

LETTER to the EDITOR

Substance P is a Major Mediator Causing Delayed Emesis in Anthracycline-Based Chemotherapy - Really?Arife Ulas¹, Kamile Silay², Sema Akinci³, Bulent Yalcin⁴*Asian Pac J Cancer Prev*, **15** (24), 10993**Dear Editor**

We read with great interest the article written by Roila et al (2014) in which they indicated that in breast cancer patients treated with anthracycline plus cyclophosphamide chemotherapy and received the same antiemetic prophylaxis (aprepitant plus dexamethasone plus 5-HT₃ antagonist) for acute emesis, aprepitant was not superior to dexamethasone. Dexamethasone had similar efficacy and toxicity in preventing delayed emesis. The study indicates that even though complete response rates are similar in delayed emesis, dexamethasone-treated patients seemed to have better results in terms of complete protection, number of emetic episodes, duration, severity of nausea and dexamethasone is relatively cost effective. Also, the authors recommend that further studies comparing combination of dexamethasone plus aprepitant with single agent needs to be planned.

We would like to share some of our comments regarding this valuable study.

First of all, the use of aprepitant, an oral neurokinin-1 (NK1) antagonist, in combination with dexamethasone plus 5-HT₃ receptor antagonist in prevention of nausea and vomiting induced by highly and moderately emetogenic chemotherapy regimens is recommended (Hesketh et al., 2003; Uchino et al., 2012). Aprepitant is a moderate inhibitor of CYP 3A4 at antiemetic doses. Co-administration of aprepitant with dexamethasone resulted in increased plasma concentrations of dexamethasone since steroids are substrates of CYP 3A4. Due to this interaction it is recommended to decrease steroid dose by 50% in this particular patient populations (McCrea et al., 2003).

Secondly, as known, one of the study in the literature demonstrated that patients who are receiving cisplatin (≥ 70 mg/m²) based chemotherapy regimen has high serum substance P levels. The plasma substance P concentration which is responsible from delayed nausea/vomiting significantly increases on days 2-4 after administration of cisplatin (Takahashi T et al., 2011). Aprepitant as a competitive inhibitor for the NK1 receptor may exert its antiemetic effect during cisplatin based chemotherapy.

In the light of these information, if placebo arm was added to the study to assess delayed emesis prophylaxis, the same results might be obtained in placebo arm. During initial prophylaxis the interaction of aprepitant

and dexamethasone would increase the effectiveness of dexamethasone via cytochrome system.

On the other hand the similar response rates in both aprepitant and dexamethasone arms during 2nd and 3rd days of treatment in patients who receives anthracycline brings up the question if other potential substances instead of substance P are responsible from delayed emesis.

As a conclusion, our proposal may be one design improvement to consider in future studies and further studies that are evaluating mechanism of emesis in non-cisplatin-containing anthracycline based chemotherapy should be considered.

References

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