

The Effect of Enteral Nutrition in Patients with Gastrointestinal Cancer: A Literature Review

Gastrointestinal Kanserli Hastalarda Enteral Beslenmenin Etkisi: Literatür İncelemesi

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ABSTRACT

Background: The gastrointestinal tract defines a wide integral system including all organs starting from the mouth and ending at the anus. With advances in science, diseases can be diagnosed early and benefits from treatment are more possible. On the other hand, the number of survivors after cancer increases with the prolongation of human life. While gastrointestinal tract cancers are among the most prevalent cancers both in the world and Turkey, their mortality rates are reported also to be high. Enteral nutrition is especially important in the prevention of mortality and morbidity in patients with gastrointestinal cancer. This review was performed to investigate the factors affecting enteral nutrition and nutrition in patients with gastrointestinal cancer.

Materials and Methods: 36 articles published in the last 5 years (2014 - 2019) were obtained in total by writing the key words "gastrointestinal tract cancer", "nutrition", "enteral nutrition" and "gastrointestinal system cancers" to various databases such as "Google Scholar", "PUBMED" and "Web of Science". 10 studies, full text of which can be accessed in Turkish and in English languages and which met the inclusion criteria, were examined as a result of the evaluation.

Results and Conclusion: As a result of the literature reviewed, the effectiveness of enteral nutrition in patients with advanced stage gastrointestinal system cancer may increase intestinal motility, reducing hospital stay, although it is seen to be useful in maintaining body mass index, In the large sample group, it is thought to be important to determine the nutritional product and nutritional time.

Keywords: Enteral nutrition; nutrition; gastrointestinal tract cancer; cancer nutrition.

ÖZET

Amaç: Gastrointestinal sistem ağızdan başlayıp anüsle sonlanan tüm organları kapsayan geniş bir bütünü tanımlar. Bilim alanında gelişmeler sayesinde hastalıklara erken tanı konulabilmekte ve tedavilerden yararlanım daha fazla mümkün olmaktadır. Bir diğer yandan insan ömrünün uzamasıyla kanserden sonra sağ kalanların sayısı da artmaktadır. Gastrointestinal sisteme ait kanserler dünyada ve Türkiye’de en sık karşılaşılan kanser türleri arasında yer alırken mortalite oranlarının da yüksek olduğu bildirilmektedir. Enteral beslenme özellikle gastrointestinal sistem kanserli hastalarda mortalite ve morbiditenin engellenmesinde önemlidir. Bu derleme gastrointestinal kanserli hastalarda enteral beslenme ve beslenmeyi etkileyen faktörleri incelemek amacıyla gerçekleştirilmiştir.

Gereç ve Yöntem: "Google Scholar", "PUBMED", "Web of Science" veri tabanlarından son 5 yıla (2014-2019) ait "gastrointestinal tract cancer", "nutrition", "enteral nutrition", "gastrointestinal sistem kanser", "nutrisyon", "enteral nutrisyon" anahtar sözcükleri yazılarak toplam 36 makaleye ulaşılmıştır. Değerlendirme sonunda İngilizce ve Türkçe 10 makalenin tam metnine ulaşılmıştır.

Bulgular ve Sonuç: İncelenen literatürler sonucunda ileri evre gastrointestinal sistem kanser hastalarında enteral nutrisyonun etkinliği bağırsak motilitesinin artırılmasında, hastane yatış süresinin azaltılmasında, beden kitle indeksinin korunmasında yararlı olduğu görülse de geniş örneklem grubunda, nutrisyon ürününün özelliği ve nutrisyon zamanının belirlenmesinin önemli olduğu düşünülmektedir.

Anahtar kelimeler: Enteral beslenme; beslenme; gastrointestinal kanser; kanserde beslenme.

