



Efficacy of commercial formulas in comparison with home-made formulas for enteral feeding: A critical review

Majid Hassan-Ghomi¹, Bahareh Nikooyeh², Soudabeh Motamed², Tirang R. Neyestani^{2*}

Received: 12 Feb 2017

Published: 5 Sep 2017

Abstract

Background: In several disease conditions, patients must inevitably be nourished by enteral feeding (EF). Though in many countries, commercial formulas are routinely used for EF, in Iran still home-made formulas are commonly employed as commercial formulas are not covered by insurance. This may pose patients to malnutrition and bring about further costs. The aim of this study was to evaluate the efficacy of EF commercial formulas in comparison with home-made formulas and thus to make further evidence for insurance policy-making

Methods: Medline, Cochrane, Embase and Center for Review & Dissemination (CRD) as well as IranDoc and SID databases were searched. Keywords included formula, ICU, and enteral nutrition or tube feeding. No clinical trial study on the efficacy of EF formulas was found. Therefore, the compositions of available formulas and their cost-effectiveness were evaluated based on the clinical guidelines of scientific bodies such as American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Parenteral and Enteral Nutrition (ESPEN) and relative articles available in PubMed. In addition, the expert opinions were also taken into consideration.

Results: Domestic commercial formulas seemed to less merit dietary recommended intakes, i.e. the amount of some nutrients were much higher, and some others were much lower than the recommended values. The amount of several micronutrients including vitamins B1, B6, C, D and K, as well as iron, calcium and magnesium were not sufficient to meet the body needs in most commercial formulas upon receiving 2000 kilocalories and less.

Conclusion: Clinical studies on the efficacy of commercial formulas in comparison with home-made formulas are needed. Meanwhile, making suitable conditions for increasing the diversity of artificial nutrition products in the market would help clinical nutritionists to make better choices according to their patients conditions and to reduce the costs, as well.

Keywords: Enteral feeding, Enteral formula, Home-made formula, Intensive care unit

Copyright© Iran University of Medical Sciences

Cite this article as: Hassan-Ghomi M, Nikooyeh B, Motamed S, Neyestani TR. Efficacy of commercial formulas in comparison with home-made formulas for enteral feeding: A review. *Med J Islam Repub Iran*. 2017 (5 Sep);31:55. <https://doi.org/10.14196/mjiri.31.55>

Introduction

Despite definition of “hospital malnutrition” in more than three decades ago, this problem still exists and is ignored somehow (1). Hospital malnutrition, particularly in the patients of intensive care unit (ICU) hospitalized for more than three days tends to be more severe, mostly due to the acute inflammatory response and consequent catabolic stress. This response is in conjunction with complications such as fatal infections, multi-organ dysfunction syndrome (MODS), and prolongation of hospitalization period and increase of mortality (2). Under these conditions, the circulating concentrations of water soluble vita-

mins, some trace elements (including selenium, zinc and iron), protein transporters and many antioxidants (particularly vitamin C) may decrease while the blood levels of some other elements, notably copper and manganese, may increase (3).

Malnutrition among ICU patients is quite prevalent. There is no report of the occurrence rate of hospital malnutrition in Iran. However, the prevalence of this problem in the United States has been reported 40% in 1995 (4). In the critically ill patients, malnutrition is along with the impaired immune function, weakness of respiratory mus-

Corresponding author: Dr Tirang R. Neyestani, t.neyestani@sbmu.ac.ir
neytr@yahoo.com

¹ Department of Technology Assessments, Standard and Tariff for Health, Deputy for Healthcare Affairs, Ministry of Health and Medical Education, Tehran, Iran.

² Laboratory of Nutrition Research, National Nutrition and Food Technology Research Institute; and Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

↑What is “already known” in this topic:

Commercial formulas are routinely used for enteral feeding. In Iran, still home-made formulas are commonly employed as commercial formulas are not covered by insurance.

→What this article adds:

The review of the literature revealed that the amount of several micronutrients including vitamins B1, B6, C, D and K, as well as iron, calcium and magnesium were not sufficient to meet the body needs in most commercial formulas upon receiving 2000 kilocalories and less.

cles, prolongation of dependence to artificial ventilation and increased mortality (5).

During the last three decades, the importance of molecular and biologic impacts of nutrients in the critical patients has been more appreciated. Studies indicate that plenty of ICU patients receive much less energy and protein than their requirements (averagely, 49-70% of the required value) (6, 7). In 1950, it was proved that energy-protein malnutrition is associated with increased mortality and disease complications and provision of adequate energy and protein for critically ill patients may improve the clinical consequences (6).

