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Case report: Nutrition therapy and side-effects monitoring in critically ill coronavirus disease 2019 patients



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ABSTRACT

An outbreak of pneumonia proved to be infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), named Coronavirus Disease 2019 (COVID-19) by World Health Organization (WHO), has rapidly and widely spread to the whole world, affecting thousands of people. COVID-19 patients have poor gastrointestinal function and microecological disorders, which lead to the frequent occurrence of aspiration pneumonia, gastric retention, and diarrhea. In the meanwhile, it takes a certain period of time for nutrition therapy to reach the patient's physiological amount. Refeeding syndrome and hypoglycemia may occur during this period, causing the high risk of death in critical patients. Therefore, we reported the nutrition therapy and side-effects monitoring as well as the adjustment of the nutrition therapy of 2 critical COVID-19 patients, thus provide clinical evidence for nutrition therapy and prevention of the side effects.

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Introduction

In December 2019, a cluster of cases of pneumonia of unknown pathogen was identified in Wuhan, Hubei, China¹. The pathogen was quickly revealed as a novel betacoronavirus named as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), and the pneumonia was named as coronavirus disease 2019 (COVID-19) by World Health Organization (WHO)². WHO declared the outbreak of the disease as a public health emergency of international concern (PHEIC) on 30 January 2020². COVID-19 is highly contagious and has rapidly spread to the world, affecting more than 180 countries and over 15,000,000 people³. Investigations are blooming worldwide to better understand all aspects of patients infected with SARS-Cov-2 in order to control the COVID-19 epidemic. As far as we know, general treatment including nutrition therapy is a prerequisite for COVID-19⁴ but it has always been overlooked during clinical practice. Nutrition support is a fundamental stone to improve the patients' body metabolism and strengthen their immune system, especially for the elderly critical patients. In this 2-case report, we aimed to investigate the nutrition therapy and side-effects monitoring of 2 critical COVID-19

patients, and further provide more information of the nutrition therapy of COVID-19.

Case 1

On Feb 1, 2020, a 78-year-old female was diagnosed as critical COVID-19, severe malnutrition, stage 5 chronic kidney disease (CKD), grade 3 hypertension (extremely high risk), hypertension heart disease with congestive heart failure, and bacterial pneumonia. The Nutrition Risk Screening 2002 (NRS-2002) score was 5, and the Mini Nutritional Assessment short form (MNA-SF) score was 1, which showed that the patient was at nutritional risk. Then a comprehensive nutritional assessment was given, the Subjective Global Assessment (SGA) score was 3, and the Mini Nutritional Assessment (MNA) score was 4.5, indicated the patient was malnutrition. As the patient was lying in bed, the calf circumference, which was 29 cm, was measured instead of body weight (Table 1). The total energy demand of the patient was 1400 kcal per day. The patient was given enteral nutritional emulsion (TPF) through nasogastric tube (NGT), 500 mL, bid, energy dense was 1.5 kcal/mL and energy supply was set at 1500 kcal on the second day of admission. Unfortunately, under this nutrition therapy, the patient had frequent occurrence of gastric retention and diarrhea along with hypophosphatemia (lowest blood phosphorus level was 0.22 mmol/L) due to poor gastrointestinal

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Table 1
Nutrition Evaluation of 2 cases

Parameters		Case 1	Case 2
calf circumference(cm)		29	23
Nutrition Risk Screening	NRS-2002 (before treatment)	5	4
	NRS-2002 (after treatment)	5	4
	MNA-SF (before treatment)	1	1
	MNA-SF (after treatment)	1	1
Nutrition Assessment	SGA (before treatment)	3	3
	SGA (after treatment)	3	3
	MNA (before treatment)	4.5	10
	MNA (after treatment)	4.5	6.5

NRS-2002, Nutrition Risk Screening 2002; MNA-SF, Mini Nutritional Assessment short form; SGA, Subjective Global Assessment; MNA, Mini Nutritional Assessment.

