Am J Transl Res 2021;13(9):10793-10800
www.ajtr.org /ISSN:1943-8141/AJTR0131690

Original Article

Effect of standardized enteral nutrition on AECOPD patients with respiratory failure

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Received February 9, 2021; Accepted June 16, 2021; Epub September 15, 2021; Published September 30, 2021

Abstract: Objective: To investigate the effects of standardized enteral nutrition (EN) on nutritional indicators and immunological functioning of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) patients with respiratory failure. Methods: We selected 92 cases of AECOPD patients with respiratory failure as the research objects, and classified them into two groups (control/observation group, n=46 respectively) according to random number table. Both groups were given conventional anti-infection and symptomatic treatment. In addition, the control group received diet support therapy, and the observation group was given standard EN treatment. Afterwards, the changes of nutritional indicators, immunological functioning, inflammatory indicators and cardiopulmonary function of the two groups before and after therapy were compared. Results: Hemoglobin (HB), serum albumin (ALB), and total protein (TP) of the two groups after treatment were critically higher than those before treatment, and the indicators in observation group in post-treatment were remarkably higher than those in control group ($P<0.05$); lymphocyte count (TLC), immunoglobulin A (IgA) and immunoglobulin G (IgG) of the two groups tremendously increased in post-treatment than before receiving treatment, and the post-treatment indicators of observation group were obviously higher than those of control group ($P<0.05$); high sensitivity C-reactive protein (hs-CRP) and procalcitonin (PCT) in two groups sharply decreased after treatment comparing to which before treatment, and the observation group had notably lower post-treatment indexes than that of the control group ($P<0.05$); Ejection minutes (LVEF), NT proBNP, partial pressure of carbon dioxide ($PaCO_2$), partial pressure of blood oxygen (PaO_2) and pH of the two groups had remarkably improved after treatment, and the improvement effect in observation group was superior to that in control group ($P<0.05$). Conclusion: The standard EN can substantially improve the nutritional status and immunological functioning of AECOPD patients with respiratory failure, reduce the inflammatory indicators, and promote their cardiopulmonary function.

Keywords: Standardized enteral nutrition, acute exacerbation of chronic obstructive pulmonary disease (AECOPD), respiratory failure, nutritional indicators, immunological functioning

Introduction

Chronic obstructive pulmonary disease (COPD) is a clinically common type of emphysema and (or) chronic bronchitis induced by restriction of airflow. COPD is irreversible and progressive, and can further progress into respiratory failure and pulmonary heart disease [1, 2]. COPD is a disease with high morbidity and mortality, and poses serious threat to the lives of patients. According to epidemiological studies, the prevalence rate among people over 40 years old has risen rapidly from 1% in the past to around 10% at present. Although the medical standards have been improved in recent years, and great progresses have been made in the treatment of COPD symptoms and prevention of acute exacerbation, there were few effective breakthroughs in reducing COPD mortality and improving its outcomes. According to statistics, over 3 million sufferers worldwide die of COPD each year [3, 4]. COPD is currently the fourth leading cause of death in the world and is expected to rise to the third by 2030 [5]. Non-invasive positive pressure ventilation is non-invasive artificial assisted ventilation, which has been clinically confirmed in treating COPD respiratory failure [6]. Patients with COPD tend to have longer stays in ICU and higher energy expenditure. 2018 European Critical Nutrition Guidelines explicitly stated that patients hospitalized in ICU for over 48 h are at risk of malnutrition, and that risk is even higher in those with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) [7]. Evidence has shown that malnutrition is an independent risk factor that affects the survival of AECOPD patients, and imposes a crucial impact on the clinical prognosis [8, 9]. Based on the above-mentioned factors, this study is targeting the exploration of the standard EN on nutritional indicators and immunological functioning in AECOPD patients with respiratory failure.

