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Narrative Review

Clinical nutrition and the role of hospital pharmacist in the management of covid patient

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SUMMARY

The nutritional status of everyone represents a fundamental element to maintain a good health and it can be related to infectious agents in some disorders. Prevention, diagnosis and treatment of malnutrition should be included in the management of SARS-CoV-2 patients in order to improve both short- and long-term prognosis.

In Covid patients the choice of route of administration for nutrition is closely related to respiratory autonomy. In subjects who are not mechanically ventilated or with non-invasive ventilation (NIV), spontaneous oral feeding is strongly indicated, while considering the patient's comorbidity, chewing ability and swallowing. If this is not possible or if it is not possible to meet the appropriate nutritional needs, it is necessary to resort to artificial nutrition (enteral or parenteral). Enteral nutrition (EN) is preferred to parenteral nutrition (PN) because it allows to maintain the trophism of the gastrointestinal tract, involving a lower risk of infectious complications and it is easier to manage. PN is usually used in patients in whom NE is not feasible, insufficient or contraindicated, or in patients with invasive total mechanical ventilation. Based on these considerations, it would be necessary to develop a targeted nutritional pathway in order to support the management of Covid patients.

In the nutritional management of these patients, the role of the hospital pharmacists is fundamental. They collaborate with clinicians, nutritionist, dieticians and speech therapists to choose the most appropriate nutrition, based on the clinical characteristics of the patient and on the availability of nutritional formulations in the therapeutic guide.

1. Introduction

Most SARS-CoV-2 positive, hospitalized, symptomatic patients arrive at the hospital in an advanced stage of illness which is usually associated with a high risk of malnutrition [1,2]. Following hospitalization, issues such as sarcopenia, reduced muscle mass, and malnutrition often occur, which may influence the outcome of the disease.

Antiviral therapy and intestinal involvement of the infection tend to further aggravate the nutritional status of the positive Covid patients, due to various side effects including inappetence, nausea, and diarrhea [3].

If the patient's nutrition is not adequately supported during the hospitalization, which often extends over long periods, the patient's health status may prove to be compromised even after discharge [4].

Malnutrition does not always result from hospitalization or infectious status, but may be related to a pre-existing condition of altered nutritional status of the subject that may modify the response to the virus:

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- Obese patients may develop an impaired immune response, may suffer from Chronic Obstructive Pulmonary Disease (COPD), cardiovascular disease, hypertension and diabetes, all risk factors that worsen the clinical condition of the SARS-CoV-2 patient; [5].
- Undernourished patients have a deficiency of adipose tissue as a source of adipocytokines and a reduction in macrophages and T cells; these conditions imply less response toward the virus by the immune system [6].

The choice the preferred nutritional methodology is closely related to the respiratory autonomy of the Covid patient, who can easily be in more or less severe artificial ventilation conditions (NIV-Non Invasive Ventilation/high flows - ECMO Extra-Corporeal Membrane Oxygenation/IOT -Orotracheal Intubation) [7].

2. Oral nutrition

Patients who are paucisymptomatic, not mechanically ventilated or with NIV, requiring only the use of nasal cannulas to receive oxygen, can feed themselves orally, which remains, when possible, the best choice [8]. Applicable nutrition is not very dissimilar to the one used for patients who are malnourished or at risk of malnutrition and must take into account the rules of a healthy diet to avoid the cascade reactions that lead to excessive synthesis of inflammatory molecules [9].

Oral food administration should be considered based on the patient's comorbidity, chewing and swallowing ability, and nutritional status [10].

Small, frequent meals and, if necessary, proteins or amino acids powder supplementation is preferred during hospitalization [9]. The need to use hypercaloric and high-protein Oral Nutritional Supplements (ONS) is especially useful in patients who are malnourished or unable to feed themselves adequately, reaching only 50–60% of their daily caloric-protein requirements with food [10]. In both hospitalization and post-Covid recovery, an improvement in immune response and side effects (fatigue, respiratory distress, etc.) has been observed when the diet is supplemented with certain micronutrients (selenium, copper, zinc, vitamins A, C, D, and E) [11,12].

To avoid a drop-in saturation, make swallowing less difficult and feeding more accepted (patients may present with gastrointestinal tract symptoms and have inappetence, nausea, or dysgeusia), administration through a straw of liquid foods or foods modified in consistency and composition may be recommended [9].

Just as with food intake, supplements, if needed, should be administered in liquid form [1].

