JBUON 2020; 25(2): 681-687
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

ORIGINAL ARTICLE

Efficacy of albumin-bound paclitaxel in the treatment of advanced refractory breast cancer and its effect on serum resistin

Xiaoting Han[1], Ziliang Wang[2]

[1]Department of Breast Surgery, Weihai Central Hospital, Weihai 264400, P.R. China. [2]Department of Thyroid Breast Surgery, Weihai Municipal Hospital, Weihai 264200, P.R. China.

Summary

Purpose: *This study aimed to investigate the efficacy of albumin-bound paclitaxel (nab-paclitaxel) in the treatment of advanced refractory breast cancer (BC) and its effect on serum resistin.*

Methods: *A retrospective study was performed based on the clinical records of 95 patients with advanced refractory BC admitted to Weihai Central Hospital from March 2012 to May 2015. Thirty-four patients were treated with traditional paclitaxel and enrolled in the control group, while the other 61 patients were treated with nab-paclitaxel and enrolled in the study group. The efficacy, toxicity and side effects, quality of life, and serum resistin levels were compared between the two groups.*

Results: *The total response rate (RR) of the study group was much higher than that of the control group ($p<0.05$). The leukopenia level of the study group during the treatment was significantly lower than that of the control group ($p<0.05$). The level of serum resistin in the study group after treatment was significantly lower than in the control group ($p<0.05$). The improvement rate of quality of life in the study group was significantly higher than in the control group ($p<0.05$).*

Conclusion: *The results indicated that nab-paclitaxel is very effective in treating advanced refractory BC and reduces the level of serum resistin. It can improve the quality of life of patients and is worthy of clinical promotion.*

Key words: *advanced refractory breast cancer, nab-paclitaxel, paclitaxel, quality of life, resistin*

Introduction

Breast cancer (BC) is a malignant tumor that occurs in the epithelial tissues of the breast [1]. It has increasingly high morbidity and tends to occure the younger populations. One in every 8 women in the United States will suffer from BC during her life [2]. At present, various treatment methods are used according to the grade of severity of BC and the patient's physical condition, including surgery, chemotherapy, radiotherapy, etc. [3]. Paclitaxel (PTX) is a commonly used chemotherapy drug which is effective for early BC but not for treating advanced BC, not to mention its easily occurring toxicity and side effects such as chest tightness, lower blood pressure, and bronchospasm. Because of its poor water solubility, it is usually combined with cosolvents such as anhydrous ethanol and polyoxyethylene castor oil. Such cosolvents may cause allergic reactions, aggravate neurotoxicity and other adverse reactions, and impact the efficacy of PTX by limiting the intensity and dosage of the drug [4,5]. Therefore, the search for effective drugs in treating advanced BC is of great significance.

Albumin-bound paclitaxel (nab-paclitaxel) is a novel formulation of PTX with human albumin as a drug carrier and stabilizer [6]. The albumin in nab-paclitaxel works as a natural carrier of hydrophobic

Corresponding author: Dr. Ziliang Wang, MM. Department of Thyroid Breast Surgery, Weihai Municipal Hospital, No.70 Heping Rd, Weihai 264200, P.R. China.
Tel: +86 130 6111 9189, Email: wccg99@163.com
Received: 23/08/2019; Accepted: 17/09/2019

molecules in the human body. It contributes to the more massive and faster distribution of paclitaxel in tumor cells and has a higher affinity with tissue and a better prevention against angiogenesis. Albumin, as a delivery carrier for hydrophobic drugs, is satisfying since it prevents nab-paclitaxel from adverse reactions such as allergy caused by the complex solubilizer required by traditional PTX [7]. No pretreatment is required before the application of nab-paclitaxel. The intravenous injection of traditional PTX costs several hours, while the injection time of nab-paclitaxel is as short as 30 min. Besides, nab-paclitaxel is suitable for a higher dosage, free of the dose limitation of traditional PTX [8]. Theoretically, nab-paclitaxel is superior to traditional PTX formulations, but its application in BC patients is still rare due to its high price and a short time to market. This study was designed to compare the efficacy and prognosis between traditional PTX and nab-paclitaxel in detail.

