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Original Article

Strategies to Improve Tolerance to Oral & Enteral Nutritional Interventions in COVID-19

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ABSTRACT

The present global pandemic due to coronavirus disease 2019 has challenged the health resources as a significant number of afflicted patients need hospitalization including admission to critical care units. Therapeutic nutrition is an essential component of treatment, in addition to the other established therapies. However, the severe gut dysfunction due to viral effects on the digestive tract and the gastrointestinal dysfunction due to critical illness can result in a significant intolerance to oral and enteral feeds. This article reviews the gastrointestinal manifestations and the strategies to improve tolerance to oral and enteral nutritional interventions.

Keywords: *COVID -19, Nutrition, digestive tract, gastrointestinal.*

1. INTRODUCTION:

Health of humanity is under severe threat since the global outbreak of coronavirus disease 2019 (COVID-19), after the first case was reported in December 2019, from Wuhan, China. The World Health Organization classified it as a pandemic in March 2020. As on 31st July 2020, more than 17 million cases of COVID-19 have been reported from more than 188 countries and territories[1]. As this global threat typhoons across the world, the disease manifests with myriad of symptoms, none of which are diagnostic of COVID-19! The common ones are cough, headache, dyspnea, myalgia, fever, lethargy and severe pneumonia. Uncommon presentations are anosmia, chest pain, cardiac arrythmias, confusion, etc. Additionally, there are several case-reports describing the varied effects on the digestive tract - anorexia, abdominal discomfort, nausea, vomiting, and diarrhea. In fact, the first reported COVID-19 case from the United States manifested with diarrhea, with a 2-day history of nausea and vomiting, in a 35-years old male. His swabs from nasopharynx and oropharynx tested positive for COVID-19[2]. Early in its course, the upper respiratory tract symptoms can be predominant, and clinicians should be aware that infectivity of patients peaks even before the onset of any symptoms. There is increasing evidence that it can present initially with gastrointestinal symptoms prior to onset of respiratory symptoms[3].

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1.1 Pathogenesis of COVID-19 and its impact on gastrointestinal functions

Soon after the exposure to the virus-laden droplets, the novel coronavirus binds tightly to cells which have a peptidase angiotensin converting enzyme 2 (ACE2) receptor. This tight binding permits rapid fusion of viral (spike) protein to host cell membranes, which enables the viral RNA to gain access to the cells and replicate. ACE2 receptors are expressed in the nasal epithelial cells, and type II alveolar epithelial cells of the lungs. It is also expressed in vascular endothelium, and many other tissues – oral mucosa, stomach, ileum, colon, liver cholangiocytes, kidneys, heart, brain and adipocytes. Ileal enterocytes have greater expression than lung epithelial cells, maybe due the nonenzymatic actions of ACE2, involved in amino acid transport[4].

Once the virus enters the host cell, it replicates exponentially, and infects other cells. Majority of the infected persons develop few clinical symptoms – dry cough, malaise, and fever, and most recover completely. However, in over 90% of the symptomatic patients, computed tomography of the chest reveals evidence of viral pneumonitis[5]. Yet, around 80% of the patients recover without specific treatment, but 20% develop severe illness, with worsening symptoms – fever, hypoxia, shortness of breath, due to complement deposition, which disrupts the lung epithelial-endothelial barrier, resulting in acute respiratory distress syndrome (ARDS) and systemic hyperinflammation. The combination of dysregulated inflammatory and immune responses due to cytokine storm (CS), and the viral binding to ACE2-bearing enterocytes, disrupts the routine digestive- and immune-functions of the gastrointestinal tract. The gut, which is resident to the maximum number of lymphocytes and has long been regarded as the "motor" of critical illness, drastically undergoes rapid dysbiosis of the commensal gut microbiota; which, within a few hours evolve into a disease-promoting pathobiome, causing increased translocation and leakiness[6].

Hence symptoms related to the digestive tract are increasingly being reported, the common ones being diarrhea, anorexia, nausea and abdominal pain[7]. The viral RNA from stool samples has been reported in up to 30% of patients. However, transmission through fecal-oral route appears to be less common, as the virus has been reported to be inactivated by human colonic fluid[8].

Patients with ARDS have an increased demand for substrates, which is provided by severe catabolism, with the net nitrogen losses between 6-7 grams in adults, and can reach up to 15 grams, culminating in acute disease-related malnutrition. This predisposes to muscle loss, reduction in visceral proteins, suboptimal organ function, nosocomial infections, multiple organ failure and fulminant death9. The complete pathological effects of COVID-19 are yet to be understood; the chronic and the long-term consequences are yet to be ascertained. The acute manifestations, scoring of the intensity of illness, assessment nutritional status and requirements (preferably by indirect calorimetry, if available), in addition to specific treatment protocols are well-documented to effectively improve the clinical outcomes[10].