tolerance. The patient received routine blood glucose monitoring after admission, postprandial blood glucose tests were normal but fasting blood glucose was low, fluctuated between 4–5 mmol/L. Therefore, nutrition therapy was adjusted by reducing the amount of feeding, applying the continuous pump feeding at the speed of 100ml/h and probiotic therapy simultaneously. However, there was no improvement in diarrhea and gastric retention. The patient had persistent low blood glucose levels during the night with a lowest blood glucose level of 3.2 mmol/L. Then, nutritional treatment was switched from TPF to rice water, but still, the patient had no improvement in diarrhea and gastric retention. On the 11th day after admission, trophic feeding was given for the patient through nasogastric tube (NGT), 50 ml, tid, energy dense was 0.3 kcal/mL, continuous pump feeding at the speed of 15ml/h, total feeding time per day was about 10 h. At the same time, total parenteral nutrition was also applied, providing 500 kcal for the patient. Under this combined treatment, the patient's gastrointestinal tolerance and bowel movements finally improved, and later parenteral nutrition (PN) was stopped when enteral nutrition (EN) can ensure sufficient nutrition supply on the 17th day after admission (Table 2).

Case 2

An 81-year-old male patient was diagnosed as critical COVID-19, severe malnutrition, severe pneumonia, type I respiratory failure, and septic shock. Nutritional status of this patient was carefully evaluated and detailed information was listed in Table 1. The total energy demand of the patient was 1200 kcal per day. The patient was given EN through NGT, 500 mL, Qd, energy dense was 0.9 kcal/mL, continuous pump feeding at the speed of 100 ml/h on the 12th day after admission. But the patient had frequent occurrence of gastric retention, diarrhea and fever, for which aspiration pneumonia cannot be ruled out. He also had persistent low blood glucose levels during the day, fluctuating between 2.9–5.7 mmol/L. Therefore, individualized enteral therapy was applied, 200 ml, bid, energy dense was 0.5 kcal/mL, continuous pump feeding at the speed of 50ml/h, energy supply

was 191 kcal along with probiotic therapy on the 20th day after admission. Maintaining this treatment for 7 days, the patient had no gastric retention and diarrhea was improved significantly. So we increased the amount of EN to 200 ml, Qd, energy supply was 381 kcal, and the patient did not experience gastric retention or diarrhea. Since the patient had a gastric retention volume of 300 ml, light yellow in color on the 34th day after admission, we decreased the amount of EN to 200 ml, bid, energy supply was 191 kcal. On the 35th day after admission, the patient presented gastric retention (465 ml), diarrhea (3 times a day, 150 g in total, yellow watery stool) and fever. Accordingly, we maintained the probiotic therapy and replaced the EN with the PN, with an energy supply of 285 kcal (Table 3). At present, the patient is still under a status of insufficient energy supply because of critical COVID-19, limited capacity, limited PN support, and the decreased heart rate as well as the unstable vital signs of the patient during several attempts to place the NJT.

Discussion

We report 2 cases of elderly and critical COVID-19 patients. Both of the patients had severe malnutrition and poor gastrointestinal function. The adverse effects of the antiviral drugs and antibiotics may cause dysbiosis and further aggravate gastrointestinal dysfunction of the patients. As a result, the patients had frequent occurrence of gastric retention and diarrhea, and the possibility of aspiration pneumonia. The first patient was fed through NGT but her nutritional status did not have significant improvement due to frequent occurrence of gastric retention and diarrhea. Therefore, early probiotic therapy and PN were given. After replacing NGT with NJT, the patient's intestinal tolerance improved and nutrition therapy finally met the patient's need, and PN was stopped. The second patient also received EN through NGT, however, he presented gastric retention and diarrhea for about one month. The patient is still under a poor nutritional status because of the limited PN and failed attempt to place NJT. But probiotic therapy was effective for diarrhea.