Case and methods

General data

92 cases of AECOPD patients with respiratory failure admitted to our hospital from November 2019 to November 2020 were enrolled as the research objects, and classified into two groups (observation/observation group, n=46 respectively) according to random number. The ethics committee of our hospital approved the conduction of study.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients included had met the diagnostic criteria for AECOPD in *Chinese Expert Consensus on the Diagnosis and Treatment of Acute Aggravation of Chronic Obstructive Pulmonary Disease (AECOPD)* [10], and were diagnosed with respiratory failure by arterial blood gas analysis; (2) Aged ≥10, yd; (3) The Nutritional Risk score (NRS) tritional I with reall patients and family members were aware of the study and signed the informed consent.

Exclusion criteria: (1) Patients with worsening condition, no spontaneous breathing or weak breathing, or those should undergo invasive ventilation with tracheal intubation immediately; (2) Those with insufficiency of important organs such as heart, liver, kidneys, lungs, etc.; (3) Patients with gastrointestinal failure or malignant tumor of digestive tract; (4) Patients accompanied by gastrointestinal bleeding, intestinal perforation, intestinal obstruction, or short bowel syndrome that not suitable for enteral nutrition support; (5) Patients with severe abdominal infection; (6) Patients in shock or deep coma that unable for treatment; or (7) Patients that allergic to mask material.

Methods

Both groups of patients received conventional treatments such as anti-infection, phlegm-resolving drugs, bronchial antispasmodics, cardiotonic drugs and non-invasive positive pressure respiratory therapy in line with their disease conditions. The respiratory therapy was conducted by Dorma200 non-invasive positive pressure ventilator made by Philips of the Netherlands. The ventilator was set to S/T mode, the initial inspiratory pressure was 8 cm H_2O, and the increase rate was 2 cm H_2O/time; gradually increase to 10-20 cm H_2O according to the condition and tolerance of patients. Positive end-expiratory pressure was set at 2-6 cm H_2O, blood oxygen saturation was maintained at 90%-95%, oxygen concentration was 25%-60%, and respiration rate was 16 times/min. The daily ventilation time of patient depends on the severity of the disease, which was generally set as 2-4 h/time, 4-6 times/day, until the index of patient's blood gas analysis return to normal degree.

The control-group-patients took regular diet support treatment, and were instructed to ingest foods rich in high protein and fiber. The patients were treated for 2 weeks with standardized EN therapy as follows: (1) A standardized EN support nursing group was established, which composed of one clinician, one pharmacist, one nutritionist, one head nurse and two nurses. The head nurse, acting as the team leader, formulated the nutrition plan after discussion with team members, and standardized the procedure of EN support. (2) Calculation and distribution of calories. Referred to Harris-Benedict formula, the nursing group determined the daily basal energy consumption of AECOPD patients with respiratory failure, and multiplied by the correction coefficient of 1.5 to calculate the patient's basal energy supply value. According to the energy

Table 1. Comparison of general data between two groups of patients

Items	Control group (n=46)	Observation group (n=46)	X^2/t	*P*
Gender (M/F, cases)	29/17	27/19	0.1825	0.6692
Age ($\bar{x}$ ± s, yd)	67.46±5.21	68.55±5.39	0.9862	0.3267
Course of disease ($\bar{x}$ ± s, years)	12.27±1.53	12.87±1.46	1.9242	0.0575
Smoking experience (yes/no, cases)	39/7	36/10	0.6494	0.4203
APACHE II score ($\bar{x}$ ± s, points)	18.84±1.66	18.75±1.84	0.2463	0.8060
Heart rate (times/min)	98.67±8.12	97.84±8.75	0.4716	0.6384
Respiratory rate (times/min)	24.55±3.34	25.35±3.28	1.1591	0.2495

supply value contained in each bag of nutrient solution, the amount of nutrient solution pumped for daily EN was determined accordingly. (3) EN support. Amoxapride tablets (Chinese National Medicine Standard H1999-0313, Chengdu Kanghong Pharmaceutical Group Co., Ltd.) and metoclopramide tablets (H61020854, Xi'an Fenghua Pharmaceutical Co., Ltd.) were used for tube feeding; If the patient had diarrhea, the nutritional formula was changed after eliminating the cause, and the treatment was carried out for 2 weeks.

