Increasing efficiency of paclitaxel administration

Paclitaxel is one of the most widely used cytostatics worldwide. New insights show that paclitaxel can be administered more efficiently, with less comedication, and in a more patient-friendly manner thus reducing use of resources and environmental impact. The Dutch NVMO Committee for Sustainability and Efficiency has formulated recommendations.

Introduction

Paclitaxel is one of the most widely used cytostatics in oncology. It is indicated for breast, lung, and ovarian cancer among others, in both weekly and three-weekly schedules. In the Netherlands there are about 70,000 administrations of paclitaxel yearly. (1) To reduce the risk of hypersensitivity reactions and nausea, a corticosteroid (dexamethasone), an H1 antagonist (clemastine), and an H2 antagonist (ranitidine) have been administered prior to paclitaxel infusion for decades. However, there has been ongoing debate about the necessity of the premedication regimen surrounding paclitaxel.

Ranitidine has no added value in paclitaxel regimens

The 'RANISTOP' study investigated whether omitting ranitidine from the premedication regimen before paclitaxel infusion affects the occurrence of clinically relevant allergic reactions. Based on this study (n=366), it was concluded that ranitidine can be safely removed from the treatment regimens. (2)

Replacing intravenous clemastine with oral cetirizine

Clemastine is often still routinely given to reduce the risk of hypersensitivity reactions. First-generation H1 antagonists, such as clemastine, have a strong sedative effect. Therefore, clemastine comes with a (auto)driving ban for 24 hours. Second-generation H1 antagonists, such as cetirizine, have an equally potent effect on preventing allergic reactions but cause less sedation. (3) Using cetirizine orally 10 mg is therefore preferred over clemastine, also because oral administration is more efficient, sustainable, and safer for the patient. (4) Cetirizine should be taken at least 30 minutes before the treatment for maximum effect.

Reducing or stopping dexamethasone

Despite being part of the standard treatment, the use of high doses of dexamethasone is controversial in preventing hypersensitivity reactions during paclitaxel infusion. Research shows that dexamethasone can be safely tapered off if no hypersensitivity reactions occur in the first two cycles. (5,6,7) There is even evidence supporting omitting dexamethasone from the first cycle, with the administered H1 antagonist (cetirizine) being sufficiently effective in preventing hypersensitivity reactions.(8) It is crucial to limit the use of dexamethasone as much as possible due to side effects such as immunosuppression, mood disorders, hyperglycemia, sleep disturbances, and weight gain. Therefore, we recommend the following two alternative dosing schedules for dexamethasone in paclitaxel monotherapy: 1) tapering

off dexamethasone or 2) completely omitting dexamethasone. The tapering schedule for dexamethasone suggested is as follows: dose 1: 8 mg, dose 2: 4 mg, dose 3: 2 mg, and stop from dose 4 onwards. (8,9) Since dexamethasone absorption is rapid and complete, it is recommended to take dexamethasone at least half an hour before the treatment. Dexamethasone can also be completely omitted during paclitaxel infusion (from the first dose). This practice is already applied in multiple centers in the Netherlands.

Shortening paclitaxel infusion duration

When paclitaxel was developed in the mid-1990s, it was administered over 24 hours due to the risk of hypersensitivity reactions. After optimizing the premedication, the administration duration was reduced to one hour for the weekly (Q1W) and three hours for the three-weekly (Q3W) schedule. Research indicates that administering paclitaxel (Q1W) over one hour does not pose additional risk of hypersensitivity reactions while maintaining efficacy. (10,11) By extrapolating the infusion rate of the Q1W schedule (e.g., 90 mg/m² in one hour), paclitaxel 175 mg/m² (Q3W) can be infused over two hours instead of three. Shorter infusion durations, as mentioned above, lead to a significantly higher percentage of hypersensitivity reactions and are therefore not recommended. (12)

Conclusion and Recommendations

By critically reviewing the administration of the paclitaxel regimen, it has been shown that it can be administered significantly more efficiently and in a more efficient, patient-friendly and sustainable manner without compromising effectiveness and safety. All recommendations are summarized in Table 1.

Table 1: Recommendations for Paclitaxel Regimen

Medication	Dosage	Administration	Savings per administration	Nationwide savings
Dexamethasone	0-8 mg	Tablet at least half an hour before the treatment	15 minutes*	17,500 hours**
Cetirizine	10 mg	Tablet at least half an hour before the treatment	15 minutes*	17,500 hours**
Ranitidine	50 mg	STOP	15 minutes*	17,500 hours**
Paclitaxel Q1W		Intravenous in 1 hour	N/A	N/A
Paclitaxel Q3W		Intravenous in 2 hours	60 minutes	2,500 hours***

- Savings include the time saved on preparing IV medication and chair time compared to a shot.
- ** Based on 70,000 paclitaxel treatments per year.
- *** Based on 2,500 Q3W doses of paclitaxel 175 mg/m² per year (2021).

Key Messages Regarding Efficiency in Paclitaxel Infusion

1. An infusion of paclitaxel can be administered more efficiently in a safe manner.
2. Ranitidine can be omitted.
3. Clemastine intravenously can be replaced by cetirizine 10 mg orally.
4. Paclitaxel 175 mg/m² can be administered intravenously in two hours instead of three hours.
5. Dexamethasone dosage can be significantly reduced or even omitted.

About the Authors:

The committee "sustainability and efficiency" of the Dutch Society of Medical Oncology (NVMO) was initiated in 2022. Their remit is to demonstrate that it is possible to increase both the sustainability as well as the efficiency of medical oncology care. The committee consists of medical oncologists and hospital pharmacists. They regularly publish specific guidelines and suggestions for daily practice based on both published literature and daily experience. All published guidelines are freely accessible at "https:www.nvmo.org/duurzaam-en-doelmatigheid/"

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