Resistin, an adipocyte-derived cytokine, is frequently studied in cancers related to inflammation and obesity [9]. The study made by Han et al showed a close relationship between serum resistin and the occurrence and development of BC [10]. Yuan et al [11] revealed in their study that serum resistin level is positively correlated with tumor stage, tumor size and lymph node metastasis in BC patients, and that they can induce epithelial-mesenchymal transition (EMT) and increase the specificity of stem cells by activating TLR4/STAT3 signaling in BC, thereby promoting the development of BC. A study [12] has shown that resistin is highly expressed in the serum of patients with BC, and it is associated with clinicopathologic factors such as TNM staging, tumor size, lymph node invasion, histological grade, etc. They also pointed out that resistin may have potential value in diagnosing BC. These studies suggest that serum resistin may be a biomarker for BC diagnosis.

This study will compare the efficacy and prognosis between nab-paclitaxel and traditional PTX and analyze the changes of serum resistin levels in BC patients after two different PTX treatments, providing more useful information for the clinical diagnosis and treatment of BC.

Methods

Inclusion and exclusion criteria

Inclusion criteria: patients diagnosed with advanced refractory BC by pathology, cytology or imaging [13]; patients aged 20-70 years; patients with complete clinical records; patients with ECOG scores ranging from 0 to 2 points; patients with an expected survival time of more than 3 months; patients whose important organ functions were basically normal; patients with normal routine blood test results before chemotherapy; patients with no chemotherapy contraindications.

Exclusion criteria: Contradictions to drugs used in this study; history of PTX; patients with hematopoietic dysfunction; patients with severe mental illness; patients with poor treatment compliance.

General information

Ninety-five patients with advanced refractory BC admitted to Weihai Central Hospital from March 2012 to May 2015 were the research subjects. Thirty-four patients were treated with traditional PTX and enrolled in the control group, while the other 61 patients were treated with nab-paclitaxel and enrolled in the study group. The patients in the control group were 22-64 years old (mean 41.25±3.45). The control group was comprised of 3 cases of lobular carcinoma, 3 cases of medullary carcinoma, 2 cases of adenocarcinoma, and 26 cases of invasive ductal carcinoma. According to the postoperative histopathological receptor expression [14], 26 patients were classified as endocrine therapy-sensitive Luminal type (ER and/or PR positive, HER-2 negative), 4 patients were epidermal growth factor receptor 2 positive and 4 had triple-negative type (ER, PR, and HER-2 negative). According to the chemotherapy situation, 12 patients were during the first-line chemotherapy, 22 patients were during second-line chemotherapy or more advanced chemotherapy. Patients in the control group were 22-64 years old (mean 41.25±3.67). The control group was comprised of 5 cases of lobular carcinoma, 8 cases of medullary carcinoma, 4 cases of adenocarcinoma, and 44 cases of invasive ductal carcinoma. According to the postoperative histopathological receptor expression [14], 43 patients were classified as endocrine therapy sensitive Luminal type (ER and/or PR positive, HER-2 negative), 8 patients were epidermal growth factor receptor 2 positive and 10 were with triple-negative type (ER, PR, and HER-2 negative). According to the chemotherapy situation, 19 patients were during the first-line chemotherapy, 42 patients were during second-line chemotherapy or more advanced chemotherapy. All the research subjects and their families signed the informed consent form after having a knowledge of this study which was approved by the ethics committee of the hospital.

Treatment methods

Patients in the study group were treated with only nab-paclitaxel (Baiaolaibo, China, item number: KFS279) at a dose of 260 mg/m^2 through 30 min intravenous infusion, once every 3 weeks. No anti-allergic treatment was used before the administration, but a 5-HT3 receptor antagonist (Shanghai Yiji, China, article number: BN65497964) was administered to prevent gastrointestinal adverse reactions caused by chemotherapy drugs.