3. Artificial nutrition (AN)

If natural oral feeding is not possible, dysphagia is significant, or the nutritional requirements cannot be met even with oral supplementation, it is necessary to use AN [3]. We use to divide AN into two different route of administration as following.

4. Parenteral nutrition (PN)

In patients with total invasive mechanical ventilation (intubated in induced coma), PN can be administered by continuous infusion, which reduces diarrhoea and the number of contacts that the health care team could have with the patient [8]. However, the enteral route, which maintains intestinal tropism, remains the preferred route, and it is recommended to try to maintain a minimum intake [9]. If this is not possible, PN can be administered to the patient.

PN can be total (TPN) and this should considered for proper/correct weaning during oral feeding re-education [7].

5. Enteral nutrition (EN)

About 20% of Covid patients show gastrointestinal symptoms (abdominal pain and diarrhoea) either due to viral infection or as consequence of antiviral drug's mechanism; these side effects may result in alteration of the intestinal microbiota.

PN could further worse this situation, as no food arrives to nourish the microbiota and the gastrointestinal tract is put at rest with consequent reduction of intestinal tropism. This argues for the choice of EN, which maintains the flow of food (nutrients) through the gastrointestinal tract whenever possible, flanked by antiemetic, anti-diarrheal drug therapy and with probiotic supplementation [9].

Maintaining gut immunity through a healthy microbiota also helps to reduce the risk of higher infectious complications in NPT due in part to central or peripheral venous catheter placement [14].

The enteral route may also be preferred in patients with NIV (mask or helmet) and can be performed through probes (naso-gastric tube, naso-duodenal, naso-digiunal) or ostomies (pharyngostomy, esophagostomy, gastrostomy, dijunostomy); in any case, nutrients will be mixed with liquids such as water or sorbitol to reduce osmolarity.

The type of enteral access choice depends on the patient's general condition, condition of digestive system function, risk of ab-ingests, and expected duration of nutritional treatment [7].

If enteral feeding is required for a period of less than 4 to 6 weeks, it is performed by means of a nasogastric tube (NG), by passing a cannula through the nasal passages to the stomach. If an injury or deformity of the nose hinders nasal placement, an oro-gastric or oro-enteric tube may be chosen.

If enteral feeding is required for more than 4–6 weeks, percutaneous endoscopic gastroscopy (PEG) or jejunostomy is required.

In the intubated patient, EN can be started at low doses (minimal enteral feeding) and then progressively increased until nutritional needs are covered.

Gastric access via NGT can be considered the standard approach for the administration of EN in the Covid patient, to be started by infusion pump at a rate of 40–60 mL/h and with subsequent increments of 10–20 mL/h every 24 h, although the rate must be customized according to the patient's starting conditions [3–15].

Enteral feeding can also be administered with boluses several times/days as it is more physiological than continuous infusion, even if it may cause nausea as side effect. Despite the greater similarity with physiological nutrition, a meta-analysis based on five studies found a significant reduction in diarrhoea with continuous infusion versus bolus administration (RR 0.42, CI 0.19, 0.91, p ¼ 0.03), and no difference was identified in outcomes [8]. EN via NG tube could persist even following estuation, as swallowing issues may continue for up to 4 months after discharge [9]. However, if the inability to feed is prolonged, the PEG represents an essential support to reduce the discomfort and side effects of the NGT, although neither this route is lacking of them. In fact the risk of infection at the level of the abdominal perforation, risk of gastric ulcers or risk of dislocation of the tube, aspiration and bleeding are not to be excluded.

An alternative to PEG is dijunostomy, even if it's more difficult and requires greater dilution and smaller volumes [16].

Nutrition typically begins at a concentration of ≤0.5 kcal/mL and a rate of 25 mL/h; after a few days, concentrations and volumes can be increased to meet caloric and water requirements. Usually, the maximum that can be tolerated is 0.8 kcal/mL at 125 mL/h, providing 2400 kcal/day.

Monitoring for potential complications of NE should be performed in all cases. The enteral route may also be impractical in the presence of compromised clinical conditions, consequent to the infectious state and characterized by hypoxia, desaturation/dyspnoea, dysphagia, dyssomnia, dysgeusia, xerostomia and important gastrointestinal symptoms (nausea, vomiting, altered alvo) [10]. It could also be difficult and present limitations in cases where the application of NGT is required, which can make NIV less efficient or cause gastric dilation, with subsequent consequences at the diaphragmatic level. In these situations, NP with vitamin and mineral supplementation is preferred [3].

