



Letters

Re-challenging Patients with Oxaliplatin Allergy – The Successful Use of a Standardised Pre-medication Protocol in a Single Institute

Sir — Reports of hypersensitivity reactions to oxaliplatin have been increasing. We have previously reported an overall incidence of 15% and grade 3–4 reactions of 2.2% [1], similar to what has been reported elsewhere. Different re-challenge and desensitisation protocols for oxaliplatin have been reported, mostly in the form of case reports or small case series. Currently, there is no established standard approach for re-challenging patients who have developed hypersensitivity reactions to oxaliplatin with the same drug. Patients may also develop more severe hypersensitivity reactions when being re-challenged with oxaliplatin, despite an increase in pre-medications [1,2].

A simple re-challenge protocol for patients who have developed grade 1–2 hypersensitivity reactions to oxaliplatin has been used in our institute since August 2009. Twenty colorectal cancer patients who developed relatively mild (considered to be grade 1–2) hypersensitivity reactions to oxaliplatin on FOLFOX4 or XELOX regimens in our institute during August 2009 to May 2010 were re-challenged with oxaliplatin using a standardised re-challenge protocol (adapted from the BC Cancer Agency) [3]. The protocol included pre-medications using intravenous dexamethasone, diphenhydramine and ranitidine, as well as prolongation of the oxaliplatin infusion time (Table 1). If there was no recurrence of hypersensitivity reactions, chemotherapy was continued using the same protocol in subsequent cycles. Chemotherapy was stopped whenever any grades of hypersensitivity reactions recurred. We did not re-challenge patients who developed relatively severe (grade 3 or above) hypersensitivity reactions, those with a poor performance status, those considered unlikely to benefit from continuing oxaliplatin combination

Table 2

Characteristics of patients reported

Number of patients	
Male	11
Female	9
Total	20
Age (years)	
Range	43–73
Median	57.5
Chemotherapy schemes (no.)	
Adjuvant FOLFOX4	15
Palliative FOLFOX4 + cetuximab	4
Palliative XELOX + cetuximab	1
Average ($\pm$ standard deviation) number of cycles when hypersensitivity reactions occurred	7.5 ($\pm$ 2.7)

chemotherapy regimens, or those who refused to be re-challenged after considering the risks.

The characteristics of the 20 patients re-challenged are described in Table 2. Their initial hypersensitivity reactions to oxaliplatin occurred after an average of 7.5 cycles (standard deviation $\pm$ 2.7). Fourteen (70%) patients re-challenged with oxaliplatin using the standardised protocol successfully completed the subsequently scheduled chemotherapy cycles without recurrence of hypersensitivity reactions. The average number of cycles added after using the re-challenge scheme was 3.5 (standard

Table 1

Oxaliplatin re-challenge protocol

Dexamethasone 20 mg intravenous 45 min before oxaliplatin
Diphenhydramine 50 mg intravenous 30 min before oxaliplatin
Ranitidine 50 mg intravenous 30 min before oxaliplatin
Prolonging oxaliplatin infusion time to 6 h

Table 3

Outcome of patients re-challenged with oxaliplatin after the first development of hypersensitivity reactions

Outcome	Number of patients
Success	14
Failure	
In first re-challenge cycle	4
In second re-challenge cycle	1
In third re-challenge cycle	1
Total	20

Table 4

Features of hypersensitivity reactions at first presentation and during re-challenge

Initials	First occurrence (grade)	Second occurrence during re-challenge (grade)
HTY	Urticarial rashes over limbs and trunk; erythema over face and hands (grade 2)	Urticarial rashes over neck and upper shoulder (grade 2)
LWF	Urticarial rashes over upper anterior chest wall (grade 2)	Area of erythema over right chest wall (grade 2)
KKS	Itchy rashes over whole trunk (grade 2)	Itchy rashes over trunk and thigh (grade 2)
CKC	Itchiness over left palm and soles of feet (grade 2)	Erythematous rashes over right palm (grade 2)
FKW	Itchiness over palms and soles; subjective feeling of shortness of breath but no suggestion of bronchospasm (grade 2)	Erythematous rashes over right upper limb and neck; chest discomfort (grade 2)
YLH	Facial flushing with subjective feeling of shortness of breath but no suggestion of bronchospasm (grade 2)	Grade 2 hypersensitivity reactions (details not available)

deviation ± 1.6). Six (30%) patients had recurrence of hypersensitivity reactions. Four had reactions during the first re-challenge cycle and the remaining two during the second and third cycles (Table 3). The timing of occurrence of hypersensitivity reactions varied from after 20 min to upon completion of oxaliplatin infusion. None of these six patients had increased severity of allergic reactions compared with their initial presentations (Table 4), and the reactions subsided after appropriate treatments.

Our standardised approach is able to achieve a 70% success rate, which is similar to other larger series [1,4,5]. Details of pre-medications were either not mentioned or not standardised in many of these larger series. Our approach provides a standardised way for our clinical staff to re-challenge patients with hypersensitivity reactions towards oxaliplatin that avoids variations in the management approach, which can result in potentially variable and possibly suboptimal outcomes.

In conclusion, our protocol is safe and efficacious, and can be considered for patients with grade 1–2 hypersensitivity reactions towards oxaliplatin, especially when clinical benefit is shown and no effective alternative is available.

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Thyroxine Dosing after I131Radioiodine Ablation for Differentiated Thyroid Cancer

Sir — Differentiated thyroid cancer comprises less than 1% of all malignancies, but is the most common endocrine malignancy [1]. It is highly curable with a good prognosis, with 5 year mortality rates as low as 1–2% in younger patients [2]. Treatment is initially surgical with radioiodine ablation recommended for tumours greater than 1 cm [3]. Thyroid-stimulating hormone (TSH) suppression after radioiodine ablation is an important part of treatment. Tala and Tuttle [4] published their protocol for TSH suppression in 2010 and recommended aggressive TSH suppression (<0.1 mIU/l) for high-risk patients, but for most other patients a range from 0.1–0.4 mIU/l (similar to the British

Thyroid Association guidelines). They also suggested a much less aggressive range of 0.5–1.5 in very low-risk patients. The British Thyroid Association guidelines suggest that a dose of 175–200 μ g daily will be adequate in most patients. This does not, however, take into account variation in patient weight and size and this can lead to over- or under-dosing within a patient population, which can lead to significant toxicities.

Current practice in Leeds is for patients to commence weight-adjusted dosing as published studies have suggested that doses of 2–2.5 μ g/kg may be sufficient to suppress TSH [5]. Our practice is to recheck the TSH at