Severe anorexia, nausea, vomiting, diarrhea, mechanical ventilation with sedation, prone-position and the underlying dysfunction of gastrointestinal tract present enormous challenges, in effectively feeding COVID-19 patients. Oral nutrition, in those who can eat and enteral nutrition (EN) remains the preferred option, given the positive effects of EN in critically ill patients[11]. However, in patients in whom the caloric and protein requirements cannot be provided due to intolerance to EN, diarrhea, and other issues, early parenteral nutrition (PN) should be initiated.

1.2 Intestinal epithelium in health and clinical benefits from enteral nutrition.

Intestinal tract has a surface area of 30 m2 and is covered by a single layer of specialized intestinal epithelial cells (IECs), which play a crucial role in intestinal homeostasis, by influencing innate and adaptive immune responses. Most of the IECs are continuously and constantly renewed, every 5-7 days, by stem cells, which are at the base of the intestinal crypts. The different types of IECs are absorptive enterocytes (which are most numerous and involved in absorption of nutrients), goblet cells (secrete protective mucus layer, anti-microbial proteins [AMPs], cytokines and chemokines), and tuft cells (involved in immunity against parasites). In the crypts are the long living Paneth cells, which secrete defensins and other AMPs. In addition, there are numerous exocrine and endocrine cells, involved in digestion. There is a constant interaction between the antigen-presenting cells and IECs which regulate T and B cell responses. Therefore, IECs, in addition to digestive functions, are also crucial in preserving immunological tolerance to commensal microbes, while maintaining local and systemic homeostasis, the main stimulus for which is the presence of nutrients in the lumen of intestines[12].

Soon after initiating even minimal amounts of feeds, the intestinal blood flow increases, and supports gut-associated lymphoid tissue (GALT). The nutrients stimulate release of trophic substances (gastrin, bile salts, motilin, etc), initiates intestinal contractility (which propels the microbes downstream), and stimulates production of secretory IgA (which prevents adherence of bacteria to mucosa), proliferation of the Th2 CD4 helper lymphocytes (which has an anti-inflammatory effect). In turn, these (secretory IgA and Th2 CD4) proliferate and migrate to various sites (liver, lungs and kidneys) to modulate immune response and reduce inflammation[13].

1.3 Pathological effects of not providing enteral nutrition

Absence of nutrients within the intestinal lumen reduces the blood flow and reduces the contractile activities, which promote bacterial overgrowth and evolution of virulent pathogenic microbes. There is a decrease in the thickness of the protective mucus layer and the paracellular channels between the intestinal epithelial cells weaken, causing loss of function and structural integrity, resulting in increased translocation of the virulent organisms. This increase in permeability further activates macrophages and effector T cells towards Th1 pathways. These immune cells gain access to the circulation, and further aggravate the systemic inflammation, especially in the pulmonary alveoli and exacerbate ARDS[14].

Hence the main objective of nutritional intervention is to initiate early oral or EN, to maintain the digestive and immune-related positive effects. This is especially important in acutely ill patients due to COVID-19, due the multiple benefits of early enteral nutrition. However, the severe systemic inflammation secondary to CS can result in intolerance to enteral feeds, due to gut dysfunction. The common causes are decreased gut perfusion, reduced gastric emptying, decreased intestinal motility, increased bacterial translocation, all of which result in reduced absorptive capacity of nutrients (Fig 1). Despite the unique challenges in utilizing gut to feed patients with COVID-19, every attempt should be made to improve the tolerance by innovative strategies.