Observation of indexes

(1) Changes of nutritional indexes such as hemoglobin (HB), serum albumin (ALB) and serum total protein (TP) in two groups in pre- and post-treatment were compared; (2) Changes in total lymphocyte count (TLC), immunoglobulin A (IgA) and immunoglobulin G (IgG) of the two groups before and after treatment were compared; (3) Changes of inflammatory indexes such as high sensitivity C-reactive protein (hs-CRP) and procalcitonin (PCT) were compared between the two groups before and after treatment; (4) Changes in cardiopulmonary function before and after treatment were compared between the two groups. Ejection minutes (LVEF) were measured by cardiac color Doppler ultrasonography and plasma NT-proBNP was measured by immunoassay; The partial pressure of carbon dioxide ($PaCO_2$), partial pressure of blood oxygen (PaO_2) and pH were detected by blood gas biochemical analyzer.

Statistical analysis

Statistical analysis and processing are conducted with SPSS19.0. The measurement data are expressed by ($\bar{x}$ ± s), the comparison between groups is by *t*-test; the enumeration data are expressed as percentage and the results are tested by χ^2. *P<0.05* is indicating that the difference is statistically significant. The graphic software was Graphpad prism9.

Results

Clinical information

The difference between the comparison of general information in two groups was not statistically significant (*P>0.05*) and comparable, as shown in **Table 1**.

Comparison of nutritional indicators of the two groups in prior-treatment

The comparison of the degree of HB, ALB and TP in pre-treatment between the two groups was not statistically significant (*P>0.05*). HB, ALB, and TP of the two groups of patients after treatment were critically higher than those before treatment, and the observation group had remarkably higher post-treatment indicators than control group (*P<0.05*) (**Table 2** and **Figure 1**).

Comparison of indexes changes in immunological functioning between the two groups before and after treatment

There was no significant difference in the degree of TLC, IgA, and IgG between the two groups of patients before treatment (*P>0.05*). TLC, IgA, and IgG of the two groups tremendously increased in post-treatment than before receiving treatment, and the post-treatment indicators of observation group were obviously higher than those of control group (*P<0.05*) (**Table 3**).

Table 2. Comparison of nutritional indicators in two groups of patients before and after treatment ($\overline{x}$ ± s, g/L)

Group	HB		ALB		TP	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=46)	86.72±6.49	103.22±7.12*	26.18±2.54	32.37±2.77*	40.45±2.36	49.97±2.48*
Observation group (n=46)	87.14±6.34	114.67±6.91*	26.47±2.73	38.43±2.82*	40.17±2.65	59.52±3.13*
t	0.3140	7.8270	0.5275	1.3977	0.5352	16.2195
P	0.7543	<0.0001	0.5992	<0.0001	0.5939	<0.0001

Note: Compared with prior-treatment, *$P<0.05$.