Recent researches indicate that nutritional care is effective in reducing the morbidity and mortality in critically ill patients (8, 9). In several disease conditions, patients must inevitably be nourished by enteral feeding (EF), in which food stuffs and liquid are given to the patient in the form of a homogenous liquid named formula via a special tube inserted in patient's digestive tract.

During recent years, the diversity of EF formulas has been rapidly increased. Nowadays, there are several kinds of formulas in the market that occasionally may make the selection difficult. In most cases, a formula is selected based on the experience of physician or nutritionist, availability and finally the price. In other words, the effectiveness and indication thereof may be less taken into consideration. On the other hand, as Food and Drug Administration (FDA) considers formulas as nutritional supplements, they are not under legal supervision similar to the drugs. Therefore, the manufacturers may make many claims without supporting scientific evidence. The most common formulas available in the Iranian market include Entramil, Milatech, Ensure, Notricamp and Fresubin. Currently, number of imported formulas is very limited and even may not be easily available in the market. Though in many countries, commercial formulas are routinely used for EF, in Iran still home-made formulas are commonly employed as commercial formulas are not covered by insurance. This may pose patients to malnutrition and bring about further costs. This study, therefore, aimed to evaluate the efficacy of EF commercial formulas in comparison with home-made formulas and thus to make further evidence

for insurance policy-making.

Methods

Medline, Cochrane, Embase and Center for Review & Dissemination (CRD) as well as IranDoc and SID databases were searched. Keywords included "formula", "ICU", and "enteral feeding" or "enteral nutrition" or "tube feeding". No clinical trial study on the efficacy of EF formulas was found. Therefore, the composition of available formulas was investigated and their cost-effectiveness was determined based on the clinical guides of scientific authorities notably American Society for Parenteral and Enteral Nutrition (ASPEN) (2, 10, 11) and European Society for Parenteral and Enteral Nutrition (ESPEN) (12-16). Moreover the composition of all formulas available in the Iranian market was compared to the composition recommended by the competent authorities. Meanwhile, the composition of a home-made formula with a recipe recommended by the Iran Nutrition Society (INS) was investigated and its cost effectiveness was compared to that of commercial formulas available in the Iranian markets. In this study, the cost needed for feeding the patients was estimated based on current prices. The sufficiency of formulas for providing the required energy and nutrients was judged based on the Dietary Reference Intakes (DRIs).

Results and discussion

Effectiveness

The commercial EF formulas can be categorized as standard, elemental and disease-specific. There are many formulas available in each category often with different compositions. Standard formulas are designed to meet the basic needs to protein together with a balanced value of other macronutrients and micronutrients. These formulas have lower price than special formulas. Special (disease-specific) formulas are designed for specific clinical conditions (Table 1) (2). Selection of an appropriate formula for EF is mostly dependent on the following factors: nutritional needs of the patient, function of the patient's digestive system, location of the tube end (stomach or intestine), food sensitivities and/or lactose intolerance in the

Table 1. Classification of enteral formulas

Class	Subgroup	Specifications	Indication
	Standard	Similar to normal diet	Normal digestion
	High protein	Protein more than 15% of total calorie	- Catabolism - Wound healing
Polymeric	High energy	More than 1 kilocalorie per ml	- Constraint of liquids - Intolerance of high volume - Abnormality of electrolytes - Adjustment of intestine function
Monomeric	Fibrous	5-15 gr of fiber per lit	Problem of digestion and absorption
	Partial hydrolysis	One or more nutrients are digested.	
For special diseases	Elemental		
	Peptide		
	Renal	Low protein and electrolyte	Renal disorder
	Hepatic	High BCAAs, low FAAs and electrolytes	Hepatic encephalopathy
	Pulmonary	High fat	ARDS
	Diabetic	Low carbohydrate	Diabetes
	Safety increaser	Arginine, glutamine, omega 3, and antioxidant	- Metabolic problem - Safety system problem

Abbreviations: ARDS: acute respiratory distress syndrome; BCAAs: branched chain amino acids; FAAs: free amino acids

patient, and the amounts of sodium, potassium, magnesium and phosphorous available in the formula, particularly in the patients suffering from renal, hepatic or cardiac-respiratory failure. To our knowledge, there is no study ever having investigated the effectiveness of formulas available in the Iranian market and other countries. Thus, attempts were made to evaluate and compare the composition and cost-effectiveness of the home-made and commercial formulas available in Iranian market based on recent recommendations of scientific authorities.

Nutrient composition of the enteral formulas

Energy, micronutrients and macronutrients available in 100 mL of each formula against the ASPEN recommended values are shown in Table 2. Standard formulas majorly contain micro- and macro-nutrients to the extent of values recommended for the healthy persons. The ASPEN guideline (2) has modified the amounts of nutrients required for people under enteral and parenteral nutrition. However, more amounts of energy and nutrients may be needed to meet critically ill patients' requirements (2).