The control group was given traditional PTX injection (Aladdin, China, item number: P106869). To avoid serious allergy, preventive medication was given before treatment. Patients were required to take oral administration of 10 ml of dexamethasone acetate (SELLECK, USA, item number: S312450mgc) 6 h and 12 h before the injection of PTX. Then, an intramuscular injection of 25

ml of promethazine (TargetMol, USA, Cat. No. 60-87-7) was administered 30 min before the injection of PTX. Last, an intravenous injection of 300 ml of cimetidine (LGC, UK, item number: MM0020.00) was given before the injection of PTX. After the preventive medication, PTX was intravenously injected at a dose of 175 mg/m^2 for more than 3 h, once every 3 weeks. The treatment for both groups lasted for 6 months.

Evaluation of efficacy

Efficacy evaluation was in accordance with the World Health Organization's evaluation criteria for clinical treatment efficacy of BC [15], which divides the efficacy into four levels: complete response (CR) which means complete disappearance of tumor lesions, partial response (PR) which means a reduction more than 50% in tumor lesion volume, stable disease (SD) which means a reduction less than 50% in tumor lesion volume, and progressive disease (PD) which means an increase more than 25% in tumor lesion volume or appearance of new lesion(s). Total response rate (RR) = (CR case number + PR case number) / total case number × 100. Adverse reactions during the treatment period of the control group and the study group were followed and registered. The main adverse reactions included neutropenia, thrombocytopenia, soreness in muscle and joint, numbness at the ends of the hands and feet, nausea and vomiting, fatigue, increased ALT/AST levels, etc.

The quality of life of patients after treatment was assessed according to the Karnofsky (KPS) score [16]. After treatment, an increase of over 10 points in KPS score was considered as an improvement in quality of life, an increase or decrease of no more than 10 points in KPS score was considered as stability of quality of life, a decrease of more than 10 points in KPS score was considered as deterioration of quality of life. Improvement rate of quality of life = improvement case number + stability case number / total case number × 100.

Table 1. Baseline data of the study group and control group

Group	*Control group (n=34)* *n (%)*	*Study group (n=61)* *n (%)*	x^2/F	*p*
Age, years			0.085	0.771
< 42	14 (41.18)	27 (44.26)		
≥ 42	20 (58.82)	34 (55.74)		
Smoking			0.031	0.860
Yes	10 (29.41)	19 (31.15)		
No	24 (0.59)	42 (68.85)		
Exercise habits			0.061	0.804
Yes	22 (64.71)	41 (67.21)		
No	12 (35.29)	20 (32.79)		
Place of residence			1.814	0.178
Urban area	18 (52.94)	39 (63.93)		
Rural area	16 (47.06)	22 (36.07)		
Nationality	0.111	0.739		
Han nationality	24 (70.59)	45 (73.77)		
Minority nationality	10 (29.41)	16 (26.23)		
Educational level			0.028	0.867
< high school	15 (44.12)	28 (45.90)		
≥ high school	19 (55.88)	33 (54.10)		
Weight, kg			0.011	0.915
< 50	13 (38.24)	24 (39.34)		
≥ 50	21 (61.76)	37 (60.66)		
Marital status			2.330	0.312
Married	27 (79.41)	45 (73.77)		
Unmarried	7 (20.59)	12 (19.67)		
Widowed	0	4 (6.56)		
Dietary preference			0.272	0.602
Light diet	17 (50.00)	33 (54.10)		
Spicy diet	18 (50.00)	28 (45.90)		
Alcohol abuse			0.041	0.840
Yes	9 (26.47)	15 (24.59)		
No	25 (73.53)	46 (75.41)		

Serum resistin detection

Before and after treatment, fasting brachial vein blood was taken from the two groups of patients in the morning and placed in 5 ml sterile blood collection tube. The blood was kept stand at room temperature for 30 min and then centrifuged at 4500 r/min for 10 min. The serum was separated and stored in a freezer at 80°C for later use. Afterwards, the serum was placed in a refrigerator at 2-8°C to begin the dissolution, and then got completely dissolved at room temperature.

