Evaluate the Clinical Outcome of Nanoparticle Albumin-bound Paclitaxel on Breast Cancer Treatment: A Systematic Review and Meta-analysis

Yasaman Shariati[a], Fatemeh Salehi Kahrizsangi[b,*], Niloofarsadat Hozhabrossadati[c], Donya Naseri[d], Mandana Ebrahimi[e]

[a] Department of General Surgery, School of Medicine, Arak University of Medical Sciences, Arak, Iran
[b] Department of pathology, Faculty of medicine, Sari Branch, Islamic Azad University, Sari, Iran
[c] School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[d] School of Medicine, Islamic Azad University, Najaf Abad Branch, Najafabad, Iran
[e] Department of Internal Medicine, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran

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ABSTRACT

Background and aim: Nanoparticle albumin-bound paclitaxel can have a higher response rate than paclitaxel in women with metastatic breast cancer. Therefore, the present study was conducted to evaluate the clinical outcome of nanoparticle albumin-bound paclitaxel on breast cancer treatment.

Material and methods: All articles published in international databases such as PubMed, Scopus, Science Direct, ISI Web of knowledge, and Embase between March 2016 and August 2022 included. 95% confidence interval (CI) for odds ratio and risk ratio with fixed effect modal and Mantel-Haenszel were calculated. Data analysis was performed using STATA.V16 software.

Results: In the initial review, the abstracts of 249 studies were reviewed, two authors reviewed the full text of 42 studies, and finally, nine studies were selected. The odds ratio of the Overall response rate in breast cancer patients between nab-paclitaxel and the control group was 0.22 (95% CI, 0.04 to 0.41; p=0.02) in breast cancer patients with been treated with neoadjuvant nab-paclitaxel, Overall response rate was higher.

Conclusions: Based on the findings of the present meta-analysis, complete pathological response and overall response rate were higher for the neoadjuvant nab-paclitaxel than conventional taxane regimens.

1. Introduction

Breast cancer is the most common malignancy among women and one of the most important causes of death worldwide.[1] Neoadjuvant systemic therapy can be mentioned among the treatments used to treat breast cancer; According to the results of the studies, this treatment increases the survival rate, of course, in patients who have achieved a pathological complete response after the treatment.[2] Using taxanes in adjuvant breast cancer treatment is necessary and helps the treatment process.[3] Among the taxanes that are widely used in the field of breast cancer treatment is Paclitaxel.[4] Based on the findings of studies, Neoadjuvant Paclitaxel can increase the survival rate.[5-8] Among the complications reported for Paclitaxel are toxicity and long-term peripheral neuropathy, and its cause can be related to polyethoxylated castor oil and its other compound ethanol, which is used as a solvent to increase the drug's solubility.[9] A novel delivery mechanism for Paclitaxel to tumors is used in nanoparticle albumin-bound (nab) paclitaxel, which is solvent-free.[10] Based on the study findings, nab-paclitaxel can have

a higher response rate than Paclitaxel in women with metastatic breast cancer.[11, 12] Based on preliminary trials, nab-paclitaxel has been approved; more studies are needed to compare nab-paclitaxel and Paclitaxel to provide stronger evidence.[13, 14] Most studies that have investigated and compared nab-paclitaxel and Paclitaxel have a small sample size, different patient groups, different drug doses, nab-paclitaxel drug combinations, and different treatment plans, which needs to be done with the consensus of the results and examining them will provide stronger evidence. In 2017, a systematic review and meta-analysis study was conducted by Zong et al.,[15] which examined and compared the efficacy and toxicity of nab-paclitaxel in the treatment of breast cancer and examined studies between 2010 and 2016. The results showed that nab-paclitaxel is an effective cytotoxic drug in the neoadjuvant breast cancer treatment. In the present study, an attempt has been made to review newer studies from 2016 to August 2022 to provide sufficient evidence in this field by consensus of results and comparison with older studies. Therefore, the

present study was conducted to evaluate the clinical outcome of nanoparticle albumin-bound paclitaxel on breast cancer treatment.