In clinical practice, the height and weight of patients could not be directly measured because the patients had disorders of consciousness and poor physical function. So their ideal weight were not indicated, which posed challenges on the determination of actual energy and protein requirements. Before the outbreak of COVID-19, we could use body composition analyzers or metabolic carts to measure the basal or resting metabolic rate of patients. However, due to the strong contagious nature of SARS-Cov-2, these equipment were inconvenient to bring into isolation wards. Therefore, we used alternative measurements, such as calf circumference, which can effectively reflect the nutritional status of elderly patients. Then MNA-SF, MNA, survey of daily intake, laboratory examination and physical examination were performed to comprehensively assess the nutritional status of patients. Based on the patient's condition and with reference to "Chinese Dietary Reference Intakes (2013 Edition)", as well as

Table 2
Nutritional characteristics of case one

Days after admission	Types of enteral feeding tubes	Enteral nutrition formula	Enteral nutrition (kcal)	Parenteral nutrition (kcal)	Diarrhea-amount(ml)/ frequency per day	Gastric retention volume(ml)	Probiotic therapy (CFU)
D2	NGT	High-energy, high-fat	1500	0	500/4	220	0
D8	NGT	High-energy, high-protein	621	0	200/2	97	1.2×10^{11}
D10	NGT	Rice water	30	0	400/6	140	1.2×10^{11}
D11	NJT	Low-fat, short peptide	58	500	600/4	0	1.2×10^{11}
D14	NJT	Low-fat, short peptide	306	700	200/2	0	1.2×10^{11}
D15	NJT	Low-fat, short peptide	600	500	0	0	1.2×10^{11}
D16	NJT	Low-fat, short peptide	800	200	0	0	1.2×10^{11}
D17	NJT	Low-fat, short peptide	1000	0	0	0	1.2×10^{11}

NGT, nasogastric tube; NJT, nasogastric tube.

Table 3
Nutritional characteristics of case two

Days after admission	Types of enteral feeding tubes	Enteral nutrition formula	Enteral nutrition (kcal)	Parenteral nutrition (kcal)	Diarrhea-amount(ml)/frequency per day	Gastric retention volume(ml)	Probiotic therapy (CFU)
D12	NGT	High-energy, high-fat	450	0	500/3	180	0
D25	NGT	High-energy, high-protein	191	0	280/3	0	1.2×10^{11}
D33	NGT	Low-fat, short peptide	381	0	0	0	1.2×10^{11}
D34	NGT	Low-fat, short peptide	191	0	0	300	1.2×10^{11}
D35	NGT	Low-fat, short peptide	0	285	150/3	465	1.2×10^{11}

NGT, nasogastric tube.

previous clinical experience on the treatment of critically ill patients, we determined the energy and protein requirements of patients and gave them nutrition therapies accordingly.

In comparison of the two patients, we witnessed the frequent occurrence of gastric retention in both cases, which may lead to poor absorption of nutrition and malnutrition, fluctuations in blood glucose, and bacterial infection⁵. We not only focused on the gastric residual volume, but also paid attention to clinical signs. In case 1, the patient vomited several times, and the vomit was white stomach contents. Physicians should pay close attention to early symptoms of gastric retention like nausea, postprandial fullness, heartburn, early satiety, bloating, and abdominal pain that may occur before vomiting⁶. Early probiotics therapy could help restore the natural balance of the gut microbiota as well as reduce the side effects, such as gastric retention and diarrhea. Although gastric access should be adopted as the standard approach to initiate EN, in patients with feeding intolerance or gastric retention that could not be solved with prokinetic drugs, postpyloric feeding should be performed⁷. For patients who are at high risk for aspiration, instead of gastric feeding, postpyloric feeding should be used if feasible^{7, 8}. 2016 ASPEN guideline⁹ also suggested that if the retention volume exceeds 250 ml, 2 times per day, prokinetics should be added, and if the retention volume exceeds 500 ml, the nasogastric feeding should be suspended or changed to nasojejunal feeding. Ultrasound was an effective way to determine gastric residual volume, especially in the monitoring of critically ill patients. However, currently, based on the condition of COVID-19 wards, unless it was necessary medical equipment, most of the large equipment was not allowed to enter the wards. We have always wanted to put the body composition analyzer and the metabolic cart into the ward, but failed under our clinical conditions. Gastrostomy should be considered if the patient needs long-term feeding and is at high risk for complications as well. But critical COVID-19 patients are always combined with other serious infections, physicians should weigh the further increased the risk of infection and the benefit of gastrostomy before procedure.