ELISA was used to detect the expression of resistin in the serum and was carried out in strict accordance with the instructions of the kit.

Statistics

Statistical analyses were performed by SPSS 21.0 software (EASYBIO), and the graphics were drawn using GraphPad Prism 7. The count data of the two groups were expressed by [n(%)] and were compared between the two groups by the chi-square test. The serum resistin levels before and after the treatment were expressed as mean±standard deviation and were compared between groups by the independent t-test. Paired t-test was used for comparison before and after treatment within the group. One-way ANOVA followed by Tukey HSD was used for comparison of measurement data between the two groups. The difference was statistically significant if $p<0.05$.

Results

Baseline data of the study and control group

There was no significant difference between the study group and the control group in baseline data including age, smoking history, exercise habits, place of residence, nationality, education level, weight, marital status, dietary preference, and alcohol abuse ($p>0.05$) (Table 1).

Clinical efficacy in the control and the study group

In the control group, the treatment outcome was CR in 2 patients (5.88%), PR in 5 (14.71%), SD in 15 (44.12%), PD in 12 (35.29%), and the RR of the control group was 20.59%. In the study group, the treatment outcome was CR in 12 patients (19.67%), PR in 24 (39.34%), SD in 15 (24.95%), PD in 10 (16.39%), and the RR of the study group was 59.02%. The RR of the study group was much higher compared with the study group, and the difference was statistically significant ($p<0.05$) (Table 2).

Toxicity and side effects in the control and the study group

Toxicity and side effects were observed in both groups, but allergies were not. In the control group, 12 patients developed thrombocytopenia (35.29%), 26 leukopenia (76.47%), 14 soreness in muscles and joints (41.18%), 25 numbness at the ends of the hands and feet (73.53%), 16 nausea and vomiting (47.06%), 17 fatigue (50.00%) and 8 increased ALT/AST levels (23.53%). In the study group, 20 patients developed thrombocytopenia (32.79%), 22 leukopenia (36.07%), 21 soreness in muscles and joints (39.34%), 42 numbness at

Table 2. Clinical efficacy of the control group and the study group

Group	*Control group (n=34)* *n (%)*	*Study group (n=61)* *n (%)*	x^2	*p*
CR	2 (5.88)	12 (19.67)	-	-
PR	5 (14.71)	24 (39.34)	-	-
SD	15 (44.12)	15 (24.59)	-	-
PD	12 (35.29)	10 (16.39)	-	-
RR	7 (20.59)	36 (59.02)	5.396	0.020

Table 3. Adverse reactions of the control group and the study group

Group	*Control group n=(34)* *n (%)*	*Study group (n=61)* *n (%)*	x^2	*p*
Thrombocytopenia	12 (35.29)	20 (32.79)	0.030	0.862
Leukopenia	26 (76.47)	22 (36.07)	4.422	0.036
Soreness in muscle and joint	14 (41.18)	21 (34.42)	0.428	0.654
Numbness at the ends of the hands and feet	25 (73.53)	42 (68.85)	0.039	0.843
Nausea and vomiting	16 (47.06)	27 (44.26)	0.026	0.872
Fatigue	17 (50.00)	27 (44.26)	0.105	0.746
Increased ALT/AST levels	8 (23.53)	13 (21.31)	0.199	0.842

the ends of the hands and feet (68.85%), 27 nausea and vomiting (44.26%), 27 fatigue (44.26%) and 13 increased ALT/AST levels (21.31%). No statistically significant differences were detected during the treatment between the two groups in the incidence rates of the main adverse reactions, including thrombocytopenia, soreness in muscles and joints, numbness at the ends of the hands and feet, nausea and vomiting, fatigue, increased ALT/AST levels, etc. The leukopenia level in the study group was significantly lower than in the control group during treatment (p<0.05) (Table 3).