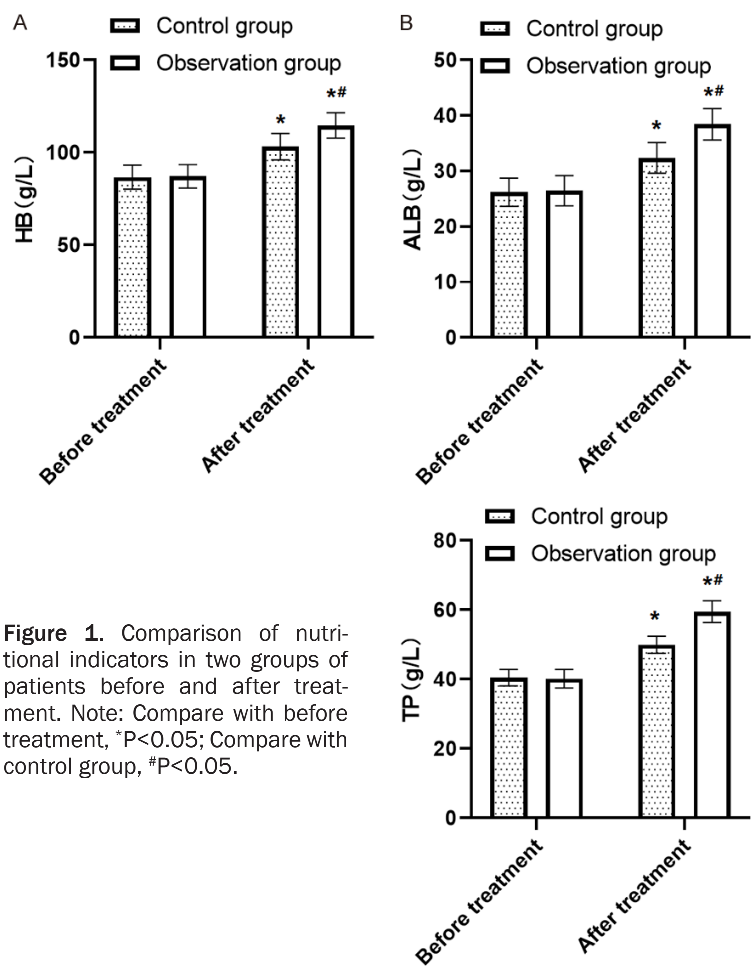

Figure 1. Comparison of nutritional indicators in two groups of patients before and after treatment. Note: Compare with before treatment, *P<0.05; Compare with control group, #P<0.05.

bly lower than control group ($P<0.05$) (**Table 4**).

Comparison of changes in cardiopulmonary function between the two groups before and after treatment

There was no statistical significance in the levels of LVEF, NT-proBNP, $PaCO_2$, PaO_2 and pH between 2 groups before treatment (P>0.05). LVEF, NT proBNP, $PaCO_2$, PaO_2 and pH of the two groups had remarkably improved after treatment, and the improving effect in observation group was superior to that in control group ($P<0.05$) (**Tables 5** and **6**).

Discussion

Chronic obstructive pulmonary disease (COPD) is a chronic and consumptive disease that is often accompanied by recurrent attacks. As suffered from respiratory disorders, COPD patients often have severely imbalanced ratio of lung ventilation and blood flow, which result into severe hypoxia and carbon dioxide retention. Such long-term hypoxia condition in turn increases the burden of respiratory function and forms a pernicious circle [11]. COPD is often accompanied by malnutrition, especially in those with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), with prevalence of malnutrition as high as 50% [12]. The causes of AECOPD with malnutrition is likely to be related with the following factors:

Comparison of changes in inflammatory indicators before and after treatment between the two groups

There was no significant difference in hs-CRP and PCT between the two groups before treatment (P>0.05). hs-CRP and PCT in two groups sharply decreased after treatment comparing to which before treatment, and the post-treatment indexes in observation group were nota-

Table 3. Comparison of indexes changes in immunological functioning before and after treatment in two groups of patients ($\overline{x} \pm s$)

Group	TLC (unit/ml)		IgA (g/L)		IgG (g/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=46)	1318.41±255.64	1543.83±273.47*	1.79±0.58	2.19±1.07*	10.37±2.45	12.75±1.64*
Observation group (n=46)	1305.16±267.47	1837.23±289.31*	1.74±0.63	2.66±1.15*	10.41±2.52	14.66±1.25*
t	0.2429	4.9985	0.3960	2.0294	0.0772	6.2822
P	0.8086	<0.0001	0.6930	0.0454	0.9386	<0.0001

Note: Compared with prior-treatment, *$P<0.05$.