Macronutrients

Most commercial formulas used in EF contain 1 kcal/mL. A few provide 2 kcal/mL that may be used for the patients with intensive limitation for liquid intake (such as patients suffering from cardiac, respiratory, renal or hepatic failures).

In most commercial formulas, the ratio of energy from non-protein nutrients to nitrogen is 150 kcal/g. This ratio

is ideal for the patients without stress. In patients with increased need to protein (e.g. those suffering from burning, infection or multiple traumas), use of commercial protein mixtures or commercial high protein formulas is recommended. Based on the ASPEN guideline, protein needs for these patients is 0.8-2.0 g/kg.d⁻¹, 25-30% of which must be provided from essential amino acids (10, 11). This value is about 15-25% of daily energy intake. The recommended ratio of non-protein calorie to nitrogen is about 70:1 to 100:1 (2). The protein in polymeric formulas is typically derived from casein, caseinate, whey protein, egg (ovo-albumin), soya (soy protein), sodium, potassium, calcium and magnesium caseinates, lactalbumin, and milk protein extract. Almost all formulas except elemental or predigested ones that have protein as di or tripeptides and amino acids, provide intact protein and are gluten free (5).

The amount of protein in polymeric formulas available in the domestic commercial products varies from 15% to 20% of total energy, with high protein formulas having the highest amount of protein among these formulas. If 1g/kg.BW⁻¹ protein is prescribed for a 70 kg man, then he must receive at least 1870 ml of a standard formula containing 15% of total energy from protein to supply his needed protein.

Fat sources in polymeric formulas are corn oil, sunflower oil with high oleate, soy, flax seed oil, soy lecithin, mono- and di-glyceride, canola oil, fish oil, date seed oil,

Table 2. Nutrient composition of Entramil formulas in comparison with the daily intake values (DV%) recommended by ASPEN

	Unit	Standard Entramil	DV%	Diabetic Entramil	DV%	High protein Entramil	DV%	Fibrous Entramil	DV%	ASPEN DRI
Formula shape	-	Powder	-	Powder	-	Powder	-	Powder	-	-
Energy	Kilocalorie	100	-	100	-	120	-	100	-	-
Protein	Percent	14	-	15	-	17	-	15.4	-	-
Carbohydrate	Percent	54.4	-	37	-	48	-	52	-	-
Fat	Percent	31.6	-	48	-	35	-	32.6	-	-
Fiber	Percent	0.4	-	0.98	-	0.5	-	1.36	-	-
Osmolality	Milliosmol	340	-	380	-	380	-	380	-	-
B1	Milligram	0.15	-	0.18	300	0.18	250	0.16	266	1.2
B2	Milligram	0.17	250	0.2	307	0.2	256	0.17	261	1.3
Niacin	Milligram	1.27	261	1.89	236	2.23	232	1.31	163	16
Pantothenic acid	Milligram	0.63	158	0.69	276	0.75	250	0.65	260	5
B6	Milligram	0.13	252	0.14	164	0.15	147	0.13	152	1.7
Folic acid	Microgram	25.4	152	27.28	136	30	125	26.3	131	400
Biotin	Microgram	15.85	127	17.05	1136	18.76	1042	16.45	1096	30
B12	Microgram	0.5	1056	0.55	458	0.59	409	0.52	433	2.4
Vitamin C	Milligram	9.72	416	10.2	226	11.25	208	9.86	219	90
Vitamin D	IU	19	216	20.47	68	22.5	62	19.75	65	600
Vitamin E	IU	2.5	63	2.73	242	2.99	221	2.62	232	22.5
Vitamin K	Microgram	6.34	222	6.8	113	7.48	103	6.56	109	120
Vitamin A	IU	209.5	105	225.2	150	247.56	137	217	144	3000
Iron	Milligram	1.53	139	1.12	124	1.11	102	0.98	108	18
Calcium	Milligram	77.2	170	73.67	122	82.58	114	72.4	120	1200
Chrome	Milligram	1.85	128	2.47	164	2.24	124	1.97	131	30
Copper	Milligram	0.09	123	0.1	222	0.1	185	0.09	200	0.9
Fluorine	Milligram	0.22	200	0.23	115	0.25	104	0.22	110	4
Iodine	Milligram	9.5	110	10.23	136	11.25	125	9.86	131	150
Magnesium	Milligram	37.4	126	25.05	119	27.92	110	24.48	116	420
Manganese	Milligram	0.1	178	0.18	156	0.18	130	0.16	139	2.3
Molybdenum	Microgram	2.85	86	3.06	136	3.38	125	2.96	131	45
Zinc	Milligram	1.2	126	0.87	158	1.11	168	0.98	178	11
Phosphorous	Milligram	77.2	218	43.7	124	80	190	72.4	206	700
Potassium	Milligram	92	220	147.5	147	192	160	162.9	162	2000
Sodium	Milligram	52.6	92	139.1	556	144	480	122.17	488	500
Chlorine	Milligram	83	210	75.83	202	92.9	206	70.1	186	750
Selenium	Microgram	3.5	221	3.75	136	4.13	125	3.62	131	55