Serum resistin levels before and after treatment in the control and the study group

No significant difference in serum resistin levels was detected between the two groups before the treatment (p>0.05). After treatment, serum resistin levels in both groups were significantly lower than before the treatment (p<0.05). The serum resistin levels in the study group were significantly lower than in the control group after treatment (p<0.05) (Figure 1).

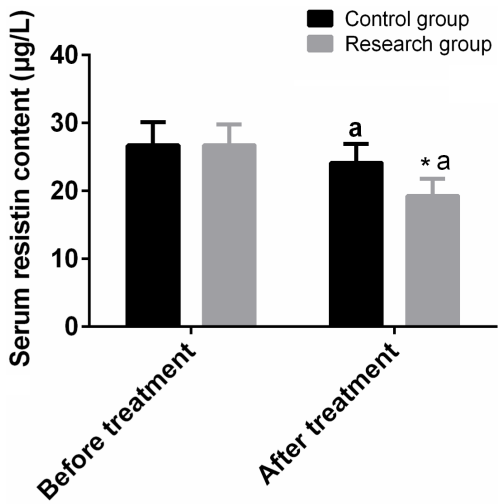

Figure 1. Changes and comparison of resistin level in serum in patients. After treatment, the serum resistin levels of the two groups of patients were significantly decreased, and the level of the study group was lower than that of the control group. *compared with the control group, p<0.05; [a]compared with before treatment in the same group, p<0.05

Quality of life in the control and the study group

Thirty days after discharge, in the control group 5 patients showed improvement in the quality of life (14.71%), 19 stability (55.88%), 10 deterioration (29.41%), and the improvement rate of quality of life was 70.59%. In the study group, 17 patients showed improvement in the quality of life (27.87%), 40 stability (65.57%), 4 deterioration (6.56%), and the improvement rate of quality of life was 93.44%. The improvement rate of quality of life of the study group was significantly higher than that of the control group (p<0.05) (Table 4).

Discussion

More than 1,1 million women worldwide get BC each year, and among them more than 400,000 die of this disease and its complications [17]. At present, an increasing number of patients have drug resistance to PTX due to the widespread use of this drug in BC clinical treatment.

According to Gradishar et al [18] who conducted a randomized controlled phase III clinical trial of 454 patients with advanced BC in 2005, the objective response rates for the nab-paclitaxel group and the conventional PTX group were 37% and 19%, respectively, and the tumor progression time in the nab-paclitaxel group was significantly prolonged from 16.9 weeks to 23 weeks. Based on the results of this study, nab-paclitaxel was approved for the treatment of recurrent or metastatic BC. One previous study pointed out that nab-paclitaxel has an advantage in treatment efficacy compared with traditional PTX [19]. Xie et al [20] analyzed the clinical efficacy of nab-paclitaxel and traditional PTX and found that the RR of the nab-paclitaxel group (53.57%) was significantly higher than the traditional PTX group (25.00%). In this study, the total effective rate of the study group was significantly higher than the control group, which was consistent with the above results, indicating that nab-paclitaxel has better efficacy than traditional PTX in patients with advanced BC.

The toxic and side effects of nab-paclitaxel include thrombocytopenia, fatigue, nausea and vom-

Table 4. Quality of life of the control group and the study group

Group	*n*	*Improvement n (%)*	*Stability n (%)*	*Deterioration n (%)*	*Improvement rate*
Control group	34	5 (14.71)	19 (55.88)	10 (29.41)	70.59
Study group	61	17 (27.87)	40 (65.57)	4 (6.56)	93.44
x^2	-	-	-	-	9.075
p	-	-	-	-	0.003

iting, and soreness in muscles and joints. Xie et al [20] found in their study that the incidence rates of toxic and side effects such as thrombocytopenia, soreness in muscle and joint pain, numbness at the tips of the hands and feet, nausea and vomiting, fatigue, and increased ALT/AST levels between patients treated with nab-paclitaxel and patients treated with traditional PTX were not significantly different. Liu et al [21] reported the same results except that the leukopenia level in the study group was significantly lower than in the control group during the treatment. The results of our study were consistent with the results of the study by Liu et al, suggesting that nab-PTX has better tolerance and lower toxic and side effects than conventional PTX, making the administration of pretreatment needless. No patients in the study group showed allergies.