2. Material and methods

Search strategy

Table1. PICO strategy.

PICO Strategy	Description
P	Population: Breast cancer patients
I	Intervention: nab-paclitaxel
C	Comparison: conventional taxane regimens
O	Outcome: clinical outcome

The following keywords were used to search:

((((((("Breast"[Mesh] OR "Inflammatory Breast Neoplasms"[Mesh] OR "Breast Neoplasms, Male"[Mesh] OR "Carcinoma, Ductal, Breast"[Mesh] OR "Breast Neoplasms"[Mesh]) OR ("Breast Neoplasms/classification"[Mesh] OR "Breast Neoplasms/complications"[Mesh] OR "Breast Neoplasms/mortality"[Mesh] OR "Breast Neoplasms/statistics and numerical data"[Mesh] OR "Breast Neoplasms/therapy"[Mesh])) OR "Neoplasms"[Mesh]) AND "taxane" [Supplementary Concept]) AND "Neoadjuvant Therapy"[Mesh]) AND "Paclitaxel"[Mesh]) AND "Albumin-Bound Paclitaxel"[Mesh]) AND "Survival Rate"[Mesh].

Study selection, Data Extraction, and method of analysis

Studies data were reported by first author name, years, study design, number of Breast cancer patients, mean of age, Receptor status, and Taxan and Neoadjuvant Regimens. Using a tool developed by the Cochrane Collaboration, the quality of the included randomized control trial studies was assessed.[17] Low risk received a scale score of 1, while high and unclear risk received a score of 0. The scale scores have a range of 0 to 6. A higher score indicates higher quality. The Newcastle-Ottawa Scale (NOS)[18] is used to evaluate the quality of cohort studies and non-randomized research; With a total of nine items, this scale evaluates three dimensions (selection, cohort comparability, and outcome). Studies having NOS scores of 1-3, 4-6, and 7 were classified as low, medium, or high quality, respectively, in the analysis. STATA.V16 software was used to analyze the data. The level of heterogeneity was evaluated using the I^2 index test ($I^2 < 50\%$ = low levels, $50 < I^2 < 75\%$ = moderate and $I^2 > 75\%$ = high levels). Calculated odds and risk ratio 95% confidence intervals (CI) for fixed effect modal and Mantel-Haenszel models.

3. Results

When the reviewed literature was searched using the studied keywords, two hundred forty-nine studies were found. Duplicate studies were removed from the initial review, which also reviewed the abstracts of 237 studies. One hundred ninety-five studies were in the first stage removed because they did not match the inclusion criteria, and in the second stage, two authors reviewed the full texts of 42 studies. Thirty-three studies were excluded from the study at this stage because of incomplete evidence, inconsistent study results, poor studies, restricted access to full texts, or data that did not align with the study objective. Finally, nine research were selected (Fig. 1).
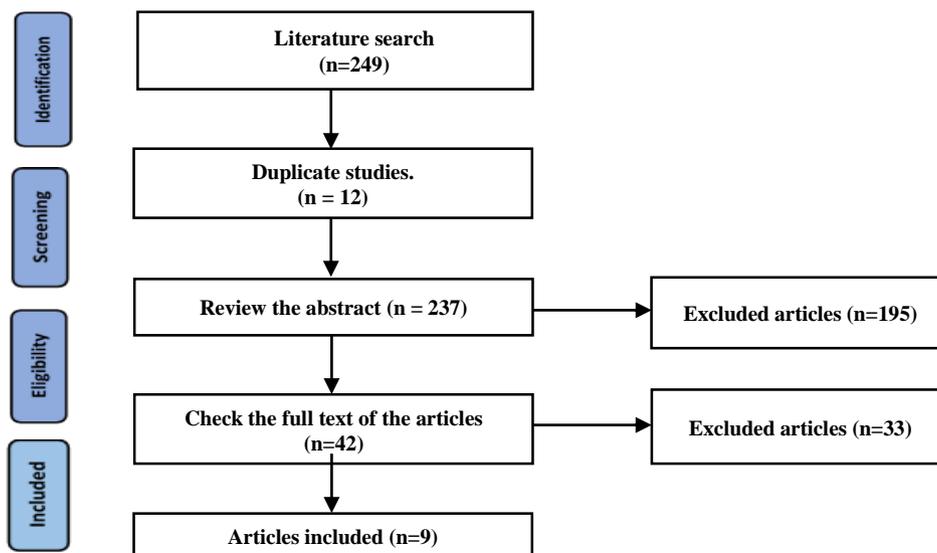
The current study is a systematic review and meta-analysis based on PRISMA guidelines(16). It includes all publications published in international databases such as PubMed, Scopus, Science Direct, ISI Web of Knowledge, and Embase between March 2016 and August 2022. Table 1 shows the response to PICO.