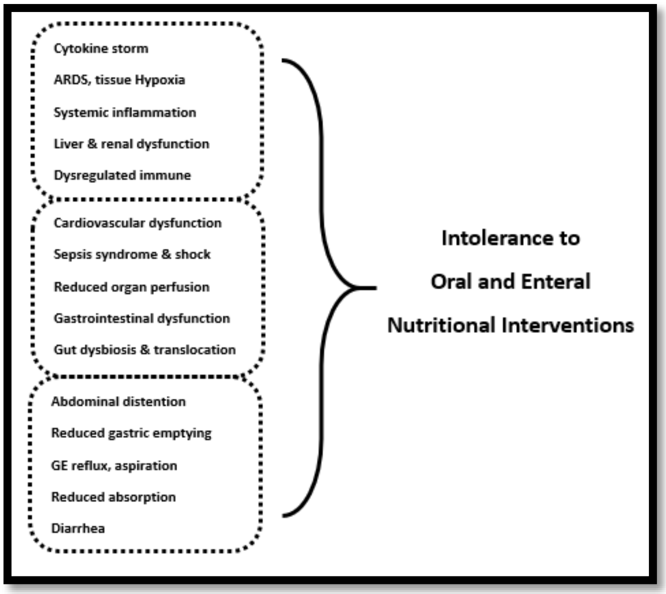

Fig 1: Mechanisms and implications on gastrointestinal functions

2. NUTRITIONAL NEEDS IN COVID-19

The following are the evidence-based strategies, based on various scientific publications, in addition to guidelines and recommendations by various societies[15-20].

In patients who can tolerate oral feeds, a high-calorie and a high-protein diet should be commenced as early as possible. ESPEN guidance recommends 30 kcal per kg body weight per day in adult, polymorbid patients with undernutrition (while monitoring for risk of refeeding syndrome) and 27 kcal per kg body weight per day in polymorbid patients over 65 years. These values are not absolute, and can be altered on physical activity, underlying nutritional status and tolerance. Protein requirements range from 1 g to 1.2 g per kg body weight per day.

The most appropriate way to estimate the energy needs of patients admitted to the ICU is by using indirect calorimetry. If it is not available, then the standard predictive equations should be utilised to calculate the nutritional requirements. After estimation, commence feeds at a low dose of 15 -20 kcal per body weight per day, but with a high dose of protein of 1.2 g up to 2.0 g body weight per day, especially over the first 2 to 4 days and progressively increased to target levels, by the end of first week of acute illness. Patients with respiratory dysfunction, and on ventilation, need a carbohydrate and fat ration of 50:5020. Malnourished patients should be supplemented with vitamins, trace elements and minerals at the standard dietary reference intake doses.

Oral nutritional supplements (ONS) will be required in patients who are unable to achieve these targets by oral diet. Patients who are unable to have oral feeds, EN should be started via tube feeds, after confirming the position of the tube, by visual inspection of the aspirate and by x-ray. If nutritional targets cannot be achieved by oral or tube feeds, then supplemental PN should be commenced[21].

The most susceptible COVID-19 patients tend to be those with co-morbid conditions (cardiovascular, metabolic, the elderly, and those with acute malnutrition due to poor oral intake 7 to 10 days prior to hospitalization). These factors further intensify the gut dysfunction, increase the intolerance to enteral feeds. The common challenges and practical issues are abdominal distention, hypomotility, presence of circulatory shock, prone position, reduced intestinal absorption increased risk of aspiration and diarrhea (Fig.2).

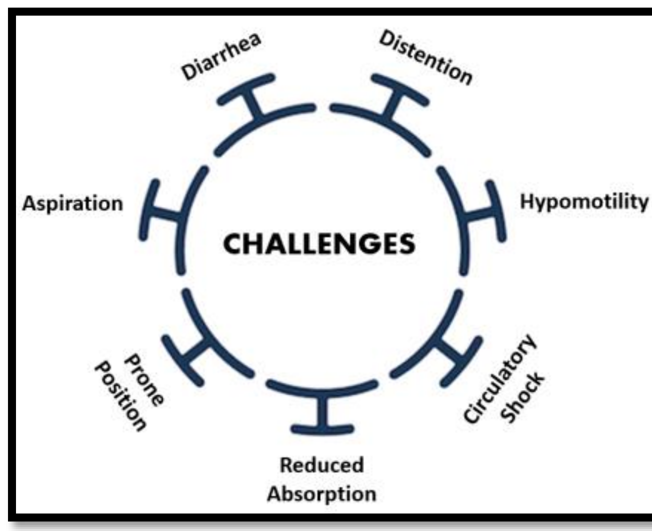

Fig 2: Challenges in feeding

Abdominal distention secondary to gastroparesis and hypomotility, which are very common, are multifactorial in origin. Some of which are due to underlying sepsis (sympathetic overactivity, nitric oxide production), metabolic (hyperglycemia, renal dysfunction), associated raised intracranial pressure and medications (sedatives, vasopressors). Distended intestines, with ileus and even pneumatosis intestinalis have been reported[22]. In addition, the intra-abdominal pressure can increase, resulting in abdominal compartment syndrome, which decrease intestinal mucosal perfusion. Patients with ARDS, are ventilated in prone position, over prolonged periods, to improve their oxygenation[23]. However, prone position has the potential to increase pressure over the abdomen, and with the use of paralytic agents, there is an increased likelihood of aspiration. Diarrhea can primarily be due to the viral effects on the enterocytes, and can also be due to medications (antibiotics) or even develops soon after the initiation of EN, due to gut dysfunction and intolerance, as a consequence of which there is a significant reduction in nutrient absorption. Therefore, the gut can be an initiator of, and a target of dysregulated systemic inflammatory and immune responses, thus posing an enormous challenge in enteral feeding, especially in the very early- and late-acute phases of COVID-19.