Table 4. Comparison of the changes in levels of inflammatory factors between the two groups before and after treatment ($\overline{x} \pm s$)

Group	hs-CRP (mg/L)		PCT (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment
Control group (n=46)	45.29±6.34	33.83±2.65*	1.92±0.34	1.17±0.15*
Observation group (n=46)	46.87±5.93	21.17±2.48*	1.95±0.29	0.61±0.14*
t	1.2344	23.6577	0.4553	18.5108
P	0.2203	<0.0001	0.6500	<0.0001

Note: Compared with before treatment, *$P<0.05$.

Table 5. Comparison of changes in cardiopulmonary function of the two groups before and after treatment ($\overline{x} \pm s$)

Group	LVEF (%)		NT-proBNP (pg/L)	
	Before treatment	After treatment	Before treatment	After treatment
Control group (n=46)	39.41±4.24	44.67±5.35*	1114.82±257.18	556.72±131.45*
Observation group (n=46)	38.37±3.96	49.82±5.14*	1137.44±243.52	423.94±108.13*
t	1.2158	4.7080	0.4332	5.2921
P	0.2272	<0.0001	0.6659	<0.0001

Note: Compared with pre-treatment, *$P<0.05$.

Table 6. Comparison of changes in cardiopulmonary function between the two groups before and after treatment ($\overline{x} \pm s$)

Group	$PaCO_2$ (mmHg)		PaO_2 (mmHg)		pH	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=46)	58.46±5.23	45.84±6.18*	60.50±3.13	72.76±4.15*	5.71±1.23	7.15±0.56*
Observation group (n=46)	58.75±5.49	36.75±7.52*	61.74±3.47	88.65±5.12*	5.66±1.35	7.38±0.22*
t	0.2594	6.3339	1.7997	16.3521	0.1857	2.6233
P	0.7959	<0.0001	0.0753	<0.0001	0.8531	0.0102

Note: Compared with pre-treatment, *$P<0.05$.

The patient's airway has been in a long-term state of obstruction, which causes the decrease in elastic retraction force of alveoli, thus increasing the breathing work and breathing energy consumption; The long-term hypoxemia and hypercapnia further damage the gastric mucosa of patient, causing imbalance of gastrointestinal flora, disorder of digestion and absorption, and ineffective digestion, absorption and oxidation of nutrients; The long-term disease sufferings lead to the decrease of appetite and the intake of nutrients; The increase in breathing work and respiratory energy consumption increases the resting energy consumption of patients and keep them in a long-term state of high metabolism; The above reasons have led to a sharp increase in the malnutrition of patients [13-15]. Nutritional status of patients is crucial to improve the disease prognosis, and it is also an independent risk factor of death in patients with COPD [16, 17]. When patients are undernourished, the quantity of elastic fibers in lung tissues and active substances on the surface of alveoli will be substantially reduced. This will lead to a disease in compliance of lung, a decrease in reversibility of lung cells, drop in quantity of alveoli, and decrease in lung diffusion capacity, which eventually aggravates emphysema [18]; In patients with malnutrition, muscle proteins and contractile proteins in their body will be excessively decomposed, which lead to atrophy of respiratory muscle and auxiliary respiratory muscle, and eventually induce the respiratory muscle fatigue [19]. AECOPD with malnutrition will also damage the immunological functioning of patients, affecting their defense and repair ability of respiratory system and reducing their body ability of anti-infections, thereby affecting the prognosis.