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INTRODUCTION

Identifies cancers in the gastrointestinal tract, mouth, pharynx, esophagus, stomach, colorectal, liver, pancreas, larynx, colon and anus (1). Cancers of the gastrointestinal tract are among the most common types of cancer. According to GLOBOCAN 2012 data, where 184 countries and 28 cancer types are registered, it ranks 3rd among the most diagnosed cancers in the world. In Turkey 163 500 people are diagnosed with cancer each year and also constitutes about 20% of these cancers, gastrointestinal cancers (2). It is foreseen that it will move to the first place as of 2015 while it is in the second rank among TUIK 2016 death data (3). With the increase in patients with gastrointestinal cancer, cancer-related anorexia-cachexia syndrome becomes even more important. Although it is generally seen in all cancer patients, 31-87% is more common in patients with gastrointestinal system cancer (4). Anorexia-cachexia syndrome is defined as a multifactorial syndrome with loss of skeletal muscle mass with or without loss of fat mass, and may cause progressive disruption of movement power with muscle loss in the skeletal system (5,6).

There are many reasons that lead to this syndrome. These causes may result from the disease itself or the treatment applied. In gastrointestinal system cancers, cytokines released from tumors as a result of systemic inflammation can lead to anorexia-cachexia. Cytokines facilitate muscle loss and development of cachexia by causing catabolism of proteins (4). In addition, obstructions may occur due to tumor formation, which may affect the oral intake of the person (7). Vomiting, diarrhea and oral mucositis may develop depending on the treatment applied (8). Especially in advanced cancer patients, it may affect dose response by making dose reduction mandatory.

It is stated that the complications that may develop enteral nutrition in patients with palliative period are directly related

to the survival and quality of life (9,10). It is also stated that enteral nutrition is effective in protecting the intestinal mucosa in recent years, maintaining immunological events, preventing systemic infection, shock and sepsis, and reducing post-operative intensive care hospitalization time (11).

AIM

In studies conducted to evaluate the effectiveness of enteral nutrition in patients with gastrointestinal cancer, it is understood that different products are evaluated with different patient groups at different times. The review prepared for this purpose was carried out to examine the factors affecting enteral nutrition and nutrition in patients with gastrointestinal cancer.

MATERIAL and METHODS

By searching the keywords of "gastrointestinal tract cancer", "nutrition", "enteral nutrition", "gastrointestinal tract cancer", "nutrition", "enteral nutrition" in the databases of "Scholar," PUBMED ", " Web of Science "for the last 5 years (2014-2019) 36 articles have been reached.

In the first stage, the database was searched independently by two researchers using keywords. The related literatures were examined in terms of subject, content, initiative, population and result sections, and those with full information were included in the review.

The total number of studies included in the review is 10. The ten studies remaining after this filtering were re-compiled by two researchers (Table 1).

Table 1. Literature review research chart

Searched databases and keywords: In the databases of "Scholar", "PUBMED", "Web of Science", "gastrointestinal tract cancer", "nutrition", "enteral nutrition", "gastrointestinal tract cancer", "nutritional", "enteral nutrition" keywords were crawled.
Total number of literature reached: 36
Inclusion criteria: <ul style="list-style-type: none"> - Research on the use of enteral nutrition in patients with advanced gastrointestinal cancer. - Published in Turkish and English languages - The full text of the research is available - Published in the last 5 years (2019-2014)
Total number of literature not considered: <ul style="list-style-type: none"> - 10 studies in which full text is not available - 7 non-english and Turkish studies - 9 studies in which sample and intervention were not fully explained
Total number of literature considered: 10

FINDINGS and DISCUSSION

In this review, the results of 10 studies published between January 2014 and January 2019 are examined. The 10 research years included in the review, author, purpose,

design, sample size and scope, application, initiative and results are presented in Table 2. In general, relationships such as the time to start feeding in gastrointestinal cancer patients, the different nutritional products used, enteral and parenteral nutrition, and the nutritional status of patients



before the operation were discussed. As a result of the researches, it is understood that hospitalization time, morbidity, mortality rates, wound healing, first fecal exit time, anastomosis leakage, body mass index are evaluated. According to the suggestions of the researches, it is understood that there are suggestions such as starting oral intake and enteral nutrition as early as possible and the use of immune nutritional products.

