. The most severe injuries result in prolonged Disorders of Consciousness (DOCs), including Unresponsive Wakefulness Syndrome (UWS) and Minimally Conscious State (MCS).

One of the main problems in rehabilitation is the management of nutrition, hampered by dysphagia, gastroparesis, tracheostomy tube, cognitive and postural-motor alterations. Therefore, an artificial nutrition must be started to provide the necessary caloric and nutrient intake [1,2]. If long-term artificial nutrition is needed, it is good practice to prefer the enteral way by means of a Percutaneous Endoscopic Gastrostomy (PEG) rather than a Nasogastric Tube (NGT) enteral nutrition through PEG can be continuous or intermittent (in boluses). The latter is not without risks, especially of inhalation and subsequent aspiration pneumonia.

In literature data about patients with disorders of consciousness are limited in terms of inhalation risk and speed of administration of enteral nutrition [3-5]. Most of the studies evaluate patients affected by various conditions, but few analyze patients with ABI and DOCs [6]. It has been assumed that there is a percentage of cases ranging between 25% and 48% that need enteral feeding after brain injury [7,8]. Medical complications, in all patients with ABI during the rehabilitation phase, reach a frequency of 0.40/week/patient [9]. Lung infections occur in 16% of patients with DOCs in the early rehabilitation phase and inhalation pneumonia represents 4.5% of the causes of death in these patients [10,11].

Among elderly patients with NGT the enteral feeding modality (continuous *vs*. intermittent bolus) does not influence the frequency of lung complications or mortality and the transition from intermittent to continuous modality does not alleviate diarrhea [12,13]. In trauma patients with critical illness the nutritional goal is achieved within 7 days with both modalities of nutrition (continuous or intermittent), but the intermittent management allows to reach it earlier and is logistically simpler [4]. The nutrition-fasting alternation has cerebral activation effects resulting from gastric filling and central neuromodulation effects resulting from the secretion of ghrelin, a hormone produced by the digestive tract during fasting; in addition, gastric stagnation significantly increases the risk of bacterial growth [3,4].

Posture is also an important factor to consider during enteral feeding and is part of a bundle of evidence-based practices for a safe and effective nutritional strategy. Good practice recom-mendations prescribe a raised position at least 30° during enteral feeding [14]. The vertical position reduces the probability of gastroesophageal reflux, both with nasogastric tube in place and with tube removed and significantly reduces (26%) the probability of nosocomial pneumonia [15,16]. The supine position increases the risk of apneas and hypopneas and most respiratory abnormalities during sleep occur in the supine posture [17,18]. During an apnea, intra-esophageal pressure decreases and facilitates reflux episodes. There is evidence that patients with Obstructive Sleep Apnea (OSA) have multiple nocturnal reflux events [19-21].

Furthermore, it has been shown that an early verticalization improves arousal in patients with DOCs, increasing the frequency and the level of behavioral responses [22,23]. Both verticalization and periodical nutrition can influence circadian rhythms that have shown to be disrupted in ABI. It is common experience that circadian rhythms in such patients are altered by anatomical-functional dysfunctions of the endogenous regulation system of circadian rhythms and by reduction in external synchronizing systems, a condition often occurring in hospital settings [24].

Therefore, it can be assumed that interventions aimed at stimulating and regulating the plasticity of the circadian function, through periodic signals modulated by the external environment, can facilitate the reorganization of normal rhythms [25]. The more manageable external signals are feed and motor rhythms as well as the sleep-wake rhythm. Bolus nutrition modalities and a sitting position during meals are more similar to the feeding patterns of healthy people than continuous nutrition, allowing the patients to experience more physiological and rhythmic bowel functions. Moreover, this management should decrease lung infections rate in patients with ABI and DOCs and promote better logistics and participation to rehabilitative and social activities, as well as a faster recovery of an adequate nutritional status, which is a basic premise to clinical stability and functional recovery.
The primary aim of this study is to estimate the incidence of respiratory infections, in a series of patients with DOCs admitted to an ABI rehabilitation unit and treated with intermittent enteral nutrition with high administration speed (> 200 ml / h), associated with a verticalized postural management (> 60° from the floor). The secondary purpose is to analyze the effect of this bundle on management of patient care, nutritional profile, sleep-wake cycle, cognitive functioning and disability.