Studies have confirmed that nutritional support can remarkably improve muscle strength and exercise tolerance in AECOPD patients, and is a variable risk factor in chronic disease progression [20]. Studies have revealed that providing AECOPD patients with a balanced diet and adequate fruits and vegetables can not only bring potential benefits of their lungs, but can also remarkably reduce the risk of cardiovascular disease and metabolic disease [21]. AECOPD patients with respiratory failure have severe malnutrition due to various reasons, and standard EN support is of particularly importance. In this study, HB, ALB, and TP of the two groups of patients after treatment were critically higher than those before treatment, and the indicators in observation group in post-treatment were remarkably higher than those in control group ($P<0.05$). It indicated that standard EN support can improve the nutritional status of AECOPD patients with respiratory failure. Related studies have pointed out that early EN support for AECOPD patients with respiratory failure can enhance their immune function and reduce inflammatory response [22, 23], which is consistent with the results of this study. According to the research outcomes, TLC, IgA, and IgG of the two groups tremendously increased in post-treatment than before receiving treatment, and the post-treatment indicators of observation group were obviously higher than those of control group ($P<0.05$); hs-CRP and PCT in two groups sharply decreased after treatment comparing to which before treatment, and the post-treatment indexes in observation group were notably lower than control group ($P<0.05$). As malnourished patients are often accompanied by disorders of myocardial energy metabolism, their respiratory muscle work will be further reduced. If sufficient energy cannot be provided by the body, cardiopulmonary diseases will be induced [24, 25]. This study results proclaimed that LVEF, NT proBNP, $PaCO_2$, PaO_2 and pH of the two groups had remarkably improved after treatment, and the improvement effect in observation group was superior to that in control group ($P<0.05$). This indicated that standardized EN support can ameliorate the cardiopulmonary function of AECOPD patients with respiratory failure.

To sum up, the standardized EN support can substantially improve the nutritional status and immunological functioning of AECOPD patients with respiratory failure, reduce their inflammatory indicators, and promote the cardiopulmonary function.

Disclosure of conflict of interest

None.

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References

[1] Zwakman M, Weldam SWM, Vervoort SCJM, Lammers JJ and Schuurmans MJ. Patients' perspectives on the COPD-GRIP intervention, a new nursing care intervention for COPD. BMC Fam Pract 2019; 20: 78.

[2] Cheng Q, Fang L, Feng D, Tang S, Yue S, Huang Y, Han J, Lan J, Liu W, Gao L and Luo Z. Memantine ameliorates pulmonary inflammation in a mice model of COPD induced by cigarette smoke combined with LPS. Biomed Pharmacother 2019; 109: 2005-2013.

[3] Murphy LA, Harrington P, Taylor SJ, Teljeur C, Smith SM, Pinnock H and Ryan M. Clinical-effectiveness of self-management interventions in chronic obstructive pulmonary disease: an overview of reviews. Chron Respir Dis 2017; 14: 276-288.

[4] Wuytack F, Devane D, Stovold E, McDonnell M, Casey M, McDonnell TJ, Gillespie P, Raymakers A, Lacasse Y and McCarthy B. Comparison of outpatient and home-based exercise training programmes for COPD: a systematic review and meta-analysis. Respirology 2018; 23: 272-283.

[5] Steindal SA, Torheim H, Oksholm T, Christensen VL, Lee K, Lerdal A, Markussen HØ, Gran G, Leine M and Borge CR. Effectiveness of nursing interventions for breathlessness in people with chronic obstructive pulmonary disease: a systematic review and meta-analysis. J Adv Nurs 2019; 75: 927-945.

[6] Ridwan ES, Hadi H, Wu YL and Tsai PS. Effects of transitional care on hospital readmission and mortality rate in subjects with COPD: a systematic review and meta-analysis. Respir Care 2019; 64: 1146-1156.

[7] Long H, Howells K, Peters S and Blakemore A. Does health coaching improve health-related quality of life and reduce hospital admissions in people with chronic obstructive pulmonary disease? A systematic review and meta-analysis. Br J Health Psychol 2019; 24: 515-546.

[8] Pleasants RA, Radlowski PA and Davidson HE. Optimizing drug therapies in patients with COPD in the US nursing home setting. Drugs Aging 2019; 36: 733-745.

[9] Early F, Wellwood I, Kuhn I, Deaton C and Fuld J. Interventions to increase referral and uptake to pulmonary rehabilitation in people with COPD: a systematic review. Int J Chron Obstruct Pulmon Dis 2018; 13: 3571-3586.

[10] Lv L, Zheng J, Zhang Y, Chen B, Yan F, Qin X, Zheng C, Wu Z and Feng K. Respiratory nursing care with Angong Niuhuang pill for patients with chronic obstructive pulmonary disease following cardiac surgery. Jpn J Nurs Sci 2021; 18: e12344.

