Management of Hypersensitivity Reactions to Taxanes

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KEYWORDS

• Taxane • Paclitaxel • Docetaxel • Allergy • Hypersensitivity • Skin test
• Desensitization and challenge

KEY POINTS

- The incidence of immediate hypersensitivity reaction (HSR) to taxanes varies greatly between molecules from 10% with paclitaxel to less than 1% with cabazitaxel.
- Two mechanisms could account for immediate HSRs to taxanes: complement activation caused by the emulsifying agents (Cremophor EL and polysorbate 80) used in their formulation and an IgE-mediated reaction.
- Almost all patients who experienced an immediate HSR to taxanes can be safely retreated and many of those do not require desensitization.
- The decision to re-expose a patient to taxanes through desensitization or challenge should be based on the severity of the reaction and on the skin test result.
- Because the risk of recurrent reaction decreases with repeated exposures to taxanes, desensitization protocols can be progressively shortened in patients with good tolerance with the aim of eventually resuming regular infusions.

INTRODUCTION

Paclitaxel (taxol) is a taxane antineoplastic agent that is widely used in the treatment of various types of cancers, such as ovarian, breast, and lung cancer.[1] However, it causes immediate hypersensitivity reactions (HSRs) in around 10% of patients despite premedication with antihistamines and a corticosteroid.[2–4] Docetaxel (taxotere) is another taxane molecule and is used for treating a wide variety of cancers.[5] It must also be administered along with a corticosteroid premedication to reduce the incidence of immediate HSRs.[5–7] The newer taxanes, nanoparticle albumin-bound

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(nab)-paclitaxel (abraxane) and cabazitaxel (jevtana) can also cause immediate HSRs, although more rarely than the older taxanes.[8–11] This article reviews the clinical presentation, diagnosis, and management of HSRs to taxanes and discusses the different options for their safe readministration.

TERMINOLOGY

The International Consensus on drug allergy defines HSRs as reactions that clinically resemble an allergic reaction even if an immunologic mechanism has not been demonstrated.[12] It also differentiates between immediate and nonimmediate HSRs depending on the onset of the reaction (immediate, $\leq$1 hour after drug administration; nonimmediate, >1 hour). Occasionally, immediate HSRs to taxanes can occur a few hours after the infusion. This terminology is used in this review.

EPIDEMIOLOGY

Table 1 gives a brief description of the different taxanes in clinical use and the incidence of immediate HSRs associated with each molecule.

Paclitaxel

Phase I studies of paclitaxel revealed that a high percentage of patients suffered from immediate HSRs, most commonly during the first administration of the drug.[13–15] Premedication with antihistamines and a corticosteroid was soon implemented to mitigate this important adverse event.[13] Currently, around 10% of patients treated with paclitaxel will develop an immediate HSR despite premedication.[2–4] Two premedication regimens can be used. Both regimens contain an H1 (diphenhydramine) and an H2 (ranitidine, cimetidine, or famotidine) antihistamine given 30 to 60 minutes before the infusion.[1,4] They differ in that the standard regimen consists of 2 doses of dexamethasone administered the night before and the morning of the infusion, whereas the simplified protocol consists of a single dose of dexamethasone given 30 to 60 minutes before the infusion.[4] Although the single-dose protocol could entail a slightly higher risk of reaction, both protocols are considered acceptable options for premedication.[4,16,17]

Docetaxel

Early clinical trials of docetaxel were also complicated by a high incidence of immediate HSRs and by an adverse event specific to this taxane: fluid retention caused by capillary protein leak.[18–21] Premedication with dexamethasone given for 3 days starting the day before docetaxel administration helped reduce the incidence of immediate HSRs to around 5% and that of fluid retention to between 3.5% and 16.5%.[6,7,22,23]

Nab-Paclitaxel

Nab-paclitaxel is a newer paclitaxel formulation that does not contain Cremophor EL, which is considered responsible for most immediate HSRs to paclitaxel.[8,24,25] Thus, it can be infused without premedication and at a faster rate than paclitaxel.[8] Although, immediate HSRs are much less frequent than with paclitaxel,[10,11] severe and even fatal reactions have been reported with nab-paclitaxel.[8] Given its ease of administration and safety profile, nab-paclitaxel is increasingly used in place of conventional paclitaxel despite its much higher cost.[26]