Resistin is a newly discovered adipokine. It is a cysteine-rich polypeptide that contains 108 amino acids [22]. Resistin can regulate inflammation and insulin resistance, mediate metabolic disorders, and promote cell proliferation and tumor progression [23]. One study [24] showed that serum resistin level is significantly increased in patients with BC. Also, it is closely related to the occurrence and development of BC and will increase the risk of incidence and metastasis of BC. The study by Lee et al [25] found that resistin can affect the expression of vimentin (a key molecule in the process of cancer cell invasion), and can promote metastasis of MDA-MB-231 BC cells through activation of Ezrin-Radixin-Moesin (ERM). They stated that resistin is a key regulator of BC metastasis. A previous study [26] pointed out the association between resistin and the incidence, malignancy, and prognosis of BC. It also revealed the importance of resistin in the growth, invasion, and metastasis of BC cells. This study showed that the serum resistin levels in the two groups after the treatment were significantly lower than those before treatment, and the serum resistin levels in the study group were significantly lower than in the control group, suggesting that nab-paclitaxel shows good treatment efficacy by decreasing serum resistin levels.

There is an increasing body of evidence that nab-paclitaxel has advantages over traditional PTX in drug tolerance and efficacy, and nab-paclitaxel has been well recognized as a treatment option for advanced BC [27,28]. In addition, our study found that the quality of life of the study group was significantly higher than that of the control group. Given the optimistic results of several clinical studies about nab-paclitaxel, conventional PTX is losing ground to nab-paclitaxel and may even be totally replaced in the future.

Conflict of interests

The authors declare no conflict of interests.

References

1. Ferlay J, Soerjomataram I, Dikshit R et al. Cancer incidence and mortality worldwide:sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2014;136:E359-86.
2. de Lorenzo F, Apostolidis K. The European Cancer Patient Coalition and its central role in connecting stakeholders to advance patient-centric solutions in the mission on cancer. Mol Oncol 2019;13:653-66.
3. Miller KD, Siegel RL, Lin CC et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin 2016;66:271-89.
4. Farhood B, Raei B, Ameri H et al. A review of incidence and mortality of colorectal, lung, liver, thyroid, and bladder cancers in Iran and compared to other countries. Contemp Oncol (Pozn) 2019;23:7-15.
5. Rawla P. Epidemiology of Prostate Cancer. World J Oncol 2019;10:63-89.
6. Bellanger M, Zeinomar N, Tehranifar P, Terry MB. Are Global Breast Cancer Incidence and Mortality Patterns Related to Country-Specific Economic Development and Prevention Strategies? J Glob Oncol 2018;4:1-16.
7. Joerger M. Metabolism of the taxanes including nab-paclitaxel. Expert Opin Drug Metab Toxicol 2015;11:691-702.
8. Wang HY, Yao ZH, Tang H et al. Weekly nanoparticle albumin-bound paclitaxel in combination with cisplatin versus weekly solvent-based paclitaxel plus cisplatin as first-line therapy in chinese patients with advanced esophageal squamous cell carcinoma. Onco Targets Ther 2016;9:5663-9.
9. Deshmukh SK, Srivastava SK, Zubair H et al. Resistin potentiates chemoresistance and stemness of breast cancer cells:Implications for racially disparate therapeutic outcomes. Cancer Lett 2017;396:21-9.
10. Li J, Han X. Adipocytokines and breast cancer. Curr Probl Cancer 2018;42:208-214.
11. Wang CH, Wang PJ, Hsieh YC et al. Resistin facilitates breast cancer progression via TLR4-mediated induction of mesenchymal phenotypes and stemness properties. Oncogene 2017;37:589-600.
12. Assiri AM, Kamel HF. Evaluation of diagnostic and predictive value of serum adipokines: Leptin, resistin and visfatin in postmenopausal breast cancer. Obes Res Clin Pract 2015;10:442-53.