When we look at the literature in general, it is seen that studies on the nutrition of patients with gastrointestinal cancer are determined to determine the best time to start feeding, differences between the products used, comparison of enteral nutrition and parenteral nutrition.

In the study in which enteral nutrition was evaluated in patients with gastrointestinal system cancer, they divided them into 3 groups after performing esophagectomy with 208 patients with esophageal cancer. The first group started feeding after the first 48 hours, the second group after 48-72 hours, and the third group after 72 hours. They found that those who started feeding within the first 48 hours between the three groups provided faster fecal passage, stayed in the hospital for a shorter period of time and had lower hospital costs. They concluded that the worst group in the postoperative period was the group that fed the latest (12). Catabolic response develops after operations especially in operated patients. This catabolic process may lead to delay in wound healing, fatigue, disruption of anastomosis, prolonged recovery time and morbidity depending on the immune system response (13,14). Therefore, it is more important to provide early nutrition in patients with gastric cancer. It is reported that starting oral feeding in the first 48 hours reduces the length of hospital stay, and reduces morbidity and mortality in the postoperative period (15). Providing nutrition is important not only in the post-operative period but also in the preoperative period. Adequate nutrition and muscle mass of the patients affect the malnutrition in the post-operative period in the preoperative period.

In the meta-analysis in which 27 randomized controlled studies were discussed, it was stated that when adequate nutritional support was provided in the perioperative period, infectious and non-infectious complications decreased and hospitalization times also decreased (16).

Nutritional status in the preoperative period was also evaluated in a study with patients with colorectal cancer. In a study with 805 patients with colorectal cancer, it was found that patients having low muscle mass caused myosteatosis and fat infiltration. Especially in obese people with low muscle mass ratio, the risk of morbidity and mortality for 30 days is also high (17).

The importance of nutrition was also highlighted in Mays et al's (2015) study in 793 patients with head and neck cancer.

In this study, they evaluated the effects of BMI on the nasogastric tube patient placed before or after tumor resection, the number of complications, complications related to the wound site / not related to hospital return, hospitalization time in the intensive care unit. They

concluded that in patients who had undergone NGT during the preoperative period, they shortened their stay in the hospital/intensive care unit, reduced return to the hospital, caused less weight loss and required less wound care. They concluded that inserting NGT in the preoperative period especially in advanced cancer patients is beneficial in providing optimal nutrition (18). Apart from NGT, jejunostomy application is also emphasized in order to reduce complications in the patient. It has been reported that jejunostomy routinely recommended in patients with esophagectomy surgery causes gastrointestinal or catheter-related complications in 91.66% of patients and re-intervention is required in 4.25% (19). Based on this, it is recommended not to routinely perform jejunostomy in patients with cancer, and to decide according to the needs of the patient. There are studies reporting that starting early feeding is effective, as well as studies reporting that it is not as effective. In the postoperative period, patients in the early feeding group (n=74) started oral intake with morning water intake after surgery. If no abdominal discomfort occurs after water intake (no nausea, vomiting), soft food (rice porridge) was switched to small ampunts 6 times a day. In the control (n=96) group, oral intake was started on the 3rd or 4th days after surgery by looking at the intestinal and gastrointestinal symptoms. Although the duration of hospitalization is reduced in the early feeding group (p <0.001), it is reported that there is no difference in terms of morbidity, mortality, development of complications, anastomosis leakage, bleeding, paralytic ileus or intestinal obstruction (20). In studies conducted, the effectiveness of enteral nutrition was compared with parenteral nutrition. In a randomized controlled study of 123 patients with rectal carcinoma, Boelens et al. (2014) provided oral intake to one group in addition to early enteral (nasojunal tube) nutrition, and to one group in addition to early parenteral nutrition (central venous catheter). They evaluated the time of first defecation, morbidity, ileus symptoms, duration of hospitalization. It was stated that the group receiving only enteral nutrition between the two groups had shorter hospitalization time in the hospital and intensive care units (21). Similarly, in metaanalysis involving 10 studies, it was stated that lower respiratory tract infections and anastomosis leakage were lower in patients fed enteral nutrition than those fed parenteral nutrition. (Peng ve ark. 2016). An ease of enteral nutrition is that patients do not need to stay in the hospital. Patients with pancreaduedonectomy were found to have less morbidity, and body weight controls and serum albumin levels were better when enteral nutrition was applied at home (22).

