Effect of dose-reduced paclitaxel pre-medication regimen on rates of hypersensitivity and corticosteroid-related adverse reactions

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BACKGROUND

Paclitaxel-based chemotherapy continues to be a fundamental component in the treatment of many solid tumors.[1] Paclitaxel hypersensitivity reactions have been reported due to the solvent Cremophor-EL.[2] In clinical trials, severe reactions characterized as dyspnea, hypotension, angioedema, and urticaria have occurred in less than 2% of patients receiving paclitaxel.[2] Minor reactions are characterized by flushing (28%), rash (12%), hypotension (4%), dyspnea (2%), tachycardia (2%), and hypertension (1%).[2] Per manufacturer and FDA guidelines, patients should receive the following to reduce the incidence of a hypersensitivity reaction: dexamethasone by mouth 12 hours and 6 hours before, diphenhydramine IV push 30 minutes before, and a histamine-2 receptor antagonist IV push 30 minutes before the paclitaxel infusion. However, multiple cycles of paclitaxel result in recurring doses of pre-medications and potential unwanted adverse events due to use of corticosteroids. In actuality, paclitaxel hypersensitivity reactions beyond the second dose have shown to be uncommon.[1] Furthermore, there is variability in the use of paclitaxel pre-medication among facilities throughout the country, with some having already successfully implemented a reduction in corticosteroid use without an increase in hypersensitivity reactions.[1]

OBJECTIVES

- Compare rates of paclitaxel hypersensitivity reactions with facility standard dose and dose-reduced pre-medication groups.
- Compare rates of common corticosteroid-induced adverse events with facility standard dose and dose-reduced pre-medication groups.
- Educate healthcare practitioners on results from the study and provide guidance for future prescribing.

METHODS

- Prospective, quality improvement study with a historical control group
- Inclusion criteria:
  - Patients at VA Connecticut Healthcare System who were treated with paclitaxel-based chemotherapy either weekly (45-90mg/m²) or every three weeks (175-200mg/m²)
- Exclusion criteria:
  - Patients who received:
    - Nab-paclitaxel
    - Prior treatment with paclitaxel
    - Paclitaxel as part of a research protocol
    - Corticosteroids for purposes other than pre-medication
    - Corticosteroids 12 and 6 hours prior to infusion (cohort group only)

PATIENT DEMOGRAPHICS

Characteristic	Control Group (N = 18)	Cohort Group (N = 9)
Gender (male)	18 (100%)	9 (100%)
Age (mean)	71.3 (60 – 88)	67.9 (52 – 82)
Diabetes at baseline	7 (38.9%)	3 (33.3%)
Diagnosis		
Lung cancer	12 (66.7%)	4 (44.4%)
Esophageal	2 (11.1%)	2 (22.2%)
Head and neck	2 (11.1%)	1 (11.1%)
Other	2 (11.1%)	2 (22.2%)
Chemotherapy regimen		
Carboplatin + paclitaxel	8 (44.4%)	2 (22.2%)
Carboplatin + paclitaxel + radiation	10 (55.6%)	6 (66.7%)
Paclitaxel + trastuzumab	0 (0%)	1 (11.1%)
Paclitaxel dosing schedule		
Weekly	10 (55.6%)	7 (77.8%)
Every three weeks	8 (44.4%)	2 (22.2%)
No. of paclitaxel doses (range)	5 (2 – 7)	5 (1 – 11)

RESULTS

	Control Group (N = 18)	Cohort Group (N = 9)	P value
Hypersensitivity reaction	0	0	1.0000*
Average dose of dexamethasone per cycle per patient (mg)	51.2	8.3	0.0013**
Hyperglycemia	11 (61.1%)	2 (22.2%)	0.1032*
Insomnia	2 (11.1%)	0 (0%)	0.5385*
Weight gain	1 (5.6%)	0 (0%)	1.0000*

METHODS

- Control group:
  - Patients who received paclitaxel between 01/01/2014 and 04/30/2014
  - Pre-medication regimen:
    - Dexamethasone 20mg PO 12 hours and 6 hours before
    - Dexamethasone 20mg IV 30 minutes before
    - Diphenhydramine 50mg PO 30 minutes before
    - Famotidine 20mg IV 30 minutes before
- Cohort group:
  - Patients who received paclitaxel between 11/01/2015 and 02/29/2016
  - Pre-medication regimen:
    - Dexamethasone 20mg IV, diphenhydramine 25mg PO, and famotidine 20mg IV 30 minutes prior to the FIRST TWO paclitaxel doses
    - For subsequent weekly infusions:
      - All pre-medications were eliminated if no hypersensitivity reaction occurred
    - For subsequent every three week infusions:
      - Only dexamethasone 8mg IV was administered 30 minutes prior to the paclitaxel dose

DISCUSSION

- There was no difference in the rate of paclitaxel hypersensitivity reactions.
- Additionally, patients experienced reduced incidence of corticosteroid-associated adverse reactions.
- Some limitations include:
  - Small sample size and patient population limited to VA population
  - Lack of assurance that patients were taking dexamethasone the night prior (control group)
  - Length of study duration
  - Subjective nature of corticosteroid-related adverse effects

REFERENCES

1. Berger MJ, et al. Feasibility of stopping paclitaxel premedication after two doses in patients not experiencing a previous infusion hypersensitivity reaction. *Support Care Cancer*. 2012 Sep;20(9):1991-7.
2. Taxol® (paclitaxel) injection package insert. Princeton, NJ: Bristol-Myers Squibb Company; April, 2011.

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Jagoda Misniakiewicz, John Szymanski, and Kristen Rychalsky: have nothing to disclose