Case Presentation

This prospective case series was collected in an ABI Rehabilitation Unit, tertiary referral specialized institute in Italy. Inclusion criteria were: diagnosis of DOCs, of vascular, traumatic, anoxic, or infective etiology, both genders, age 18 years-75 years, time from event between 1 month and 4 months. Patients with unstable hemodynamics, critical illness polyneuropathy, or not weaned from mechanically assisted ventilation were excluded.

All patients underwent a protocol of gradual increase in nutritional speed and early trunk verticalization. Enteral nutrition was administered starting from a speed of 64 cc/h; in the absence of signs of delayed gastric emptying, the rate of administration was increased every 3 days by 50 ml/h, maintaining the 80° vertical posture. A postural diary was used to monitor postures and time in and out of bed.

At baseline (T0), the Disability Rating Scale (DRS), Levels of Cognitive Functioning (LCF), and Coma Recovery Scale–Revised (CRS-R) were admninistered to all patients meeting the inclusion criteria. Somatosensory Evoked Potentials (SEPs), Electro Encephalon Graphic (EEG), Event-Related Potentials (ERPs), and sleep evaluation with polysomnography were performed, along with blood tests to evaluate nutritional status (lymphocyte count, creatinine, albumin, total protein, transferrin, and retinol-binding protein, pre-albumin). The percentage of time in/out of bed recorded in the postural diary. After 6 weeks (T1) and 12 weeks (T2), the postural diary was updated and DRS, LCF and CRS-R scales were administered [26-33].

In addition, at 12 weeks a second sleep evaluation with polysomnography was performed. Between T0 and T2 the following data were recorded weekly: nutritional status, infections occurrence, feeding modality (intermittent/continuous) and speed of the enteral nutrition.
The study includes a T3 follow-up evaluation (12 months after the acute event) in which the DRS and LCF scales were administered during an outpatient visit. The sleep study (polysomnography) was carried out with the PSG BE Micro Recorder EEG system GALILEO was used with Sandmann System B9700073000 (16 EEG channels + 5 bipolar channels + REF and GND); the type of assembly was F4-C4-O2-Cz-F3-C3-O1, oronasal thermocouple, abdominal breath, chest breath, EMG milo, EOG [34].

Outcome measures

The primary outcome measure was the rate of inhalation episodes. The occurrence of inhalation was evaluated through clinical signs (cough, temperature, low peripheral oxygen saturation), laboratory (C-reactive protein, white blood cells count) and radiological (chest x-rays) tests. The secondary outcomes were the percentage of time out of bed, nutritional status (lymphocyte count, creatinine, albumin, total proteins, transferrin, retinol binding protein, pre-albumin), sleep-wake rhythm (polysomnographic record), disability level (DRS) and cognitive functioning (LCF and CRS-R). The DRS is a 30-point scale with a higher score indicating greater disability. It rates 8 areas of functioning: eye-opening, verbalization, motor response, level of cognitive ability for daily activities of feeding, toileting, and grooming, overall level of dependence and employability.

The LCF scale is one of the earlier developed scales used to assess cognitive functioning in post-coma patients. It classifies patients in eight levels of cognitive impairment from 1 (non-responders) to 8 (purposeful-appropriate person). The CRS-R scale consists of 29 hierarchically organized items divided into 6 subscales evaluating auditory, visual, motor, oromotor, communicative and arousal functions. The total score ranges between 0 and 23, with higher scores indicating better neurobehavioral responses. The CRS-R allows clinicians to perform a reliable differential diagnosis between Vegetative State (VS) and MCS, as well as to record the emergence from MCS.

Statistical analyses

Continuous variables were summarized using mean or median when asymmetrically distributed, and range (min-max). Categorical variables were summarized using absolute and percentage frequencies.
The Wilcoxon signed rank test was used to analyze changes in continuous variables over time. Benjamini and Hockenberg correction for multiple comparisons was applied. The significance level was set at $p<0.05$. All statistical analyses were performed using Stata statistical software version 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

Standard protocols approvals, registrations, and patient consents

The study was approved by the local ethics committee CE AVEC (603/2019/OSS/AUSLIM-19109, 23/10/2019) and did not receive funding. Informed consent was obtained from the subject or the subject's legally authorized representative, in agreement with the declaration of Helsinki.