Efficacy of enteral feeding formulas

Table 3. Nutrient composition of Milatech formulas in comparison with the recommended daily intake values (DV%)

	Unit	Standard Milatech	DV%	Standard fibrous Milatech	DV%	High protein Milatech	DV%	High energy Milatech	DV%	Intensive Milatech	DV%	Elemental Milatech	DV%	Safety Milatech	DV%	Pehatic Milatch	DV%	ASPEN DRI
Formula shape	-	Solution	-	Solution	-	Solution	-	Solution	-	Solution	-	Solution	-	Solution	-	Solution	-	-
Energy	Kilocalorie	100	-	100	-	100	-	-	-	130	-	100	-	133	-	-	-	-
High protein	Percent	15	-	15	-	20	-	-	-	20	-	20	-	20	-	-	-	-
Carbohydrate	Percent	55	-	55	-	50	-	-	-	40	-	70	-	55	-	-	-	-
Fat	Percent	30	-	30	-	30	-	-	-	40	-	10	-	25	-	-	-	-
Fiber	gr	0	-	1.5	-	0	-	-	-	0	-	0	-	0	-	-	-	-
Osmolarity	Milliosmol	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
B1	Milligram	0.07	116	0.07	116	0.07	116	116	288	0.07	107	0.07	116	0.14	175	175	153	1.2
B2	Milligram	0.08	123	0.08	123	0.08	123	123	307	0.08	94	0.08	123	0.16	185	185	177	1.3
Niacin	Milligram	1	125	1	125	1	125	125	250	1.3	125	1	125	1.62	152	152	159	16
Pantothenic acid	Milligram	0.2	80	0.2	80	0.2	80	80	80	0.2	61	0.2	80	0.33	99	99	92	5
B6	Milligram	0.11	129	0.11	129	0.11	129	129	235	0.12	108	0.11	129	0.24	212	212	162	1.7
Folic acid	Milligram	20	100	20	100	20	100	100	150	20	76	20	100	30	112	112	115	400
Biotin	Microgram	8	533	8	533	8	533	533	355	8	410	8	533	8	401	401	410	30
B12	Microgram	0.15	125	0.15	125	0.15	125	125	150	0.15	96	0.15	125	0.36	225	225	96	2.4
Vitamin C	Milligram	3	66	3	66	3	66	66	296	3	51	3	66	6	100	100	102	90
Vitamin D	IU	20	66	20	66	20	66	66	133	26	66	20	66	33.6	84	84	66	600
Vitamin E	IU	0.75	66	0.75	66	0.75	66	66	331	0.75	51	0.75	66	1.9	126	126	102	22.5
Vitamin K	Microgram	3.5	58	3.5	58	3.5	58	58	116	4.55	58	3.5	58	5.33	66	66	76	120
Vitamin A	IU	150	100	150	100	150	100	100	177	150	76	150	100	333	166	166	93	3000
Iron	Milligram	0.9	100	0.9	100	0.9	100	100	148	0.9	76	0.9	100	1.57	131	131	115	18
Calcium	Milligram	45	75	45	75	45	75	75	112	54	69	45	75	60	75	75	69	1200
Chrome	Microgram	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	30
Copper	Milligram	0.1	222	0.1	222	0.1	222	222	222	0.1	170	0.1	222	0.16	267	267	273	0.9
Fluorine	Milligram	0.1	50	0.1	50	0.1	50	50	50	0.1	38	0.1	50	0.16	60	60	76	4
Iodine	Microgram	7.5	100	7.5	100	7.5	100	100	128	7.5	76	7.5	100	12	120	120	115	150
Magnesium	Milligram	17.5	83	17.5	83	17.5	83	83	111	18.5	67	17.5	83	30.87	110	110	105	420
Manganese	Milligram	0.12	104	0.12	104	0.12	104	104	197	0.12	80	0.12	104	0.22	147	147	160	2.3
Molybdenum	Microgram	5	222	5	222	5	222	222	222	5	170	5	222	6.5	217	217	222	45
Zinc	Milligram	0.75	136	0.75	136	0.75	136	136	254	0.75	104	0.75	136	0.94	128	128	163	11
Phosphorous	Milligram	40	114	40	114	40	114	114	185	60	131	40	114	66.6	143	143	131	700
Potassium	Milligram	130	130	130	130	130	130	130	86	130	100	130	130	130	97	97	100	2000
Sodium	Milligram	50	200	50	200	50	200	200	133	50	153	50	200	50	150	150	153	500
Chlorine	Milligram	95	253	95	253	95	253	253	266	105	215	95	253	146.6	293	293	287	750
Selenium	Microgram	2.5	90	2.5	90	2.5	90	90	164	3.5	97	2.5	90	3.6	98	98	97	55