Fig. 1. PRISMA flowcharts.

Characteristics

Four Non-Randomized controlled trials (RCT) studies and five Randomized controlled trial studies have been included in the present article. The number of Patients in the nab-paclitaxel group and conventional taxane regimens was 1658 and 1671, respectively, and a total was 3329 with an average age of 47.5 years (Table 2).

Bias assessment

According to the NOS instrument and Collaboration's tool, the risk of bias was low in Non-RCT and RCT studies (Tables 3 and 4).

Table 2. Summary of demographic and clinical data of studies selected.

No	Study. Years	Study Design	Number of Patients		Dose of Taxane		Mean of Age (years)		Neoadjuvant Regimens	
			Nab-paclitaxel	Control	Nab-paclitaxel	Control	Nab-paclitaxel	Control	Nab-paclitaxel	Control
1	Zhang et al., 2022[19]	Non-RCT	118	117	-----	-----	NR		Nanoparticle albumin-bound paclitaxel	Liposomal paclitaxel
2	Untch et al., 2019[20]	RCT	606	600	150 or 125 mg/m2 d 1,8,15, q3w*4	80 mg/m2 d1,8,15, q3w*4	48	47	nab-p → EC	sb-p → EC
3	Patel et al., 2019[21]	RCT	14	16	80 mg/m2 qw *12	80 mg/m2 qw*12	53	57	T-DM1 + L → T-DM1 + L + nab-p	TP → TP + sb-p
4	Xie et al., 2019[22]	Non-RCT	83	79	260 mg/m2 q 2w*4	175 mg/m2 q2w*4	47	52	EC → nab-p	EC → sb-p
5	Gianni et al., 2018[23]	RCT	346	349	125 mg/m2 week 1,2,3, q4w*4	90 mg/m2 week 1,2,3, q4w*4	50	50	nab-p → AC/EC/FEC	sb-p → AC/EC/FEC
6	Moebus et al., 2018[24]	RCT	298	300	330 mg/m2 q 2w*3	60–100 mg/m2 q2w*4	49	50	nab-p + EC	Docetaxel + EC
7	Kuwayama wt al., 2018[25]	RCT	75	77	100 mg/m2 d 1,8,15, q4w*4	75 mg/m2 q3w*4	51	50	nab-p → FEC	Docetaxel→FEC
8	Nahleh et al., 2016[26]	Non-RCT	98	113	100mg, qw*12		NR		nab-P(+/-bev) →ddAC	
9	Matsuda et al., 2016[27]	Non-RCT	20	20	125mg, d1,8,15, q4w*4		54	54	EC→nab-P(H	

Table 3. Bias assessment (NOS tool).