Results

Eight patients (7 males and 1 female, median age 37.6 years) were enrolled in the study from January 2020 to April 2021. Etiology was: 4 traumatic, 3 vascular (1 anoxic and 2 hemorrhagic) and 1 infective. Six patients (75%) were diagnosed as MCS, while two patients (25%) as VS. Time after the acute event was, on average, 3.25 months. Table 1 lists patients' demographic and clinical features, as well as the scores on the clinical scales at enrollment.

Table 1. Patient's characteristics at baseline.

ID	Gender	Age	Months from injury	Aetiology	Comorbidity	CRS-R	LCF	DRS
1	M	18	3,7	Infective	None	9	2	26
2	M	21	2,9	Traumatic	None	7	2	24
3	M	57	3,8	Anoxic	Previous cholecystectomy	6	2	26

4	F	54	2,5	Hemorrhagic	Recurrent meningioma	9	3	20
5	M	45	2,1	Traumatic	Favism	2	2	26
6	M	23	2,4	Traumatic	None	10	3	21
7	M	18	2,1	Traumatic	Scoliosis	14	2	25
8	M	65	2,1	Hemorrhagic	Hypertension, type 2 diabetes	4	2	26

CRS-R=Coma Recovery Scale-Revised
LCF=Levels of Cognitive Functioning
DRS=Disability Rating Scale

No lung infections occurred during the time of the study. One patient died before the follow-up evaluation at 12 months after the event. The median percentage of time spent out of bed increased from 20.8% at T0 to 29.2% at T1 and 40.6% at T2 (Figure 1).

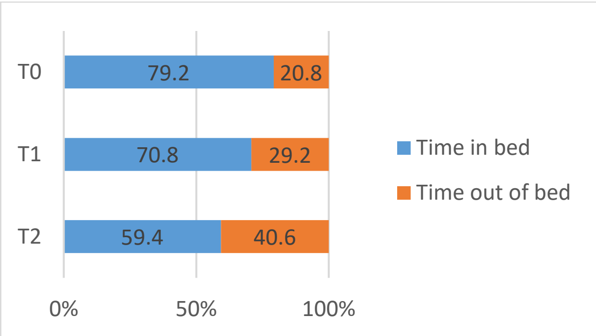

Figure 1. Median percentage time in/out of bed (24 h) at T0, T1 and T2.

Regarding nutritional status, table 2 shows the blood tests levels at T0, T1 and T2. Protein, albumin and transferrin values increased significantly between T0 and T1 but not between T1 and T2. The mean value of prealbumin gradually increased, with a significant difference between T0 and T2.

Table 2. Mean change in nutritional status from baseline (T0) to 12 weeks after (T2) and range (min - max).

	T0	T1	T2	T0 *vs.* T1	T0 *vs.* T2	T1 *vs.* T2
				p-value*	**p-value***	**p-value***
Protein	640%	690%	690%	3%	4%	62%
	(5.7-7.2)	(5.8-7.9)	(5.4–7.7)			
Albumin	3050%	3540%	3590%	3%	3%	48%
	(27.9–35.7)	(30.1–43.1)	(27.4–43.7)			
Prealbumin	2870%	3200%	3400%	14%	4%	78%
	(26.1–31.6)	(21.4–39.2)	(26.9–40.1)			
Transferrin	17600%	21000%	21200%	4%	5%	89%
	(135–211)	(160–254)	(154–290)			
White Blood Cells	770%	710%	620%	31%	31%	33%
	(5.6–9.8)	(4.6–8.3)	(4.2–8.6)			
CRP	169%	91%	67%	2%	2%	26%
	(0.24–3.34)	(0.04–1.89)	(0.06–2.64)			

Note: Benjamini and Hockenberg correction for multiple comparisons; T0 baseline, T1 6 weeks from baseline; T2 12 weeks from baseline. CRP=C-Reactive Protein

Concerning sleep/wake rhythm, no difference between T0 and T2 was detected in 4 patients. In the other 4 patients' polysomnographies, K-complexes, delta waves and spindles were recorded only at T2 (Table 3).