Table 4. Nutrient composition of some imported commercial formulas in comparison with the recommended daily intake values (DV%)

	Unit	Ensure	DV%	Standard Nutricamp	DV%	High energy Nutricamp	DV%	Standard Fresubin	DV%	High protein Fresubin	DV%	ASPEN DRI
Formula shape		Powder	-	Solution	-	Solution	-	Solution	-	Solution	-	-
Energy	Kilocalorie	100	-	100	-	150	-	100	-	150	-	-
Protein	Percent	14	-	15	-	20	-	15	-	20	-	-
Carbohydrate	Percent	54	-	55	-	50	-	55	-	45	-	-
Fat	Percent	32	-	30	-	30	-	30	-	35	-	-
Fiber	gr	0.84	-	0	-	0	-	0	-	0	-	-
Osmolarity	Miliosmol	395	-	250	-	344	-	250	-	300	-	-
B1	Milligram	0.17	283	0.2	333	0.2	222	0.13	216	0.01	88	1.2
B2	Milligram	0.19	292	0.2	307	0.2	205	0.17	261	0.11	112	1.3
Niacin	Milligram	2.3	287	1.8	225	1.8	150	1.6	200	1.06	88	16
Pantothenic acid	Milligram	1.2	480	0.6	240	0.6	160	0.47	188	0.31	82	5
B6	Milligram	0.23	270	0.2	235	0.2	156	0.16	188	0.1	78	1.7
Folic acid	Milligram	46	230	30	150	30	100	27	135	18	60	400
Biotin	Microgram	35	2333	5	333	5	222	5	333	3.33	148	30
B12	Microgram	0.72	600	0.3	250	0.3	166	0.27	225	0.18	100	2.4
Vitamin C	Milligram	16	355	4	88	20	296	6.67	148	4.46	66	90
Vitamin D	IU	22	73	40	133	40	88	40	133	26.4	58	600
Vitamin E	IU	2.6	231	1.55	137	3	177	1.99	176	5.6	331	22.5
Vitamin K	Microgram	4.2	70	7	116	7	77	6.67	111	4.44	49	120
Vitamin A	IU	149.8	99	166.6	111	166.6	74	250	166	500	222	3000
Iron	Milligram	1	111	1.2	133	1.2	88	1.33	147	0.88	65	18
Calcium	Milligram	65	108	75	125	75	83	80	133	53.33	59	1200
Chrome	Microgram	4.6	306	7	466	7	311	6.7	446	4.46	198	30
Copper	Milligram	0.12	266	0.15	333	0.15	222	0.13	288	0.08	118	0.9
Fluorine	Milligram	0	-	0.1	50	0.1	33	0.13	65	0.08	26	4
Iodine	Microgram	7.9	105	13	173	13	115	13.3	177	8.86	78	150
Magnesium	Milligram	21	100	20	95	20	63	25	119	18	57	420
Manganese	Milligram	0.28	243	0.2	173	0.2	115	0.27	234	0.18	104	2.3
Molybdenum	Microgram	8.8	391	10	444	10	296	10	444	6.66	197	45
Zinc	Milligram	1.3	236	1.2	218	1.5	181	1.2	218	0.8	96	11
Phosphorous	Milligram	53	151	65	185	65	123	63	180	42	80	700
Potassium	Milligram	155	155	150	150	150	100	125	125	156	104	2000
Sodium	Milligram	84	336	100	400	100	266	75	300	80	213	500
Chlorine	Milligram	142	378	100	266	100	177	115	306	122	216	750
Selenium	Microgram	4.4	160	7	254	9	218	6.7	243	4.46	108	55

Table 5. A sample of a home-made formula* (28)

Food composition	Value (g or ml)	Energy	Carbohydrate	Protein	Fat	Iron	Zinc	Calcium	Vitamin D (IU)	Vitamin A (IU)	Vitamin C (mg)
Meat (cooked and water-removed)	210	403	-	49	35	35	8.8	17	---	---	---
Vegetable (cooked and water-removed)	600	294	30	12	-	-	2.94	150	---	25662	19.2
Fruit (cooked and water-removed)	600	348	90	-	-	-	0.42	42	---	2574	15
Milk powder	300	1074	30	20	15	15	13.23	3693	---	45	16.8
Pasteurized milk	720	403	36	24	15	15	2.95	1030	---	540	7.9
Vegetable oil	30	265	-	-	30	30	---	---	---	---	---
Water	As Required	---	---	---	---	---	---	---	---	---	---
Total	-	2787	186	105	95	95	28.34	4932	---	28821	58.9