Study	Selection (5 Scores)				Comparability (2 Scores)	Outcome (2 Scores)		Total Score
	Representative Sample	Sample Size	Non-respondents	Ascertainment of the Exposure	Based on Design and Analysis	Assessment of Outcome	Statistical Test	
Zhang et al., 2022[19]	*	*	*	*	*	*	*	7
Xie et al., 2019[22]	*	*	*	*	**	*	*	8
Nahleh et al., 2016[26]	*	*	*	*	*	*	*	7
Matsuda et al., 2016[27]	*	*	*	*	*	*	*	7

*= 1 score; **= 2 score; -=0 score.

Table 4. Risk of bias assessment (Collaboration's tool).

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Total Score
Untch et al., 2019[20]	+	?	+	+	+	+	5
Patel et al., 2019[21]	+	+	-	+	+	+	5
Gianni et al., 2018[23]	+	+	+	+	+	+	5
Moebus et al., 2018[24]	+	?	+	+	+	+	5
Kuwayama wt al., 2018[25]	+	?	+	+	+	+	5

(Low (+), unclear (?), high (-)).

Pathological complete response

Odds ratio of Pathological complete response in breast cancer patients between nab-paclitaxel and control group was 0.41 (95% CI, 0.25 to 0.57; p=0.00) (I^2<0%; P=0.78; low heterogeneity). According to Fig. 2, a statistically significant difference was observed in pathological complete response between the two groups (p=0.00); in the intervention group, the pathological complete response rate was higher than the control group. These findings show that the pathological complete response rate was higher in breast cancer patients treated with neoadjuvant nab-paclitaxel.
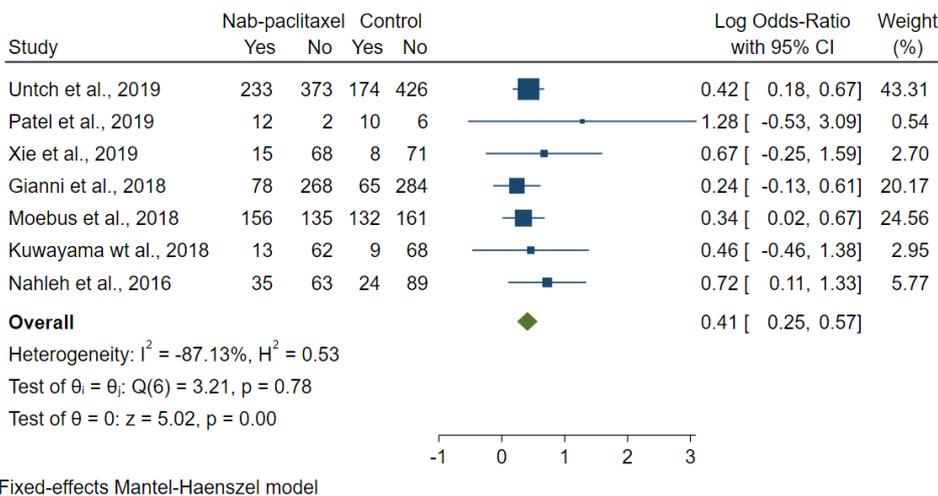

Fig. 2. Forest plot showed Pathological complete response in breast cancer patients.