In the literature, it is seen that the enteral product contents are also compared. Especially in recent years, immune nutritional products that are prepared or enriched by researchers with different products are used in cancer patients. Chapman et al. (2015) in the study of patients with gastrointestinal cancer (n = 338) investigated the effect of immune nutritional support on the development of wound complications. Immune nutrition is a form of nutrition that contains fatty acids such as arginine, glutamine, omega-3. Ready-made nutrition products containing these products were provided to patients 3 times a day (247 ml /1 package



product) for 5 days postoperatively. The control group was given the standard diet of the hospital. They found that patients receiving immune nutrition experienced fewer wound complications. When the World Health Organization is evaluated based on the list of the development of surgical site infections, they stated that the 2nd and 3rd class infections decreased by 78% (23). The effect of immune nutrition has also been evaluated in a randomized controlled trial with patients with esophageal cancer. When immune nutrition was given 7 days before and 7 days after esophagectomy operation, it was found to be effective in terms of nutritional status, protein level, complication development, morbidity and mortality compared to the standard fed group. Considering the 5-year overall survival rates, it was seen that it was 75% in patients receiving immune nutrition and 55% in patients receiving normal enteral nutrition (24). However, in another randomized controlled study with patients with pancreatic duodenectomy, it was stated that when immune nutritional products were started in preop period, there was no difference in terms of postop infection rates and contribution to immunity compared to enteral nutrition (25). In studies conducted, it is understood that besides nutrition products, the way of giving products to patients is compared. In the study of Yang et al. (2015) with patients with malignant esophageal obstruction, they investigated hospital stay, calorie intake, survival rates. In the retrospective study, the data were collected according to 3 groups. It was observed that group 1 was given a nasogastric tube (n = 12), group 2 was given stent to the esophagus (n = 10), and group 3 was given supportive therapy (n = 9) without oral intake. Supportive therapy consists of hydration support and a small amount of oral fluid intake. They found that the group that applied the nasogastric tube and stent had higher serum albumin levels and received more calories. At the same time, it is stated that while hospital stay times are shortened, survival times increase. However, it is also stated that patients who received nasogastric tube had more dislocation problems than the stent group (p=0.01) (26). In general, it is understood that enteral and parenteral nutrition products are compared in patients with gastrointestinal cancer. In addition, it is seen that these products are sometimes preferred from immune nutritional supplements. It has been known for many years that early feeding was effective in initiating gastrointestinal motility and reducing infections. However, depending on the underlying pathologies in patients with cancer of the gastrointestinal tract, nutrition becomes more important in increasing the quality of life. The presence of malnutrition before surgery in these patients increases morbidity and

mortality in the postoperative period. It also reduces long-term life expectancy. Another issue with early nutrition is how early it should be started and how tolerable patients can tolerate enteral nutrition. However, no randomized controlled studies on this subject were encountered. Although it is suggested to provide nutrition in the first 48 hours in the comparative study reached, it is thought that it is not possible to generalize the result.

CONCLUSIONS

Within the scope of the review, it is seen that only 3 of the literatures reached in the last 5 years are randomized controlled studies and others are retrospective or prospective descriptive studies. In general, it is understood that nutrition is important in patients diagnosed with gastrointestinal cancer, either parenterally or enterally. It is stated that when the nutrition is provided via the enteral route, the days of hospitalization in the hospital and ICU decrease, the surgical site infections decrease, the development of anastomosis leakage is low, and the serum protein and albumin values increase. Due to the increasing nosocomial infections in recent years, the early discharge of patients has been mentioned more. Similarly, it is reported to be effective in preventing morbidity and malnutrition when enteral feeding is provided at home by discharging patients early. When looking at the studies carried out with immune nutritional products, ready-made immune nutritional supports were used as well as products supplemented with additional products such as arginine and omega 3. However, the results of these studies do not support each other. In addition, standardization of the added products cannot be achieved.