*The energy and micronutrients values were estimated using USDA tables. Obviously, the received energy and micronutrients values will vary depending on the water added to these materials as well as the amount of the solution prescribed to the patient.

borage oil, and meat butter or fat; they are majorly enriched with medium chain triglycerides (MCTs) (17). Use of products containing fish oil and borage oil may reduce the need to artificial ventilation and hospitalization period in ICU (5). A few researches indicated that formulas containing MUFAs have been effective in the control of hyperglycemia after feeding without increasing insulin secretion (18).

According to ASPEN, total intake of lipid should not exceed from 2.5 g/ kg.d⁻¹, and 1-2% of daily energy intake should be provided by linoleic acid (omega 6) and 0.5% by alpha linolenic acid (omega 3) (19). Approximately 31-40% of total energy of formulas available in the market are provided by lipids. Nonetheless, fat content of available formulas is not specified on the labels.

Maltodextrin, corn syrup, hydrolyzed starch, sucrose, fructose and sugar alcohols are usually the carbohydrates found in polymeric formulas (17). ASEPN recommends that carbohydrate intake should not exceed 7g/ kg.d⁻¹ (2). The percent of total energy provided by carbohydrate in formulas available in Iran varies from 40% to 55%.

It has been shown that soluble fibers may reduce diarrhea episodes in patients but no significant effect on duration of artificial ventilation and hospitalization has been reported yet (2). The increase of viscosity due to soluble fibers must be taken into account in making formulas (17). Currently, progress of technology has extremely solved this problem. The results obtained from the assessment of enteral formulas containing fiber for diarrhea control are contradictory. It is chiefly due to the use of all types of fibers. Fibers are classified based on their solubility in water. Soluble

fibers such as pectin and gum, by absorption of water and sodium, may be effective in treatment of EF-related diarrhea. Insoluble fibers, on the other hand, increase the weight of feces and reduce the intestinal transit time (17). Some researchers have shown that the insoluble fibers may not reduce the occurrence of diarrhea. Besides, a few cases of intestinal obstruction have been reported in patients received insoluble fibers (2, 20). One study compared the effect of enteral formula with and without soluble fiber and concluded that diarrhea episodes were significantly decreased in the patients received fiber containing formula (21). Recently, fructo-oligosaccharide (FOS) is used in formulas as it is fermented quickly by colon bacteria and produces short chain fatty acids (SCFAs) that affect the bowel function and digestive health via several ways. These fatty acids serve as fuel for colon cells, and enhance intestinal mucus and water and sodium absorption (22). Fibrous formulas are closer to a regular diet. Notwithstanding, the evidence for their use is not adequate. It should be noted that fibrous formulas should not be given to the patients at risk of intestinal obstruction or ischemia.

Micronutrients

Upon daily intake of 1300-1900 ml of commercial formulas, the needs to vitamins and minerals in most patients are met. In contrast, in patients with fluid restriction, vitamins and minerals supplementation may be necessary.

Formulas supplemented with antioxidants (such as vitamin E and ascorbic acid) and minerals (like selenium, copper and zinc) have been demonstrated to favorably affect the outcomes of diseases (particularly in burns and traumas) and to reduce the period of ventilation in artificially ventilated patients (2). Based on the Canadian clinical guideline, use of antioxidants is useful for the patients suffering from acute respiratory distress syndrome (5).

Use of antioxidant nutrients may reduce mortality and days of artificial ventilation though may not affect the infectious complications in these patients (5). In a clinical study, intake of a fortified formula containing 67 µg/dL vitamin A (DV%¹=148), 13.3 mg/dL vitamin C (DV%=295) and 4.98 mg/dL vitamin E (DV%=658) compared with isocaloric and isonitrogenic formulas resulted in improvement of antioxidant defense but did not affect the mortality, infection rate and hospitalization period (23).

Overall, trace element and vitamin supplementation improves the antioxidant capacity in the critically ill patients (24). As selenium and vitamins E and C contribute in recycling of other water- and fat-soluble antioxidants, using a mixture of antioxidant micronutrients is preferred to the single antioxidant supplementation (25).

