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Editorial

Historical perspective on parenteral and enteral nutrition in oncology

Although there were accounts of tube feeding into the esophagus in the 1600s and 1700s, modern enteral nutrition (EN) began when Einhorn introduced bolus nasoduodenal tube feeding in 1910 using milk, raw egg, and a lactose mixture [1]. EN was then taken up by other practitioners using a continuous flow approach [1]. The first case of jejunal feeding was in 1918. Pump feeding was introduced in the 1940s. National Institutes of Health–funded work looking at enteral formulas date from 1955 to 1965 and modern-day formulas were introduced in the 1970s [1]. Most of the evidence for EN is in patients with head and neck or upper gastrointestinal cancers. Due to the challenges with ethically performing studies in these groups, the evidence for EN is not strong [2]. However, there is fair to moderate evidence that EN improves nutrient intake when oral intake is inadequate and may decrease unplanned hospital admissions and treatment interruptions in patients with cancer [2].

Modern parenteral nutrition (PN) was officially born in the United States in 1968 [3] and the first clinical contribution regarding its use in patients with cancer on oncologic therapy was published in 1971 in an American journal [4]. Shortly after, the first papers investigating the potential of PN in patients with cancer receiving chemotherapy in Europe were published [5,6]. It is interesting to note that the first patient receiving home parenteral nutrition (HPN) was a 36-y-old woman with metastatic ovarian cancer discharged from the University of Pennsylvania group in 1968 [7,8]. The first published case report [9] also involved a patient with a malignant disease (a 37-y-old woman with a recurrent desmoid tumor involving the small bowel mesentery) who survived several months on HPN and finally died of postoperative complications due to an intestinal transplant. The first experiences with HPN in European patients with cancer were published in 1972 in France [10].

In the subsequent 15 y, only small-size randomized controlled trials (RCTs) were performed, mainly in the United States, to assess whether PN could potentiate the effects of chemotherapy or decrease its toxicity. At that time, nutritional admixtures, regimens, and modalities of administration were still rough and most of these studies were unsuccessful. Koretz et al. [11], in a meta-analysis of 19 RCTs commissioned by the American Gastroenterological Association (AGA) Clinical Practice and Practice Economics Committee, concluded that PN was useless and potentially deleterious in patients with cancer. Such a conclusion was quickly endorsed by the AGA, which warned against the use of PN in patients receiving cancer therapy [12] in keeping with a previous position paper by the American College of Physicians [13]. The oncologists promptly accepted this indication because at that time it was not realized that a strong limitation of these RCTs was the entry into the trial of patients who were not malnourished. Therefore, the recommendation for PN in those RCTs relied on invalid premises and the wrong indication.

Despite this “cultural brake” and the poor knowledge of the clinical nutrition and of the nutritional status assessments by the health care professionals [14] and oncologists [15,16], research in the field of nutritional oncology went on through several steps, which were not strictly sequential.

Many studies documented the prevalence of cachexia [17], which according to the European Society of Clinical Nutrition and Metabolism (ESPEN) [18], is the state of malnutrition associated with cancer in different types of primary tumors and has a negative effect on survival [19] and quality of life of patients [20]. It soon became apparent that cachexia cannot be equated with simple starvation, and hence it cannot be expected to be fully reversed by a standard nutritional approach [21]. Even if the metabolic pattern of cachexia, with reference to the alterations of protein, glucose, and lipid metabolism, has been relatively well defined [22], our knowledge regarding the causes and the intermediate pathways is still incomplete [23,24].

Clinical nutrition research of patients with cancer has then progressed following two parallel routes: On one side defining the standard macronutrients [25,26] and energy requirements [27] that have to be met in clinical practice to try to offset the progressive nutritional deterioration of the patient, and on the other hand, a better understanding of the role of nutrients, which could act as potential anabolic or anticatabolic agents in cachectic cancer patients [28,29].

Current use of PN in patients with cancer

Currently, following the classic recommendation, once more emphasized by the ESPEN guidelines [30], nutritional intervention privileges the oral/enteral route whenever possible and PN often is used in patients with cancer in an advanced stage when the gut is not working nor accessible. Due to the recent advances of anticancer pharmacology, it is more frequent that some patients enter into a chronic phase of slowly evolving malignant disease where nutritional deterioration rather than tumor progression is a determinant for survival. Some of these patients, severely hypophagic or with chronic intestinal obstruction, can benefit from HPN [31,32].

However, it is a common experience that many patients have problems with oral alimentation because of severe anorexia, taste alteration or early satiation, or temporary nausea and vomiting due

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to chemotherapy, which make oral nutrition difficult even if the gut is technically working. These patients might benefit from supplementary PN in the hospital or at home, which is facilitated by the availability in the market of all-in-one, ready-to-use bags. Therefore, we are now facing a new reality: PN, which was originally born to totally replace a non-working gut and for such the aim was employed to keep alive malnourished (hypo)aphagic subobstructed patients with cancer, is now evolving, more frequently toward a supplementary supportive care of both in- and outpatients with the purpose of increasing the tolerance of patients with cancer to their anticancer therapy and to improve their quality of life.

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