Table 3. Sleep-wake rhythm at baseline (T0) and 12 weeks after (T2).

ID	T0	T2
1	Presence of spindles	Presence of spindles
2	Absence of K complexes	Presence of K complexes and delta waves during phase 2
3	Absence of spindles and K complex (during REM phase)	Presence of spindles and K complex (during REM phase)
4	REM phase not detected	REM phase not detected
5	REM phase not detected; absence of spindles and K complexes	REM phase not detected; presence of spindles and K complexes
6	Presence of K complexes and delta waves during sleep	Presence of K complexes and delta waves during sleep
7	Presence of spindles	Presence of spindles and K complexes
8	REM phase not detected	REM phase not detected

Finally, regarding the trend of the level of consciousness, cognitive profile and disability the CRS-R scale score increased significantly between T0 and T1 (p-adjusted = 0.02) and further between T1 and T2 (p-adjusted = 0.047). The median value was 8 at T0, 9 at T1 and 10.5 at T2 (Figure 2).

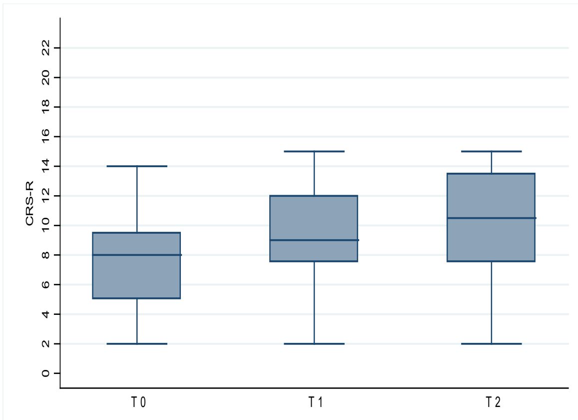

Figure 2. Box-plot of the CRS-R scores at T0, T1 and T2.
CRS-R - Coma Recovery Scale-Revised.

The median LCF score increased from 2 to 6 between T0 and T3 (Figure 3).

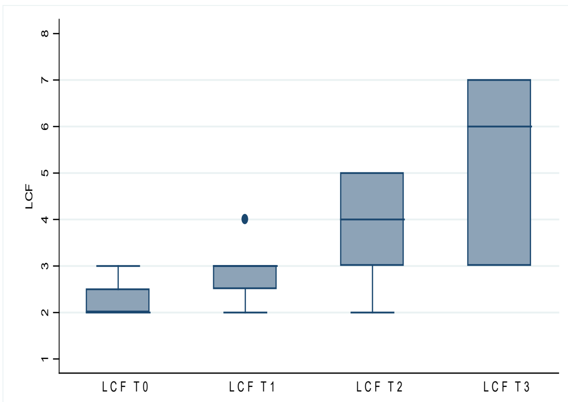

Figure 3. Box-plot of the LCF score at each assessment.
LCF - Levels of Cognitive Functioning

There was a significant variation between T0 and T1 (p-adjusted = 0.034) and also between T1 and T2 (p-adjusted = 0.034), while the variation between T2 and T3 obtained borderline significance (p-adjusted = 0.05).

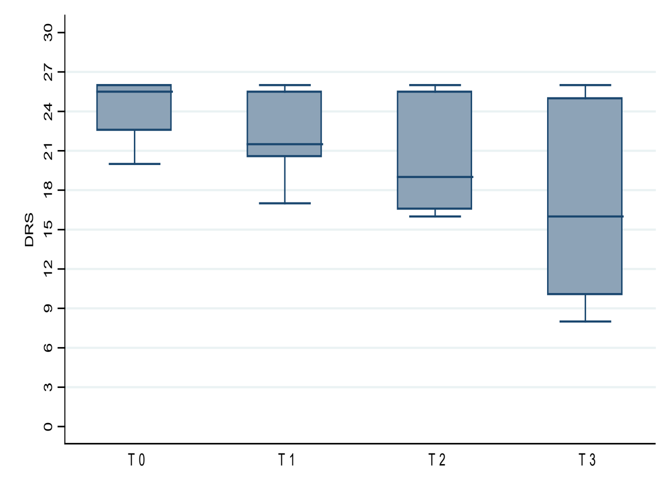

Figure 4. Box-plot of the DRS score at each assessment.
DRS - Disability Rating Scale

The DRS scale score decreased from T0 to T3 (Figure 4), however only changes from T0 were significant (p-adjusted = 0.044).