In conclusion, although it is stated that nutrition is effective in reducing morbidity, mortality, surgical site infections, hospital and ICU hospitalization period in gastrointestinal cancer patients, it is thought that randomized controlled studies conducted in large sample group are needed to generalize the results.

Conflict of interest: None

Author Contributions: Concept- D.B., D.Y.; Design- D.B., D.Y.; Supervision- D.B., D.Y. Data Collection and/or Processing- D.B., D.Y.; Analysis and/or Interpretation- D.B., D.Y.; Literature search- D.B., D.Y.; Writing Manuscript- D.B., D.Y.; Critical Review- D.B., D.Y.

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Table 2. Features of the investigated studies

Year	Authors	Aim	Design	Sample size and scope	Intervention	Results
2014	Jeong et al.	Investigation of the availability and safety of early oral nutrition 1 day after postop gastrectomy.	Prospective study (2010-2011)	74 consecutive op. patient diagnosed with gastric cancer. According to the hospital protocol, patients who underwent gastrectomy before September 2010 started the diet 2-3 days after postop (n=96), after September 2010, the post-feeding started 1 day later (n=74).	The average time to start an early diet is 1.8 days, the time to start a late diet is 3.2 days. Hospital stay is 7.4 days in the group who started the diet early, 8.9 days in the group who started late diet. There is no difference between the two groups in terms of postop morbidity, gastrointestinal system comp., anastomosis leak or ileus development.	It is feasible and safe to start oral feeding on the first day after gastrectomy. Regardless of the type of gastric resection and lymph node dissection, early oral feeding shortens hospital stay and increases compliance with oral intake. However, adaptation to early oral nutrition decreases over the age of 70.
2014	Boelens et al.	Starting early enteral nutrition, accelerating the transition to a normal diet and ensuring the effect of reducing postop ileus development	RCT's	Major rectal op. with recurrent or recurrent carcinoma patients. The early enteral nutrition group *(n=61) or the group receiving oral in addition to early parenteral nutrition (n=62). * Early enteral nutrition starts at 8 hours after surgery.	In the study, the time of first defecation, morbidity development, ileus symptoms, hospital stay were evaluated. In the early enteral nutrition group, the first defecation time is shorter, anastomosis leakage is less developed and the average hospitalization day is shorter.	Early enteral nutrition is safe and is associated with less development of ileus. Early enteral feeding is associated with less anastomosis leak development.
2015	Wang et al.	Determination of the best time for standard enteral nutrition with early enteral nutrition	Comparative groups 3	n=101 (48 h) n=87 (48-72 h) n=20 (more than 72 h)	Postoperative in the period, the same enteral nutrition product was started from 500 ml, more than 48 hours / 48-72 hours / 72 hours, depending on the tolerance of the patients. At the same time, the researchers followed abdominal side effects (distension, nausea, etc.) in the patient.	Postoperative when early enteral feeding is applied within 48 hours. pulmonary inf. is effective in improving nutritional status, early intestinal movements, shortening hospital stay.