Overall response rate

Odds ratio of Overall response rate in breast cancer patients between nab-paclitaxel and control group was 0.22 (95% CI, 0.04 to 0.41; p=0.02) (I^2<0%; P=0.55; low heterogeneity). According to Figure 3, a statistically significant difference was observed in the Overall response rate between the two groups (p=0.02); in the intervention group, the Overall response rate was higher than the control group. These findings show that the overall response rate was higher in breast cancer patients treated with neoadjuvant nab-paclitaxel.
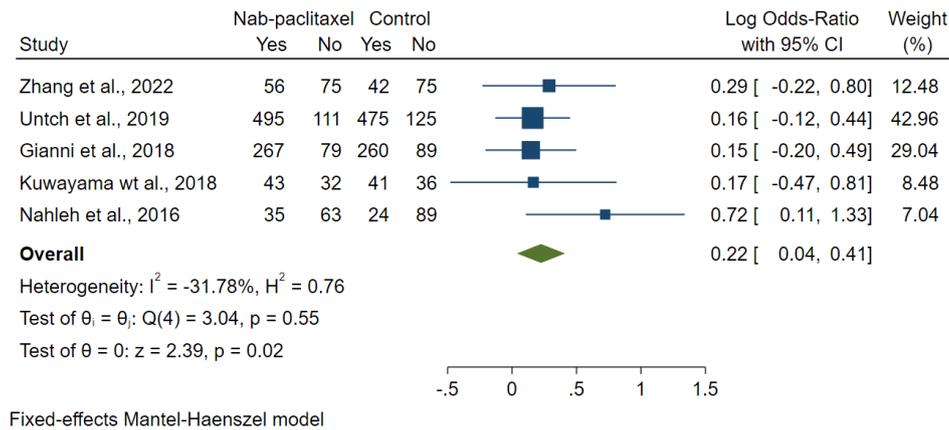
Fig. 3. The Forest plot showed the Overall response rate in breast cancer patients.

4. Discussion

In this study, the effects of nab-paclitaxel versus conventional taxane regimens were compared in treating breast cancer. Based on this meta-analysis, it was determined that neoadjuvant nab-paclitaxel has a higher rate than conventional taxane regimens in terms of pathological complete response and overall response rate and is more effective; It also has reasonable toxicity. The results of the present study were consistent with the informed findings of the meta-analysis of Zong et al., 2017.[15] Studies have shown that the better efficacy of nab-paclitaxel can be due to drug retention, increased penetration, and increased local concentration of the drug at the tumor site.[28, 29] Based on the findings of the selected studies, it was observed that pathological complete response could be related to the characteristics of the patient and the degree of illness. Therefore, according to the findings of the studies, pathological complete response in HER2-positive patients was higher for nab-paclitaxel. According to research, the rate of ballooning in this group of patients can be due to the use of targeted treatment.[30] Also, the overall response rate was higher in the nab-paclitaxel group, which corresponds to the high rate in the metastatic environment of TNBC.[31, 32] A systematic review and meta-analysis reported similar findings to the present study.[30] Gianni et al., 2018 reported that the improved pathological complete response rate after nab-paclitaxel was not statistically significant.[23] Zhang et al. 2022[19] showed that Nab-paclitaxel might be superior to liposomal Paclitaxel in the neoadjuvant systemic breast cancer treatment. Untch et al., 2019 reported a significantly higher pathologic complete response rate with Nab-paclitaxel translated than solvent-based Paclitaxel.[20] Patel et al., 2019 reported similar results.[21] Compared to conventional taxanes, nab-paclitaxel is more cost-effective since it reduces the incidence of severe adverse events and the costs associated with managing critical clinical situations. It is supported by several clinical-economic studies.[33, 34] The quality of the selected studies was high, and the heterogeneity between the studies was very low, which is an advantage for meta-analysis and shows that the results of the present study can be relied upon. In the search conducted from 2016 to August 2022, few RCT and Non-RCT studies were found, and the sample size of some studies was small, which can be one of the limitations of the present study. Also, not all selected studies were RCTs, which could lead to potential bias. Also, the dosage should be considered because it was not the same in the studies; each of the studies reported different types of side effects, so a meta-analysis was not performed; among the things that can cause bias was the selection of studies that were published in English, and the full text was available.

5. Conclusion

Based on the findings of the present study, it can be stated that in comparing two groups of neoadjuvant nab-paclitaxel and conventional taxane regimens in the treatment of breast cancer, pathological complete response and overall response rate were higher for the neoadjuvant nab-paclitaxel group and this difference is significant. More RCT studies with higher sample sizes and follow-up periods are needed To confirm the current evidence. It is also suggested that studies with the same doses be performed to provide stronger results.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgements

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