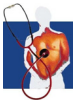
Premedication for prophylaxis of hypersensitivity reactions after weekly or 3-weekly paclitaxel:

a comprehensive literature review



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Elien DEWAELE, Caroline VERSCHUEREN, Pol SPECENIER

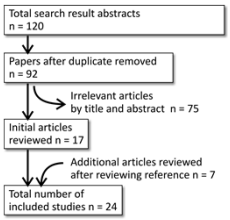
Medical Oncology, University Hospital Antwerp, Belgium
University of Antwerp, Belgium

Background

Early phase I trials with paclitaxel were complicated by a high incidence of hypersensitivity reactions. For paclitaxel administered 3-weekly, the FDA recommends the use of premedication with dexamethasone (DXM) 20 mg administered orally 12 and 6 h prior to paclitaxel, histamine 1 antagonist diphenhydramine 25-50 mg, and a histamine 2 antagonist 30-60 min prior to paclitaxel. There are no guidelines for the use of premedication when paclitaxel is given weekly. Repeatedly administered high dose of corticosteroids can induce unacceptable side effects.

Methods

MEDLINE was searched using the keywords premedication, paclitaxel and hypersensitiviy reactions at december 2014. Articles were surveyed for additional citations.



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Results

We retrieved 11 papers on prospective trials (3 on weekly paclitaxel, 8 on 3-weekly paclitaxel).

- Using a dexamethasone tapering regimen in patients without hypersensitivity reactions after the 1st weekly paclitaxel administration, hypersensitivity reactions were reported in 1.0, 2.3 and 5.7% of patients, respectively.
- Zidan reduced dexamethasone to 10 mg, 12 and 6h prior to subsequent cycles in patients without hypersensitivity reactions after the 1st 3-weekly administration and observed no hypersensitivity reactions.
- Hypersensitivity reactions rates in sequential cohorts treated at ICHNT, London, with an intravenous or oral dexamethasone regimen were 14.5% and 5.4% respectively (p= 0.07).
- Using a modified premedication regimen, Sasada et al. observed hypersensitivity reactions in 14/22 patients.

Weekly paclitaxel, prospective trials

Trial	Paclitaxel schedule	Premedication corticosteroids	Premedication H1 and H2 blockers	N	No. patients	Percent patients
Bravermann et al. 2005	80-100 mg/m²	* Cycle 1: DXM 20 mg oral 12h & 08h *No reaction:* * Cycle 2: DXM 20 mg IV * Cycle 3 – 4: DXM 10 mg IV * Cycle 5 - ...: DXM IV 2 mg until 0 mg	H1 blocker IV *No reaction:* * Cycle 5 - ... H1 blocker oral	122	7	5.73%
Green et al. 2009	80 mg/m²	* Cycle 1 – 3: DXM 10 mg IV * Cycle 4 – 12: DXM 4 mg IV	H1/ H2 blockers IV, only by previous reaction	302	6	2.30%
Zidan et al. 2008	60-80 mg/m²	* Cycle 1: DXM 10 mg oral 12h & 06h *No reaction:* * Cycle 2: DXM 6 mg oral 12h & 06h * Cycle 3: DXM 4 mg oral 12h & 06h * Cycle 4 - ...: DXM 2 mg oral 12h & 06h	H1 blocker po/ H2 blocker IV H1 blocker po/ H2 blocker IV	100	1	1%

Three-weekly paclitaxel, prospective trials

Trial	Paclitaxel schedule	Premedication corticosteroids	Premedication H1 and H2 blockers	N	No. patients	Percent patients
O' Cathaill et al. 2013	175 mg/m²	DXM 20 mg oral 12h and 06 h	H1/ H2 blockers IV	93	5	5.4%
		versus DXM 20 mg IV	H1/ H2 blockers IV	55	8	***P= 0.07*** 14.5%
Tsavaris et al. 2005	175-225 mg/m²	DXM 20 mg IV	H2/ H1 blockers IV	52	4	7.7%
Joly et al. 2011	175 mg/m²	DXM 20 mg IV	H1/ H2 blockers IV	502	166	33.1% 1% due to paclitaxel
Yamada et al. 2001	210 mg/m²	DXM 20 mg IV	H1/ H2 blockers IV	60	9	15%
Langer et al. 1995	135-215 mg/m²	DXM 20 mg IV	H1/ H2 blockers IV	54	0	0%
Kosmas et al. 2006	175-225 mg/m²	DXM 20 mg IV	H1/ H2 blockers IV	100	7	7.0%
Zidan et al. 2008	175 mg/m²	Cycle 1 - ... and no reaction: DXM 20mg oral 12h and 06 h DXM 8 mg IV	H1 blocker po/H2 blocker IV	80	3	4.0%
Sasada et al. 2007	175 mg/m²	DXM oral 8mg 12h before paclitaxel + DXM 20mg IV	H2 blocker IV H1 blocker (difenhydramine + 437.5 mg calcium bromide IV)	22	14	63.6%

Conclusion

Data from randomized trials on the optimal premedication regimen are lacking.

Tapering of dexamethasone is safe when paclitaxel is given weekly.

3-weekly paclitaxel: hypersensitivity reactions rates might be higher with a single-dose IV dexamathasone administration.

CONTACT: ...

Poster Design: Dirk De Weerdt
www.ddwdesign.be (Po735)