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Effect of enteral feeding with ginger extract in acute respiratory distress syndrome

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Abstract

Purpose: The purpose of this study is to evaluate the effects of an enteral diet enriched with ginger extract on inflammatory factors, respiratory profile, and outcome of patients with acute respiratory distress syndrome (ARDS).

Materials and methods: Thirty-two patients with ARDS were randomized to receive a high-protein enteral diet enriched with ginger or placebo. Serum levels of interleukin (IL) 1, IL-6, tumor necrosis factor α, and leukotriene B4; red blood cell glutathione; oxygenation; and static compliance were measured on days 0, 5, and 10.

Results: Patients fed enteral diet enriched with ginger had significantly lower serum levels of IL-1, IL-6, and tumor necrosis factor α and higher level of RBC glutathione on days 5 and 10 compared with control group ($P < .05$). Significant improvement in oxygenation was observed on day 5 ($P = .02$) and 10 ($P = .003$) in ginger group compared with control group. Static compliance was increased on day 5 ($P = .01$) in ginger group compared with control group. A significant difference was found in duration of mechanical ventilation ($P = .02$) and length of intensive care unit stay ($P = .04$) in favor of ginger group. We did not find any difference in barotraumas, organ failure, and mortality between the study groups.

Conclusions: An enteral diet supplemented with ginger in patients with ARDS may be beneficial for gas exchange and could decrease duration of mechanical ventilation and length of stay in intensive care unit.

1. Introduction

Clinical acute respiratory distress syndrome (ARDS) occurs primarily as the result of inflammatory injury to the alveoli producing diffuse alveolar damage [1]. The lungs probably are particularly vulnerable to inflammatory injury because mediators are released into the bloodstream and the lungs receive the entire cardiac output. Proinflammatory cytokines such a tumor necrosis factor α (TNF-α), interleukin (IL) 1, IL-6, and IL-8 are released into the interstitial and alveolar spaces with subsequent active and release of injurious protease and reactive oxygen species [2]. As a result, normal barriers to alveolar edema are lost. These

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patients almost always depend on mechanical ventilation. Mechanical ventilation can exacerbate lung injury and lead to an additional inflammatory response [3]. Ginger has a long history of medicinal use, particularly as an anti-inflammatory and antioxidant agent for some diseases such as arthritis [4,5]. Active components of ginger, shogaols, and gingerols have shown to inhibits both cyclooxygenase and lipooxygenase enzymes [6]. Recent studies have shown that the use of specialized enteral nutrition formulas with omega-3 fatty acids with their anti-inflammatory potential is becoming a useful adjuvant therapy in the clinical management of critically ill patients [7,8], although a recent study has shown that patients receiving the omega-3 supplement had fewer ventilator-free days and fewer intensive care unit (ICU)–free days [9]. On the other hand, ginger is a potent antioxidant agent. Studies in patients with ARDS have demonstrated both a decrease in total glutathione and a relative increase in oxidized glutathione in alveolar fluid [10].

To our knowledge, there is no study evaluating anti-inflammatory and antioxidant activity and clinical outcome of ginger extract in ARDS; we selected patients with ARDS who are hospitalized in ICU to evaluate these effects.

2. Materials and methods

Study protocol and patient selection have been demonstrated previously [11]. Briefly, 32 patients with ARDS who were admitted to a 21-bed medical/surgical ICU of a tertiary care teaching hospital were included in this randomized, double-blind study. Patients were well matched for age, sex, and type of disease (medical, surgical, and trauma). Acute Physiology and Chronic Health Evaluation II score calculated for each subject was used to match disease severity. Patients were eligible for the study if they were in ICU, required positive pressure ventilation via endotracheal tube or tracheostomy, and were on enteral nutrition support. In addition, they had to have an acute onset of significantly impaired oxygenation with a pressure of arterial oxygen (Pa_{O_2})–to–fraction of inspired oxygen (Fi_{O_2}) ratio equal or less than 200, bilateral pulmonary infiltrates on frontal chest radiograph, and no clinical evidence of left atrial hypertension according to the American-European Consensus Conference on ARDS [12]. Patients had to be enrolled within 48 hours of developing these criteria. The study protocol was approved by responsible ethics committee, and informed consents were obtained from all patients or their surrogates before enrollment. Subjects who were in the study for 8 days or more were analyzed.

Exclusion criteria were younger than 18 years, participation in other interventional trials in the previous 30 days, neurologic conditions that could impair weaning from ventilatory support, severe chronic respiratory disease, pregnancy, lactation, active bleeding, head trauma, intracranial hemorrhage, peptic ulcer, HIV infection, food allergy, morbid obesity, malignancy or other irreversible conditions for which 6-month mortality was estimated to be 50% or more, and who were receiving nonsteroidal anti-inflammatory drugs *N*-acetyl cysteine or ketoconazole. Before the initiation of enteral feeding, a baseline medical history, physical examination, and primary diagnosis were recorded for subjects to determine the etiology of pulmonary infiltrate thought to be responsible for the development of ARDS. Ventilation settings and decisions regarding readiness for extubation were left to the discretion of ICU physicians who were blinded to the nutritional prescription. All subjects were started on intermittent enteral feeding through a nasogastric tube. The diet was a high-protein formula, which was prepared in hospital kitchen (Table 1). Daily energy consumption was calculated by multiplying ideal body weight in 25 kcal. A complete analysis of diet is outlined in Table 1. At 4-hour intervals, aspiration of feeding tube was carried out to measure the residual volume. In those with continued feed intolerance with gastric residual volume greater than 150 mL, erythromycin was given. Study group received 120 mg of ginger extract, and control group, 1 g of coconut oil as placebo (Yasdarou, Iran). These supplements were added to diet during tube feeding in 3 divided doses per day. Treatment was continued in all patients until the end period of 21 days of trial, death, or discharge from ICU. The nurse was unblinded to the treatment assignment and preparation, whereas the patients, investigators, and all clinical personnel remained blinded to the randomization.

Participants were evaluated for occurrence of organ failure or death in 21 days of study.

Table 1 Macronutrient composition of the formula

Nutrient	% of total calorie	g/L
Protein	21	53.08
Carbohydrate	43	109.2
Fiber	0	2.17
Total lipids	36	40.62
Saturated	5	6.40
Monounsaturated (oleic)	15	17.48
Polyunsaturated	12	13.94
Linoleic acid	11.5	13.36
Linolenic acid	0.5	0.3
Ecosapentanoic acid	0	0
Decosahexanoic acid	0	0
Cholesterol	0	0.084
Unknown fat	4	3

2.1. Laboratory data

Serum samples were obtained on study days 0 (before initial study supplement diet), 5 and 10 for the measurement of leukotriene B4 (LTB4), IL-1, IL-6, and TNF-α. Sera were frozen at −70°C and were analyzed in duplicate by enzyme-linked immunoassay (ELISA) in dilutions that allowed interpolation from simultaneously run standard curves.