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Asthma, drug allergies and iodinated contrast media: A retrospective evaluation and proposed CT workflow

Dear Editor,

Contrast-enhanced computed tomography scans (CECT) are frequently employed in clinical practice. However, there are adverse reactions associated with the administration of intravenous iodinated contrast media (IOCM). Apart from contrast nephropathy, patients with asthma and multiple drug allergies have an increased risk of contrast-related reactions compared to the normal population.[1,2]

Reactions can be divided into minor (e.g. rash and itch), intermediate (e.g. hypotension and bronchospasm) or severe (e.g. angioedema and cardiorespiratory collapse), and further classified into immediate, delayed and late reactions.[3] Immediate reactions occur within the first hour after contrast administration. The incidence of mild immediate reactions has been reported to be up to 3%, and severe reactions in up to 0.04%.[3] Delayed reactions are classified as occurring from 1 hour to 1 week post-contrast injection, while late reactions are defined as hypersensitivity reactions occurring more than 1 week post-contrast administration. Both of these are usually self-limiting, requiring only symptomatic treatment or none at all.[4]

At Tan Tock Seng Hospital in Singapore, the Department of Radiology's standard protocol requires patients with asthma or multiple drug allergies (excluding allergy to contrast media) scheduled for CECT to be premedicated with oral prednisolone 10mg 3 times a day for 3 days prior to the scheduled scan. Those who did not take or complete this regimen had to have their CECT postponed and rescheduled. Outpatient scans are not deemed medically urgent and intravenous hydrocortisone is discouraged.

However, in practice, we find a degree of non-compliance to the steroid premedication guidelines, particularly so for outpatient scans. There are 3 main reasons for this: (1) referring clinicians fail to prescribe the required medications; (2) patients forget to purchase or collect the medications from the pharmacy; and (3) patients overlook completing the regimen prior to their scan. In the preceding 6 months prior to implementation of our modified workflow, the number of postponements was 181 cases with a rate of 30.2 cases per month. Similar statistics in 2017 and 2018 revealed 18.5 and 21.8 postponements per month, respectively, illustrating an increasing trend.

Recent literature is equivocal regarding the benefits of steroid prophylaxis in the prevention of adverse reaction to IOCM in these patients. While steroid premedication reduces occurrence of mild and moderate reactions, it appears to have minimal impact on severe reactions.[5] There is also suggestion that the use of premedication prophylaxis in patients with asthma is not necessary prior to contrast media administration, particularly when asthma is the sole indication or if it is well controlled.[4-7] Several major guidelines now do not mandate steroid premedication for patients with asthma or multiple drug allergies.[1,3,6-8] Furthermore, steroid premedication itself carries potential risks of hyperglycaemia and infection. Postponement may result in possible delay in diagnosis. Multiple sources have also shown a disproportionately large number of patients who need to be given prophylaxis, in order to prevent a reaction in a few, particularly for severe reactions.[1]

Based on the evidence, our institution has modified the existing protocol. Over a 6-month period from 1 August 2019 to 31 January 2020, outpatients who had inadequate steroid premedication on their day of scan were allowed to proceed with contrast administration for CECT if they had asthma (which had to be stable and well controlled) or multiple drug allergies, but not both. The Asthma Control Test (ACT) was used as screening tool, with stable well-controlled asthma defined as an ACT score of ≥20.[9] This questionnaire is easy to apply in an outpatient setting and has been locally peer reviewed to show good accuracy.[10] Multiple drug allergies was defined as being allergic to ≥4 classes of drugs (excluding contrast media).[1,5,6] Patients must also have been counselled, understood risks of IOCM administration and were agreeable to a 1-hour observation period after the scan. This was more conservative compared to the recommended 30 minutes.[4] Follow-up for adverse reactions was done in one of 2 ways: via phone for patients who consented to be contacted; or review of the electronic medical records up to the time of the next clinic appointment.