3. STRATEGIES TO ENHANCE TOLERANCE TO ORAL AND ENTERAL FEEDS AND TO MAINTAIN METABOLIC FUNCTIONS

1. Route of feeds, nausea, vomiting – In all patients who can eat, a high-protein and high-calorie diet are advised. ONS might be required to ensure the adequacy of protein-calorie requirements. Promotility medications should be prescribed in presence of severe nausea and vomiting. Patients who are ventilated or are unable to have oral diet, EN should be via nasogastric tube feeds.

2. Abdominal distention – Reducing the volume of feeds and the flow rate to 15 mls to 20 mls per hours will lessen the distention, and by allowing better absorption, will have a positive impact on intestinal function and integrity. The feeds can gradually increase, every 12 hours, by a further 15 mls to 20 mls an hour, till the patient tolerates about 60 mls every hour. All patients need to be closely monitored for signs of intolerance.

3. Delayed gastric emptying – Reducing, both the rate and volume of feed administration has the potential to improve gastric emptying. Promotility drugs (intravenous metoclopramide or erythromycin or even both) improve gastric emptying. There are no clear recommendations regarding gastric residual volumes (GRV). Routine measurement of GRV are not being advocated, even in patients who are stable, despite being ventilated in a prone position. A prospective study in 51 patients with ARDS, who were ventilated in prone position, gastric feeds were well tolerated in majority of the patients[24]. However, a recent resource document, endorsed by ASPEN-SCCM recommend measuring GRVs in all unstable patients, who are ventilated in prone position, and those on high doses of vasopressors[25].

4. Type of ONS: polymeric, elemental and semielemental – Most tolerate polymeric feeds. In patients with abdominal distention, an energy-dense formula, with high-calorie and less volume enhances absorption. Pure elemental feeds have a higher osmolality and are to be avoided, as it can provoke an osmotic diarrhea. Peptide containing semielemental are better tolerated and improves the tolerance in patients who are intolerant to polymeric formula.

5. Diarrhea – Semielemental feeds, soluble fiber and hypoosmotic formulas improves the nutrient absorption and reduces diarrhea. Peptide-based semielemental formula improves absorption in malnutrition, maldigestion and especially in malabsorption due to gastrointestinal intolerance[26]. Avoid hyperosmolar and bolus feeds. Review medications that are known to cause diarrhea – antibiotics, proton pump inhibitors, sorbitol, magnesium, and prokinetic agents.

6. Vasopressors – There is no established data in COVID-19 patients on vasopressors. However, a recent publication states that enteral nutrition can be given safely in stable patients who are minimal dose of vasopressors, with a MAP of > 65 mmHg[27]. EN is risky in patients on multiple and escalating doses of vasopressors.

7. Despite the above strategies, if patient continues to be persistently intolerant to feeds due to gastrointestinal dysfunction, or the if the energy and protein needs cannot be achieved, then total or supplemental PN, are advocated[28]

Nutritional interventions are the cornerstone in every patient with COVID-19, due to increased requirements. Oral and or enteral nutritional interventions maintain the immune functions of GIT and minimise systemic inflammation. However, the effects of acute illness and those of the virus on the digestive tract significantly diminishes the functions of gastrointestinal tract. Hence evidence-based protocols ought to be the standard care, while closely monitoring for metabolic and iatrogenic complications. Equally important are the safety precautions which have mandatory and every attempt should be made to minimise bedside procedures that have the potential for generating aerosols.
This review elucidates the digestive tract manifestations of COVID-19 and also the effects of critical illness on the function of gastrointestinal tract and elucidates strategies to enhance tolerance to gastrointestinal feeds.