Discussion

This study shows that enteral nutrition through intermittent bolus administration (speed > 200 ml/h) in a seated position in wheelchair or semi-sitting in bed (with trunk > 80°) did not in-crease the risk of inhalation and consequent aspiration pneumonia on severe ABI patients. In fact, the risk of aspiration pneumonia was lower than that reported in the literature [10,11].

In addition, this practice is associated with a better management of both assistance and caregivers with regards to rehabilitation activities, especially in the gym, which became logistically simpler with a feeding time reduced to less than 3 hours. Increased time out of bed allowed our patients to participate more efficiently in the rehabilitation programs and to spend more time with their relatives in more socially stimulating settings than the hospital room or the rehabilitation unit. As regards nutrition, adequate blood test levels indicators were reached in a relatively short time and, in most cases, there was a transition from nutrition via PEG to oral feeding. Specifically, 5 out of 8 patients switched to full oral feeding.

Cognitive functioning also improved over the course of the study. The small number of patients and the absence of a control group did not allow to find a correlation between feeding modalities and cognitive improvement. However, the change in patient management, with increased time spent in a vertical posture, the possibility to be involved in more stimulating activities during the day, a physiological sleep-wake rhythm and a low infection rate may have contributed to reach a better cognitive performance and a neurobehavioral improvement. Probably this is a result of a better activation of the endogenous arousal systems as well as a more physiological external stimulation of the circadian rhythm. Further research in needed to support this hypothesis.

Finally, the analysis of the polysomnographic characteristics showed a stable or better representation of sleep patterns at T2, with the appearance of sleep spindles and K-complexes in 4 out of 8 patients. The absence of sleep elements and of spindles may predict a poor outcome, as their pathophysiological mechanism is presumed to be the preservation of thalamo-circuital circuits.

The main contribution to better clinical scores may be determined by the concomitant presence of Rapid Eye Movement (REM) sleep and sleep spindles. The presence of spindles like other EEG patterns as a diagnostic or prognostic marker is controversial depending on numerous etiologies, depth of coma and EEG reactivity to external stimuli. Neurophysiological evaluation of sleep is in our opinion an important tool in monitoring ABI patients during the rehabilitation phase, as it allows clinicians to obtain objective information about their circadian rhythms. However, polysomnography is not yet included in the bundle of diagnostic and prognostic in-struments concerning ABI patients and further research is needed to draw conclusions about its weight in the assessment of these patients and to elucidate its possible prognostic role.

Limitations

The small sample size and the absence of a control group prevented from investigating the relationship between the nutritional and postural management and clinical outcomes. In addition, the lack of a video-EEG recording did not allow to collect information on patients' behavior during sleep.

Conclusion

The results of the present study indicate that high-speed enteral nutrition via PEG with the trunk in a vertical position (>80°) in dysphagia ABI patients can reduce the risk of aspiration pneumonia. Furthermore, the implementation of a nutritional-postural protocol accompanied by an increase of the time out-of-bed, which reached the target of 40% within 12 weeks, without negatively influencing sleep patterns, recovery of consciousness, cognitive functioning and disability and allowing the patients a better participation in social activities with their families. This preliminary study suggests that the nutria-postural protocol is worthy of further investigation in larger samples, in order to allow clinicians to optimize the management of patient with severe neurological impairment and swallowing disorder.

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization: V.C. and P.S.
Methodology: R.P., V.C and E.M.
Software and Formal analysis: E.M.
Validation: V.C., F.C.C. and P.S.
Investigation: V.C., A.R.P. and F.C.C.
Resources and Supervision: P.S.
Data curation: V.C., A.R.P., G.B., F.C.C. and E.M.
Writing—original draft preparation: V.C., F.C.C., P.S. and E.M.
Writing—review and editing: V.C., E.M., and P.S.
Project administration: V.C.

All authors have read and agreed to the published version of the manuscript.

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