13. Quiroga-Morales LA, Sat-Muñoz D, Martínez-Herrera BE et al. Obesity and adipocytokines in breast cancer and benign breast disease. Rev Med Inst Mex Seguro Soc 2018;56:246-54.
14. Wolff AC, Hammond MEH, Allison KH et al. Human epidermal growth factor receptor 2 testing in breast cancer:American Society of Clinical Oncology/College of American Pathologists clinical practice guideline focused update. Arch Pathol Lab Med 2018;142:1364-82.
15. Wolchok JD, Hoos A, O'Day S et al. Guidelines for the evaluation of immune therapy activity in solid tumors:immune-related response criteria. Clin Cancer Res 2009;15:7412-20.
16. Chang JY, Verma V, Li M et al. Proton Beam Radiotherapy and Concurrent Chemotherapy for Unresectable Stage III Non–Small Cell Lung Cancer: Final Results of a Phase 2 Study. JAMA Oncol 2017;3:e172032-e172032.
17. Wolff AC, Hammond MEH, Allison KH et al. Human Epidermal Growth Factor Receptor2 Testing in Breast Cancer: American Society of Clinical Oncology/College ofAmerican Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol 2018;36:2105-22.
18. Dalamaga M. Obesity, insulin resistance, adipocytokines and breast cancer: New biomarkers and attractive therapeutic targets. World J Exp Med 2013;3:34-42.
19. Chen N, Brachmann C, Liu X et al. Albumin-bound nanoparticle (nab) paclitaxel exhibits enhanced paclitaxel tissue distribution and tumor penetration. Cancer Chemother Pharmacol 2015;76:699-712.
20. Hou WK, Xu YX, Yu T et al. Adipocytokines and breast cancer risk. Chin Med J (Engl) 2007;120:1592-6.
21. Fan Y, Jiang Y, Zhou X et al. Phase II study of neoadjuvant therapy with nab-paclitaxel and cisplatin followed by surgery in patients with locally advanced esophageal squamous cell carcinoma. Oncotarget 2016;7:50624-34.
22. Yingchoncharoen P, Kalinowski DS, Richardson DR. Lipid-Based Drug Delivery Systems in Cancer Therapy: What Is Available and What Is Yet to Come. Pharmacol Rev 2016;68:701-87.
23. Codoner-Franch P, Alonso-Iglesias E. Resistin:insulin resistance to malignancy. Clin Chim Acta 2014;438:46-54.
24. He MM, Wang F, Jin Y et al. Phase II clinical trial of S-1 plus nanoparticle albumin-bound paclitaxel in untreated patients with metastatic gastric cancer. Cancer Sci 2018;109:3575-82.
25. Bartsch R, Bergen E, Galid A. Current concepts and future directions in neoadjuvant chemotherapy of breast cancer. Memo 2018;11:199-203.
26. Di Lorenzo G, Ricci G, Severini GM, Romano F, Biffi S. Imaging and therapy of ovarian cancer: clinical application of nanoparticles and future perspectives. Theranostics 2018;8:4279-94.
27. Wong NS. Primary medical therapy and breast conservation treatment: the medical oncology perspective. Gland Surg 2018;7:560-75.
28. Omarini C, Guaitoli G, Pipitone S et al. Neoadjuvant treatments in triple-negative breast cancer patients: where we are now and where we are going. Cancer Manag Res 2018;10:91-103.