[11] Storgaard LH, Hockey HU, Laursen BS and Weinreich UM. Long-term effects of oxygen-enriched high-flow nasal cannula treatment in COPD patients with chronic hypoxemic respiratory failure. Int J Chron Obstruct Pulmon Dis 2018; 13: 1195-1205.

[12] Hong Y and Lee SH. Effectiveness of tele-monitoring by patient severity and intervention type in chronic obstructive pulmonary disease patients: a systematic review and meta-analysis. Int J Nurs Stud 2019; 92: 1-15.

[13] Paneroni M, Simonelli C, Vitacca M and Ambrosino N. Aerobic exercise training in very severe chronic obstructive pulmonary disease: a systematic review and meta-analysis. Am J Phys Med Rehabil 2017; 96: 541-548.

[14] Martinez FJ, Mannino D, Leidy NK, Malley KG, Bacci ED, Barr RG, Bowler RP, Han MK, Houfek JF, Make B, Meldrum CA, Rennard S, Thomashow B, Walsh J and Yawn BP; High-Risk-COPD Screening Study Group*. A new approach for identifying patients with undiagnosed chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2017; 195: 748-756.

[15] He B, Zhang W, Qiao J, Peng Z and Chai X. Melatonin protects against COPD by attenuating apoptosis and endoplasmic reticulum stress via upregulating SIRT1 expression in rats. Can J Physiol Pharmacol 2019; 97: 386-391.

[16] Lloyd C and Garside J. Care bundles in the management of a COPD exacerbation. Br J Nurs 2018; 27: 47-50.

[17] Dumas O, Varraso R, Boggs KM, Quinot C, Zock JP, Henneberger PK, Speizer FE, Le Moual N and Camargo CA Jr. Association of occupational exposure to disinfectants with incidence of chronic obstructive pulmonary disease among US female nurses. JAMA Netw Open 2019; 2: e1913563.

[18] Li XX, Du XW, Song W, Lu C and Hao WN. Effect of continuous nursing care based on the IKAP theory on the quality of life of patients with chronic obstructive pulmonary disease: a randomized controlled study. Medicine (Baltimore) 2020; 99: e19543.

[19] Houben CHM, Spruit MA, Luyten H, Pennings HJ, van den Boogaart VEM, Creemers JPHM, Wesseling G, Wouters EFM and Janssen DJA. Cluster-randomised trial of a nurse-led advance care planning session in patients with COPD and their loved ones. Thorax 2019; 74: 328-336.

[20] Long R, Stracy C and Oliver MC. Nutritional care in chronic obstructive pulmonary disease. Br J Community Nurs 2018; 23: S18-S26.

[21] McCabe C, McCann M and Brady AM. Computer and mobile technology interventions for self-management in chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2017; 5: CD011425.

[22] Thom DH, Willard-Grace R, Tsao S, Hessler D, Huang B, DeVore D, Chirinos C, Wolf J, Donesky D, Garvey C and Su G. Randomized controlled trial of health coaching for vulnerable patients with chronic obstructive pulmonary disease. Ann Am Thorac Soc 2018; 15: 1159-1168.

[23] Peng Z, Zhang W, Qiao J and He B. Melatonin attenuates airway inflammation via SIRT1 dependent inhibition of NLRP3 inflammasome and IL-1beta in rats with COPD. Int Immunopharmacol 2018; 62: 23-28.
[24] Yohannes AM, Kaplan A and Hanania NA. COPD in primary care: key considerations for optimized management: anxiety and depression in chronic obstructive pulmonary disease: recognition and management. J Fam Pract 2018; 67 Suppl: S11-S18.
[25] Sun J, Li Y, Ling B, Zhu Q, Hu Y, Tan D, Geng P and Xu J. High flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: an observational cohort study. Int J Chron Obstruct Pulmon Dis 2019; 14: 1229-1237.