Another important and well recognized issue that we need to notice is refeeding syndrome (RFS) caused by the reintroduction of feeding after a period of fasting or starvation¹⁰. Physicians and nutritionists should evaluate the risk factors of RFS before introduction of nutrition therapy¹¹. If the patient had any of the RFS-related risk factors, then careful monitoring during refeeding should be applied and the feeding regimen needs to be adjusted accordingly. Refeeding should be started with an individualized, low-dose, low-concentration plan (trophic feeding), and vitamin supplementation should be given immediately¹¹. If EN was not satisfying, which referred to situations when enteral nutrition alone is unable to meet at least 60% of energy and protein requirements after 7–10 days⁹, early total parenteral nutrition should be considered to avoid the occurrence of complications like RFS during hospitalization.

A plasma glucose concentration less than 3.9 mmol/L (70 mg/dL) is generally accepted as an alert value of neuroendocrine responses to falling glucose in non-diabetes patients^{12, 13}. Since hypoglycemia is associated with higher in-hospital mortality because of the increased disease burden^{14, 15}, early detection and careful

management is required for effective clinical practice. For critically ill patients, compared with a blood glucose target of 7.8–10.0 mmol/L (140–180 mg/dL), blood glucose concentration of 4.4–6.1 mmol/L (80–110 mg/dL) was associated with a greater chance of developing hypoglycemia and a higher mortality rate¹⁶. We summarized the characteristics of blood glucose of the first patient as nocturnal hypoglycemia. This patient had suffered hunger and malnutrition for a long time. After the placement of a nasogastric tube on the second day of admission, he was given high-energy, high-protein EN therapy. But the patient rapidly developed gastrointestinal side effects and hypophosphatemia. Therefore, the EN treatment only provided limited improvements on the nutritional status of the patient, thus lead to the frequent hypoglycemia at night. After adjusting the nutrition therapy, the patient's intestinal tolerance gradually improved and his blood glucose level returned to normal. In case two, the patient had low blood glucose level during the day. Due to the frequent occurrence of gastric retention, EN treatment was settled at 7:00 and 22:00. Since the patient was placed in a prone position to assisted expectoration in the afternoon, EN was not performed, and nutrition support was limited because the patient underwent PN and bedside hemodialysis simultaneously. As a result, the patient had persistent hypoglycemia during the day. We noticed that nutrition therapy often takes a long time to meet the patient's physiological needs, especially in elderly patient with critical COVID-19. So we should pay attention to the patient's blood glucose level. Moreover, critical COVID-19 patients may have a relatively high risk of sudden death for the reason that most of them had underlying comorbidities¹⁷, such as cardiovascular disease, chronic obstructive pulmonary disease (COPD), CKD, obstructive sleep apnea-hypopnea syndrome (OSAHS), etc. Therefore, blood glucose of critical patients should be controlled between 7.8–10 mmol/L (140–180 mg/dL), more attention should be paid and appropriate nutritional support is needed to avoid the occurrence of asymptomatic hypoglycemia in critical patients with random blood glucose of 4.4–6.1 mmol/L (80–110 mg/dL). Besides, continuous glucose monitoring should be initiated if available.

In summary, we reported the nutrition therapy of 2 critical patients with SARS-Cov-2 infection. This report highlights the importance of appropriate nutrition therapy and side-effects monitoring for the critical COVID-19 patients, in order to ensure their nutrition supply and elevate patients' general status to overcome the disease.

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Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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