Currently, the commonly available formula products in the market are Entramil and Milatech, DV% of both of which is 65% for vitamin D. By intake of lower than 3000 kcal, none of them can supply the required value of this vitamin. DV% for vitamins E and K are 66% and 58%, respectively. The concentration of vitamin C and fluorine of Nutricamp formula is lower than the recommended value, and upon receiving less than 4000 kilocalories, the recommended value of fluorine is not provided. The concentration of micronutrients B1, niacin, pantothenic acid, B6, folic acid, biotin, vitamins C, D and K, calcium, fluorine, iodine, magnesium, phosphorous of high protein Fresubin is not supplied by receiving 2000 kilocalories and less. As for other micronutrients, the composition of the commercial products is almost similar (Tables 3 and 4).

Comparison of cost-effectiveness

There are few studies (and no study in Iran) on the cost-effectiveness of commercial formulas as compared to the home-made formulas. In a clinical trial on 82 patients with intestinal fistula, home-made formula was compared versus hospital (commercial) formula. The results showed a shorter hospital stay in home EF group with a significantly lower costs and increased quality of life. However, there were no significant difference in duration of EF and the incidence of complications between two groups (26). Another study reported that implementation of home enteral nutrition improved clinical outcomes and decreased health care costs through weight gain in patients, reduced incidence of infectious complications and the cost of hospitalization (27). However, the amount of nutrient intakes from home-made formulas should always be taken into consideration as the amount of some micronutrients may be

higher and that of some others be lower than the recommended values. Considering an effective process in order to standardize home-made formulas and to ensure their nutritional adequacy is essential.

A sample of food stuffs used for a recipe for a home-made formula (28) is demonstrated in Table 5. This composition contains 2019 kilocalorie, 186 g carbohydrate, 105 g protein and 95 g fat. Considering the current price of the foodstuffs, the cost of providing this composition for one day is about 110,000 Rials. On the other hand, the cost of using commercial formulas is 170,000 Rials daily. This difference and the fact that current nutritional services are not covered by insurance may cause patients and their care-givers prefer using a home-made formulas. However, the issues of safety and ease of preparation of commercial formulas should not be ignored. Additionally, in cases of a need for using such especial formulas as elemental formulas, it is very hard, if not impossible, to make it at home.

Overall, the attempts of scientific bodies of clinical nutrition should be towards both improvement of the quality and reduction the costs of commercial formulas and provision guidelines for making efficient home-made formulas. Nonetheless, assuming the cost of one night stay in ICU is averagely 10,000,000 Rials (annually 3,650,000,000 Rials) and the cost of one day use of commercial formulas is 170,000 Rials (annually 62,050,000), if using these formulas can reduce the length of stay in the ICU and overall length of hospitalization even for one night, they can reduce the cost of treatment and save money by 3,587,950,000 Rials annually.

Conclusion

According to the present study the composition of the commonly available commercial formulas in the Iranian market need to be improved. It is necessary to investigate the effectiveness of the imported and domestic commercial formulas available in the markets using precise clinical trials. Meanwhile, appropriate guidelines for making home-made formulas are also needed.

Limitations

Some limitations of this study are acknowledged. We did not estimate the costs in relation to the outcomes (efficiency) of home-made and commercial enteral formulas in patients. For instance, we did not analyze the length of hospital stay, costs of care and nosocomial infection rates. Further studies are needed to evaluate and compare outcomes in relation to using different commercial formulas and home-made formulas in the patients.

Acknowledgements

This study was funded by National Institute of Health Research and Administration of Health Technology Evaluation, Health Deputy, Iran Ministry of Health. MHG was the executive manager. Data were gathered and analyzed by BN. The preliminary paper was written by SM. TRN supervised the whole work and finalized the manuscript. Authors have no conflict of interest to declare.

¹ Percent of daily value

Conflict of Interests

The authors declare that they have no competing interests.

