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Safety of nab-paclitaxel following an allergic reaction to paclitaxel: A single institution retrospective study

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ABSTRACT

The goal of this study was to assess the safety of nab-paclitaxel in patients with ovarian cancer or endometrial cancer who had an allergic reaction to paclitaxel. We performed a retrospective review of patients with endometrial cancer or ovarian cancer with an allergic reaction to paclitaxel who were subsequently treated with nab-paclitaxel at the Mayo Clinic Florida from January 2016 to June 2023. A total of 43 patients with ovarian cancer (31) or endometrial cancer (12) and a paclitaxel allergic reaction were identified. All patients were premedicated against allergic reactions prior to paclitaxel and subsequent nab-paclitaxel. Allergic reactions to paclitaxel were mild in fourteen patients (33%), moderate in twenty-five patients (58%) and severe in four (9%) patients. None of the 43 patients had an allergic reaction to subsequent nab-paclitaxel. Our data suggests that the administration of nab-paclitaxel to endometrial cancer or ovarian cancer patients with allergic reactions to paclitaxel is safe and should be considered a preferable treatment option in this clinical situation.

1. Introduction

Gynecological cancers are the third leading cause of cancer in US women, following breast cancer and lung cancer (Siegel et al., 2024). Paclitaxel in combination with carboplatin is the standard first line treatment for most metastatic ovarian and endometrial cancers (Ledermann, 2018). Hypersensitive reactions to paclitaxel infusions are relatively common (varying from 2-42 %) and vary from severe anaphylactic shock to mild skin rashes (Haine et al. 2022). These hypersensitive reactions are believed to be secondary to the Cremophor which is used as a solvent to paclitaxel. Different approaches have been used to manage hypersensitivity reactions to paclitaxel including increased doses of steroids, anti-histaminics, a trial of docetaxel and desensitization procedures (Haine et al. 2022). Nab-paclitaxel has also been successfully used in patients with allergic reactions to paclitaxel as it is dissolved in protein albumin nanoparticles and does not require Cremophor (Maurer et al. 2017). In this study, we report a single institution's experience using nab-paclitaxel in patients with paclitaxel allergies.

2. Methods

A retrospective review of medical records of consecutive patients with endometrial cancer or ovarian cancer and a history of an allergic reaction to paclitaxel seen at the Mayo Clinic in Florida from January 1, 2016, through June 30, 2023, was performed. Patients were identified by doing a search of the electronic medical records for diagnosis of paclitaxel allergy and manually reviewing identified records for subsequent treatments. All patients with endometrial or ovarian cancer treated at Mayo Clinic in Florida during the study period were cared for by authors of the manuscript (S.K. and G.C.O.) and all of them were subsequently treated with nab-paclitaxel. Demographic data on the patients, number of cycles of treatment and information on the severity of the observed allergic reactions were collected. Hypersensitivity reactions (HSR) were classified according to Brown's classification (Brown, 2004). IRB approval was obtained (Mayo Clinic IRB17-006677).

3. Results

Forty-five patients were identified. Among these 45 patients, two

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were excluded from the analysis due to lack of specific information about the allergic reactions. Demographics of the study population are included in Table 1.

Prior to the treatment with paclitaxel or subsequent nab-paclitaxel, all the patients were pre-medicated with dexamethasone 12 mg IV, hydrocortisone 100 mg IV (for first 2 doses of paclitaxel), famotidine 20 mg IV, and diphenhydramine 50 mg IV. Most of the patients had a reaction to the first dose of paclitaxel (N=23) with 7 patients having the reaction after the second dose, 10 after the third dose and 3 to subsequent doses. The clinical presentation or symptoms reported during the allergic reaction to paclitaxel ranged from anaphylactic shock, skin rash/erythema, flushing, dyspnea, shortness of breath, hypoxia, hypotension, hypertension, chest pain, nausea, throat tightness, syncopal episodes, abdominal pressure, back pain/spasm, tachycardia, pruritus, hives, facial tingling, numbness, lightheadedness, and angioedema (Fig. 1). Fourteen patients (33 %) had mild reactions, twenty-five patients (58 %) had moderate reaction and four (9 %) patients had severe reactions, including two of them who needed hospital admission.

After these HSR, all patients were switched from paclitaxel to nab-paclitaxel and treated in the outpatient setting. All patients tolerated the nab-paclitaxel treatment without any allergic reactions. None of these 43 patients subsequently discontinued nab-paclitaxel due to allergic reactions. Patients received a median of 5 doses of nab-paclitaxel (range 1–19 doses). The dosing of nab-paclitaxel ranged from 50 mg/m2 weekly (n = 1), 60 mg/m2 weekly (n = 2), 80 mg/m2 weekly (n = 30) and 175 mg/m2 every 3 weeks (n = 10) in combination with carboplatin doses of AUC2 weekly or AUC5-6 every 3 weeks respectively or Gemcitabine 800 mg/m2 given weekly.

Table 1
Demographic data.