4. FINANCIAL DISCLOSURE

None

5. CONFLICT OF INTEREST

None

6. REFERENCES

1. World Health Organisation Coronavirus disease (COVID-19) Situation Report 31st July 2020.

2. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States NEJM,2020; 382: 929-936

3.Ungaro RC, Sullivan T, Colombel JF, Patel G. What gastroenterologists and patients should know about COVID-

19? Clinical Gastroenterology and Hepatology. 2020; 18(7):1409-1411

4. Qi F, Qian S, et al. Single cell RNA sequencing of 13 human tissue identify cell type and receptors of human coronaviruses. Biochemical and Biophysical Research Communications. 2020; 526(1):135-140

5. Bernheim A, Mei X, et al. Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. Radiology. 2020; 295;3: 200463

6. Otani S, Coopersmith CM. Gut integrity in critical illness. Journal of Intensive Care. 2019; 7:17. doi.org/10.1186/s40560-019-0372-6

7. Cheung KS, Hung IFN, et al. Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from Hong Kong cohort and systemic review and meta-analysis. Gastroenterology.2020; 159 (1): 81-95

8. Matheson NJ, Lehner PJ. How does SARS-CoV-2 cause COVID-19? Science. 2020; 369 (6503): 510-511

9. Peter B. Soeters. Macronutrient Metabolism in Starvation and Stress. 2015; 82: 17-25

10. Singer P, Blaser AR, et al. ESPEN guidelines on clinical nutrition in the intensive care unit. Clinical Nutrition 2019; 38: 48-79

11. Moore FA, Moore EE. The Evolving Rationale for Early Enteral Nutrition Based on Paradigm of Multiple Organ Failure: A Personal Journey. 2009;24 (3): 297-304

12. Lu JT, Xu AT, et al. Crosstalk between intestinal epithelial cell and adaptive immune cell in intestinal mucosal immunity. Journal of Gastroenterology and Hepatology 2017; 32(5): 975-980

13. Peterson LW, Artis D. Intestinal epithelial cells: regulators of barrier function and immune homeostasis. Nature Reviews Immunology 2014; 14: 141-153

14. Deitch EA. Role of the gut lymphatic system in multiple organ failure. Current Opinion in Critical Care. 2001; 7: 92-98

15. B Ravinder Reddy. Enteral Nutrition: Whom, Why, When, What and Where to Feed? Nestle Nutrition Institute Workshop Series 2015; 82: 53-59. Doi: 10.1159/000382002

16. B Ravinder Reddy, Niyoti Reddy. Strategies ti Improve tolerance to peri-operative enteral feeding. Journal of Medical and Allied Sciences.2016; 6: (1): 03-07

17. Hiroomi Tatsumi. Enteral tolerance in critically ill patients. Journal of Intensive Care. 2019; 7:30. Doi: 1186/s40560-019-0378-0

18. Stephanie Zoeller, Matthew L. Bechtold, et al. Dispelling Myths and Unfounded Practices About Enteral Nutrition. Nutrition in Clinical Practice 2020; 35(2): 196-204

19. Enrick JT Aguila, Ian HY Cua, et al. Gastrointestinal manifestations of COVID-19: Impact on Nutritional Practices. Nutrition in Clinical Practices. Online 16 July 2020. Doi: 10.1002/ncp.10554

20. Rocco Barazzoni, Stephan C. Bischoff, et al. ESPEN expert statement and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clinical Nutrition. March 2020. Doi: 10.1016/j.clnu.2020.03.022

21. Diana W Mulherin, Renee Walker, et al. ASPEN Report on Nutrition Support Practice With COVID-19: The First Response. Nutrition in Clinical Practice. Online 16 July 2020. Doi: 10.1002/ncp.10553

22. Haytham M. Kaafarani, Mohamad El Moheb, et al. Gastrointestinal complications in critically ill patients with COVID-19. Annals of Surgery 202; 1:10.109. PMC 7268843

23. Claude Guérin, Jean Reignier, et al. Prone Positioning in Severe Acute Respiratory Distress Syndrome. New England Journal of Medicine. 2013; 318: 2159-2168

24. Raymond D Savio, Rajalakshmi Parasuraman, et al. Feasibility, tolerance and effectiveness of enteral feeding in critically ill patients in prone position. Journal of Intensive Care Society January 2020. Doi: 10.1177/1751143719900100

25. Resource for Clinicians Caring for Patients with Coronavirus. nutritioncare.org /COVID19. Updated July 28, 2020

26. Jefferey L. Nelson. A pilot intervention study to evaluate compliance to a peptide-based oral nutritional supplement with impaired gastrointestinal function. Clinical Nutrition Experimental. August 2019 Doi: 10.1016/j.yclnex.2019.08.001

27. Paul E. Wischmeyer. Enteral Nutrition Can Be Given in Patients on Vasopressors. Critical Care Medicine January 2020; 48 (1): 122-125

28. Robert Martindale, Jayshil J Patel, et al. Nutrition Therapy in the Patient with Coronavirus Disease (COVID-19). Journal of Parenteral and Enteral Nutrition. May 2020. Doi: 10:1002/jpen.1930

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