2015	Mays et al.	Determination of the possible protective effects of gastrostomy tube (GT) placed in the periop period compared with placement in the postop period.	Retrospective study (2007-2013)	793 head and neck surgery patient	Patients' preop nutritional status, comorbidities, TNM phase, surgical treatment type and wound healing according to GT placement time, medical comp, re-hospitalization, stay in hospital and ICU were taken into consideration. 8% of the patients were applied in the GT preop period and 25% in the post-op period.	GT practice in preop period The patients stayed in the hospital for a shorter period of time, lost less weight and needed less wound care. Placing GT in high-risk patients during the preop period is effective in correcting the postop results of the patients
2015	Yang et al.	Comparison of the reflection of enteral tube feeding and esophageal stent application on clinical findings in patients with malignant esophageal obstruction and short life expectancy	Retrospective study	31 patients were evaluated in 3 groups. n = 12) Nasogastric tube (NGT) group, esophageal stent (n= 10), receiving supportive therapy only (n = 9).	Apply NGT and stent. Groups have higher calorie intake, higher albumin levels, and longer life expectancy. Dislocation is more in the NGT group. In stents, the cost is higher.	Palliative enteral nutrition has a safe, cheap and low complication rate with NGT. In patients with short life expectancy with malignant esophageal obstruction, NGT may be a good choice with the help of fluoroscopy.
2015	Chapman et al.	Peri-op immune modular diet (IMD) supplements wound comp. determine whether or not.	Retrospective study	Since July 2013, immune modulation diet is started for patients undergoing laparotomy. They compared patients between July 2012 and June 2014. Standard diet (n=226), IMD (n=112)	Wound comp. In 26% of patients receiving IMD, inf. advanced. Compared to the other group, less wound comp. advanced.	Patients who have had gynecological cancer laparotomy use IMD less postoperatively and less surgical inf. is related to its development.
2019	Alvarez Sarrado et al.	Benefits of feeding with jejunostomy (JB) and analysis of complications	Retrospective study (2008-2016)	100 patient with esophageal cancer esophagectomy	JB was applied to 47 patients. Enteral nutrition was started in 82.98%. 51.06% of the directly related JB comp., 91.66% of the gastrointestinal or catheter related comp., 4.25% of the	Although nutrition does not threaten life with jejunostomy, it is associated with many complexes. The benefit of JB for nutrition is not clear. Routine use should not be recommended after esophagectomy.



		directly related to jejunostomy			catheters were required. There is no difference in total protein and albumin levels, anastomosis leakage.	
2019	Ito et al.	Benefits of feeding with jejunostomy (JB) and analysis of complications directly related to jejunostomy. Evaluation of the effect of enteral nutritional (EEN) at home after pancreatic duodenectomy.	Retrospective study	63 patients between January 2013 and July 2016. EEN group (n= 24), non-EEN group (n= 39). All patients were given enteral nutrition until they were discharged in the postoperative period. Between January 2013 and February 2015, EEN was not started at the hospital. The EEN group started enteral nutrition at home, starting from March 2015, at 400 or 800 kcal/day.	Less morbidity was observed in the EEN group and BMI was higher. Serum albumin levels are also higher.	EEN is a safe and effective application. It may be effective in patients with post-discharge morbidity and malnutrition.
2019	Kanekiyo et al.	Esophagectomy with thoracic esophageal carcinoma practice. Periop in patients IMD practice in the period determine the effects of postoperative results and long-term survival of the patient.	RCT's	The patients were randomly divided into two groups. Immune nutritional product (impact) was given to the IMD group (n=20) and standard enteral nutrition (n=20) product was provided to the other group (ensure). Nutritional status, protein motion, ICU and hospital stay, morbidity and mortality rates were compared 7 days before and 7 days after the operation.	Protein and retinol binding protein levels are higher in IMD group. Also postop inf. comp. the incidence and changes in therapeutic antibiotics are also less. There is no difference between 2 groups in terms of ICU or length of hospital stay. The 5-year progression-free and overall survival rates were higher in the IMD group, although not significant.	Esophageal cancer esophagectomy practice. Giving IMD in the perioperative period may improve early postop nutritional status and postop inf. comp. can reduce its development.
2019	Miyauchi et al.	To investigate the effect of IMD use on immunity, postop inf rate in preop, periop period in patients	RCT's	Patients were randomly divided into preop group (n=30) and periop group (n = 30). Arginine was applied to the enteral product periop group enriched with omega 3	There was no difference between Con A and PHA stimulated lymphocyte proliferation levels between the 2 groups. Again, postop inf between the 2 groups.	Pancreatic duodenectomy op. app. The use of IMD in the preop period with periop has no effect on postop immunity and infection development in patients.



		with pancreaticoduodenectomy.		fatty acids and dietary nucleotides before and after surgery, the same product was applied to preop group before and during the operation. The effect of Con A or PHA on the level of stimulated lymphocyte proliferation, especially on post op 7th day. and post op inf. its effect on the rate of development was compared.	It was found that there was no difference between the speeds.	
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