Variable	Number (percentage)
Patients	43
Ovarian Cancer	31 (72.09 %)
Endometrial Cancer	12 (27.91 %)
Median age (in years, range)	63 (31 – 88)
Race (self-reported)	
White	39 (90.68 %)
African American	1 (2.33 %)
Middle Eastern	1 (2.33 %)
Asian	1 (2.33 %)
Not listed	1 (2.33 %)
Ovarian cancer	31
Staging	
Stage 1	0 (0%)
Stage 2	5 (16.13%)
Stage 3	14 (45.16%)
Stage 4	11 (35.48%)
Recurrent	1 (3.23%)
Histology	
High Grade Serous	25 (80.64%)
Low Grade Serous	1 (3.23%)
Endometroid	2 (6.45%)
Mixed	3 (9.68%)
Clear cell	0(0%)
Treatment	
Neo-Adjuvant	20 (64.52%)
Adjuvant	10 (32.26%)
Recurrent	1 (3.23%)
Endometrial Cancer	12
Staging	
Staging	
Stage 1	4 (33.33%)
Stage 2	2 (16.67%)
Stage 3	4 (33.33%)
Stage 4	0 (0%)
Recurrent	2 (16.67%)
Histology	
Endometroid	6 (50.00%)
Carcinosarcoma	4 (33.33%)
Serous	2 (16.67%)
Treatment	
Neo-Adjuvant+Adjuvant	1 (8.33%)
Adjuvant	9 (75.00%)
Recurrent	2 (16.67%)

4. Discussion

Hypersensitivity reactions (HSR) to paclitaxel are a significant clinical problem, varying from 2- 42 %, and sometimes can be lethal (De Leon et al. 2013; Haine et al. 2022). These allergic reactions, predominantly type 1 HSR, are manifested by hypotension, tachycardia, flushing, respiratory distress, abdominal and chest pain, as well as dermal reactions (Haine et al. 2022). Of all 43 patients in the current series, as many as 9 % of them developed severe symptoms like hypotension, hypoxia, confusion, and anaphylactic edema to paclitaxel. Current preventive strategies for taxane-induced HSR include premedication with H1 and H2 receptor antagonists, and intravenous corticosteroids. For patients who develop severe HSR despite these measures, currently recommended options include desensitization protocols or the use of alternative taxanes like docetaxel (Haine et al. 2022). Cross sensitivity to docetaxel in patients with allergic reactions to paclitaxel are quite common, varying from 41 % to 90 % (Sanchez-Munoz et al., 2011; Dizon et al., 2006) and desensitization procedures require significant time commitment and frequently hospitalizations (De Leon et al. 2013) which makes the option of nab-paclitaxel a preferable and safer option in these cases.

The incidence of allergic reactions to nab-paclitaxel are rare enough to not merit any allergic premedications in its current FDA approved indications, contrary to paclitaxel and docetaxel which require steroid premedications in order to prevent allergic reactions to its lipid solvents. Allergic reactions to nab-paclitaxel had been described in the literature, although usually these reactions are not severe, and therefore the absence of any allergic reactions in our series may had been in part due to the relatively small size of our cohort. For example, in a randomized phase 3 clinical trial of 460 patients with metastatic breast cancer, comparing nab-paclitaxel with paclitaxel, less than 1 % of patients receiving nab-paclitaxel had an allergic reaction, with none of the allergic reactions been classified as severe, compared to 2 % patients receiving paclitaxel (Gradishar et al, 2005). Additionally, it is possible that the use of premedications with steroids and H1 and H2 blockers prior to nab-paclitaxel in our series may had prevented allergic reactions and mitigated any cross sensitivity to nab-paclitaxel. We decided to use premedications in our patients in order to mitigate the possibility of cross sensitivity to nab-paclitaxel.

The majority of the patients in our study developed HSR during the initial cycles of paclitaxel. Upon switching to nab-paclitaxel, all patients tolerated the treatment well, including the four patients with severe HSR to paclitaxel, with no reports of allergic reactions, and none discontinued treatment due to subsequent allergic reactions. Our report is the largest single institution series on the use of nab-paclitaxel in patients with an allergic reaction to paclitaxel (Table 2). Previous reports were mostly case reports except for three series, one by Maurer et al. of 37 patients previously experiencing a HSR to paclitaxel, who had no immediate reactions to subsequent treatment with nab-paclitaxel (Maurer et al. 2017). Parisi et al reported a series of 10 patients with no reported reactions to nab-paclitaxel after an allergic reaction to paclitaxel (Parisi et al., 2020). Fader et al. reported a series of five patients treated successfully with nab-paclitaxel after discontinuation of paclitaxel (Fader and Rose, 2009). Our series adds important data supporting the use of nab-paclitaxel following a paclitaxel HSR.