References

- Klinkenberg M, Thijs A. Profile of the malnourished patient. *Eur J Clin Nutr.* 2005;59(10):1129-35.
- McClave SA, Martindale RG, Vanek VW, McCarthy M, Roberts P, Taylor B, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *J Parenter Enteral Nutr.* 2009;33(3):277-316.
- Berger MM, Shenkin A. Update on clinical micronutrient supplementation studies in the critically ill. *Curr Opin Clin Nutr Metab Care.* 2006;9(6):711-6.
- Giner M, Laviano A, Meguid MM, Gleason JR. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists. *Nutr.* 1996;12(1):23-9.
- Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. *J Parenter Enteral Nutr.* 2003;27(5):355-73.
- Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhaliwal R, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. *Intensive Care Med.* 2009;35(10):1728-37.
- Heyland DK, Schroter-Noppe D, Drover JW, Jain M, Keefe L, Dhaliwal R, et al. Nutrition support in the critical care setting: current practice in canadian ICUs--opportunities for improvement? *J Parenter Enteral Nutr.* 2003;27(1):74-83.
- Visser J, Labadarios D, Blaauw R. Micronutrient supplementation for critically ill adults: a systematic review and meta-analysis. *Nutr.* 2011;27(7):745-58.
- Manzanares W, Dhaliwal R, Jiang X, Murch L, Heyland DK. Antioxidant micronutrients in the critically ill: a systematic review and meta-analysis. *Crit Care.* 2012;16(2):1.
- Bankhead R, Boullata J, Brantley S, Corkins M, Guenter P, Krenitsky J, et al. Enteral nutrition practice recommendations. *J Parenter Enteral Nutr.* 2009.
- White JV, Guenter P, Jensen G, Malone A, Schofield M, Group AMW, et al. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Acad Nutr Diet.* 2012;112(5):730-8.
- Lochs H, Dejong C, Hammarqvist F, Hébuterne X, Leon-Sanz M, Schütz T, et al. ESPEN guidelines on enteral nutrition: gastroenterology. *Clin Nutr.* 2006;25(2):260-74.
- Loser C, Aschl G, Hébuterne X, Mathus-Vliegen E, Muscaritoli M, Niv Y, et al. ESPEN guidelines on artificial enteral nutrition—percutaneous endoscopic gastrostomy (PEG). *Clin Nutr.* 2005;24(5):848-61.
- Arends J, Bodoky G, Bozzetti F, Fearon K, Muscaritoli M, Selga G, et al. ESPEN guidelines on enteral nutrition: non-surgical oncology. *Clin Nutr.* 2006;25(2):245-59.
- Kreymann K, Berger M, Deutz Ne, Hiesmayr M, Jolliet P, Kazandjiev G, et al. ESPEN guidelines on enteral nutrition: intensive care. *Clin Nutr.* 2006;25(2):210-23.
- Plauth M, Cabre E, Riggio O, Assis-Camilo M, Pirlich M, Kondrup J, et al. ESPEN guidelines on enteral nutrition: liver disease. *Clin Nutr.* 2006;25(2):285-94.
- Malone AM. Enteral formula selection: a review of selected product categories. *Pract Gastroenterol.* 2005;29(6):44.
- Yokoyama J, Someya Y, Yoshihara R, Ishii H. Effects of high-monounsaturated fatty acid enteral formula versus high-carbohydrate enteral formula on plasma glucose concentration and insulin secretion in healthy individuals and diabetic patients. *J Int Med Res.* 2008;36(1):137-46.
- Mehta NM, Compber C. ASPEN Clinical Guidelines: nutrition support of the critically ill child. *J Parenter Enteral Nutr.* 2009;33(3):260-76.
- Scaife CL, Saffle JR, Morris SE. Intestinal obstruction secondary to enteral feedings in burn trauma patients. *J Trauma Acute Care Surg.* 1999;47(5):859.
- Rushdi TA, Pichard C, Khater YH. Control of diarrhea by fiber-enriched diet in ICU patients on enteral nutrition: a prospective randomized controlled trial. *Clin Nutr.* 2004;23(6):1344-52.
- Sabater-Molina M, Larque E, Torrella F, Zamora S. Dietary fructooligosaccharides and potential benefits on health. *J Physiol Biochem.* 2009 Sep;65(3):315-28.
- Preiser J-C, Van Gossum A, Berré J, Vincent J-L, Carpentier Y. Enteral feeding with a solution enriched with antioxidant vitamins A, C, and E enhances the resistance to oxidative stress. *Critic Care Med.* 2000;28(12):3828-32.
- Heyland DK, Dhaliwal R, Suchner U, Berger MM. Antioxidant nutrients: a systematic review of trace elements and vitamins in the critically ill patient. *Intensive Care Med.* 2005;31(3):327-37.
- Heyland DK, Dhaliwal R, Day AG, Muscedere J, Drover J, Suchner U, et al. Reducing Deaths due to Oxidative Stress (The REDOXSC Study): rationale and study design for a randomized trial of glutamine and antioxidant supplementation in critically-ill patients. *Proc Nutr Society.* 2006;65(03):250-63.
- Wang Y, Kang Y, Zhou JR. [Comparison of two types of enteral nutrition in patients with intestinal fistula]. *Zhonghua Yi Xue Za Zhi.* 2013 Aug 13;93(30):2364-6.
- Klek S, Hermanowicz A, Dziwiszek G, Matysiak K, Szczepanek K, Szybinski P, et al. Home enteral nutrition reduces complications, length of stay, and health care costs: results from a multicenter study. *Am J Clin Nutr.* 2014 Aug;100(2):609-15.
- Iran Nutrition Society Guide for Diet-Therapy (Persian). Tehran: Salemi; 2003.