In any case, PN to support EN should be considered until the desired nutritional targets are achieved. In such cases, the extent of supplementation will need to be evaluated on a case-by-case basis.

6. Calculation of Resting Energy Expenditure and determination of nutritional requirements

The estimation of energy needs can be done through indirect calorimetry, a technique that aims to measure the Resting Energy Expenditure (REE), that is the amount, of calories burned and therefore necessary for normal physiological and vital functions. Through indirect calorimetry, using a calorimeter, it is possible to measure the heat that is produced by biochemical reactions which occur in our body. Energy expenditure is thus measured by changes in the concentration of oxygen and carbon dioxide in respiratory gases [17].

If indirect calorimetry is not available, REE is determined through the VCO_2 (Volume of Carbon Dioxide) detected by the ventilator [18].

The formula applied is:

$REE = VCO_2 \times 8.19$;

VO_2 (Volume of Oxygen) according to Fick's method (pulmonary arterial catheter) can also be used.

Initially, the nutritional intake is less than 20 kcal/kg, later reaching a maximum of 25–30 kcal/kg, only if tolerated.

It is alternatively possible to proceed directly, without measuring VCO2, with the predictive equation that recommends an intake of 20–25 kcal/kg/day [10].

REE can also be measured indirectly using the Harris-Benedict formula:

- Women: 655.095 + (9.563 x weight in kg) + (1.8496 x height in cm) - (age x 4.6756);
- Men: 66.473 + (13.7516 x weight in kg) + (5.0033 x height in cm) - (age x 6.755) [19].

In the early phase of acute disease, caloric intake is 30% of that determined by calorimetry, and is then increased progressively, reaching 80–100% of REE by day 3. If REE is calculated by predictive equations, caloric intake will be maintained below 70% for the first week, and then slowly increased.

In patients with gastric intolerance (gastric stagnation >500 mL/6 h) or high risk of aspiration, post-pyloric nutrition is used [3].

Once the REE is calculated, it is important to follow some recommendations for the nutritional management of the Covid patient, formulated by experts and specialists in metabolism and nutrition, in order to improve the prognosis in the short and long term:

- the indicated protein intake is 1.3 g/kg/day to be achieved gradually by day 3 or 5;
- caloric intake is 20–25 g/kg/day within the first three days, but not more than 70% of REE measured by calorimetry; after the third day it can be increased to 80–100% of measured REE;
- the use of mixtures containing ω-3 fatty acids could lead to an improvement in oxygenation levels, even if there is no scientific evidence to support this. However, they should not be administered as bolus and used routinely. Instead, nutritional mixtures enriched in ω-3 at nutritional doses can be used. Intravascular lipid administration should not exceed 1.5 g/kg/day; [3–8].
- total fluid requirements are approximately 1.2–1.5 l/day [8].

All this must in any case consider that the daily requirement is related to the clinical condition of the subject (oedema, fever, diarrhoea) [3].

7. Conclusions

The role of the hospital pharmacists in the management of clinical nutrition of positive covid patients is fundamental; they collaborates with the multidisciplinary team to choose the most appropriate nutrition.

For patients with special needs, if the facility allows it, pharmacists will prepare ad hoc PN bags or, when it is not possible to use a drug of industrial origin or to prepare a magistral preparation, it may be necessary to resort to the manipulation of solid oral pharmaceutical forms as indicated by the recommendation number 19 of the Italian Ministry of Health. Manipulation is a practice not free of risk; in fact, if it is not properly performed, it can cause instability of the drug and consequently compromising efficacy and safety of the drug itself, as well as risk of side effects for the patient. It is therefore necessary for pharmacists to make available their pharmaceutical, technological and pharmacological skills to prevent complications related to nutritional intervention: for example, they must consider both the type of active ingredient and excipients, which can modify absorption and bioavailability. In addition, as part of the nutritional team, pharmacist may evaluate the administration of the manipulated pharmaceutical form, which can take place, as mentioned above, through probes and ostomies mixed with liquids.

When the preparation activities are not carried out by the pharmacy, in order to prevent errors in therapy and ensure the quality and safety of care as a prerequisite, pharmacists must give correct information on the handling of solid oral pharmaceutical forms.

Therefore, the role of the hospital pharmacists appears to be fundamental both for the assessment of nutritional needs and also for the design, composition, dispensing and quality management of formulations [20].

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Declaration of competing interest

None of the authors has conflicts to declare regarding this review.

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