5. Conclusions

This retrospective single institution experience shows that the use of nab-paclitaxel in patients with ovarian cancer or endometrial cancer who have experienced HSR to paclitaxel is safe and not associated with allergic reactions. Nab-paclitaxel should be considered a safe and

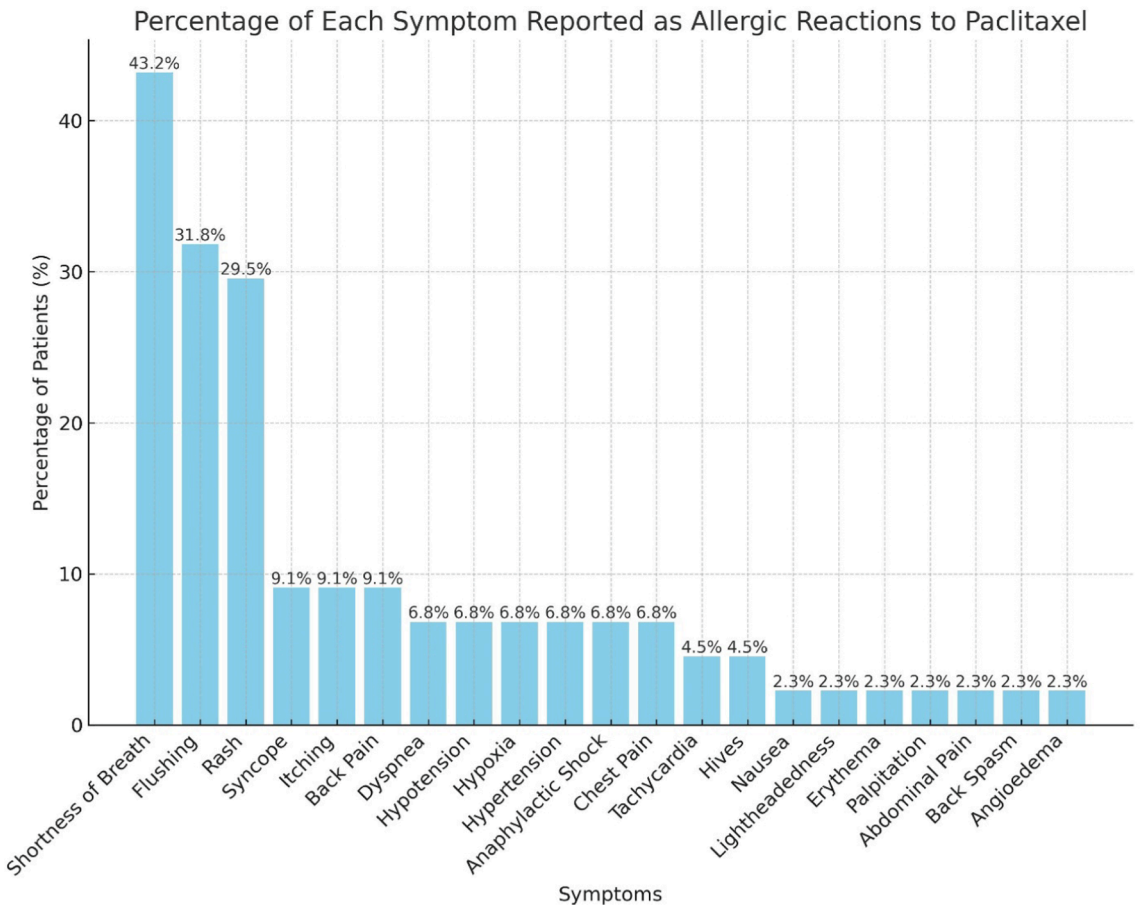

Fig. 1. Observed manifestations of hypersensitivity reactions (HSR) to paclitaxel in the current series (more than one symptom was observed in some patients).

Table 2
Reports on nab-paclitaxel use after hypersensitivity reactions to paclitaxel.

Reference	Number of patients	Taxane which caused hypersensitivity	Cycles after which HSR occurred	Premedication	Hypersensitivity caused by Nab-paclitaxel	Type of cancer
Maurer et al., 2017	37	Paclitaxel and Docetaxel	1—3	yes	no	Ovarian, uterine and cervical
Parisi et al., 2020	10	Paclitaxel	_	yes	no	Ovarian
Pellegrino et al., 2017	1	Docetaxel	2	yes	no	Breast
Kimura et al., 2013	1	Docetaxel	2	yes	no	Breast
Fader and Rose, 2009	5	Paclitaxel	1	yes	no	Ovarian, uterine, cervical
de Leon et al, 2013	1	Paclitaxel and Docetaxel	1	yes	no	Ovarian
Micha et al., 2006	1	Paclitaxel	1	yes	no	Ovarian

acceptable treatment option in patients with paclitaxel induced HSR, with clear benefits over the alternative use of docetaxel or desensitization procedures.

CRediT authorship contribution statement

Swapna Kochuveettil: Writing – review & editing, Writing – original draft, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Roberto Angeli Morales:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Alicja Kaminska:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Gerardo Colon-Otero:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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Authors contribution

Swapna Kochuveettil: Conceptualization; Data curation; Formal analysis; Methodology; Writing – original draft. Roberto Angeli

Morales: Data curation; Formal analysis; Methodology; Writing – original draft. Alicja Kaminska: Formal analysis; Writing – original draft. Gerardo Colon-Otero: Conceptualization; Data curation; Formal analysis; Methodology; Writing – original draft; and Writing – review & editing.

IRB review concluded that written informed consent was not needed for this retrospective chart review that included only de-identified patient information.

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