Over the study period, there were 120 outpatients who did not receive optimal steroid premedication but proceeded with their scans. Of these, there were 2 patients with asthma having ACT scores of 16 and 17 who were inadvertently included after being counselled. This occurred in the first month of implementation due to possible lack of clarity, and it was reiterated that having a suboptimal ACT score despite patient agreeing were not mutually exclusive criteria. Details of these patients are summarised in Table I.

Follow-up of our patients revealed that 5 patients had documented adverse reactions. Three had background of asthma while two had multiple drug allergies. The adverse reactions were rash and pruritus (n=3), wheal below the eye (n=1) and wheeze (n=1). Four of these patients developed symptoms during the 1-hour observation period and were managed accordingly before leaving the department. Phone review the next day revealed no recurrence of symptoms. One patient who was followed-up by phone described symptoms beginning only after leaving the department, but which had resolved at the time of review. All the adverse reactions were categorised as mild, and at worse, borderline moderate in the case of wheezing. They were self-limiting or resolved with simple treatment. The 2 asthmatic patients with ACT scores of 16 and 17 remained asymptomatic after the scan and on follow-up. Fischer's exact test shows no significant difference between the asthma and allergy cohort developing a reaction (P=0.227) and no difference by gender (P=0.647).

Over this period, another 24 patients' scans were postponed either because they did not meet the criteria or were not keen to proceed with the modified protocol. They had their scans after completing the premedications. Of these, 22 had asthma and 2 had multiple drug allergies. Only 1 patient with asthma developed a rash that was self-limiting and could be discharged from the department. The delay for these 24 patients ranged from 3 to 21 days, with an average of 7.25 days per patient. The risk ratio of a patient with asthma or multiple drug allergies developing contrast reaction if they did not take their premedication was 1.00, suggesting no significant benefit of steroid premedication in this group of patients.

Under the modified workflow, this translated to a reduction in computed tomography scan postponement number averaging 20 patients per month and a salvage rate of 83.3%. This achieves our aim of reducing

Table 1. Patient demographics

	Value	Mean age (years)
Age	20–88 years **n (%)**	60.9 (SD=14.99)
Sex		
Male	47 (39.2)	61.0 (SD=15.40)
Female	73 (60.8)	60.9 (SD=14.82)
Race		
Chinese	81 (67.5)	63.3 (SD=14.63)
Malay	15 (12.5)	52.5 (SD=11.58)
Indian	16 (13.3)	63.1 (SD=15.43)
Others	8 (6.7)	48.1 (SD =13.43)
Diagnosis		
Asthma	98 (81.7)	60.9 (SD=15.40)
Allergy	22 (18.3)	61.1 (SD=13.30)
Premedication		
Not premedicated	109 (90.8)	
Not prescribed	79 (65.8)	
Forgot to collect from pharmacy	17 (14.2)	
Forgot to begin the course	13 (10.8)	
Partially completed	8 (6.7)	
Uncertain status	3 (2.5)	
Mode of follow-up		
Phone call	100 (83.3)	
Review of electronic medical records	20 (16.7)	

SD: standard deviation

wastage of precious scan slots, lowering cost, preventing delays in diagnosis, as well as overcoming patient and caregiver inconvenience and dissatisfaction. Nevertheless, there are limitations to our study. Firstly, the sample size is small and selective, and not generalisable. Secondly, we relied on medical record review for 20 patients. The number of delayed or late reactions may be under-reported, particularly if the outpatient visit was too long from the time of scan or deemed unimportant compared to the main clinical problem. Fortunately, these reactions are usually mild and may thus be considered clinically inconsequential.

In conclusion, although steroid premedication is still currently part of our local institution guidelines for patients with asthma or multiple drug allergies undergoing CECT, in the event that steroid premedication was inadvertently not administered, it is generally safe to allow patients with asthma (stable and well controlled) or multiple drug allergies (other than contrast allergy) to receive intravenous IOCM, after counseling for risks. This would reduce CT scan postponement rates without compromising patient safety.[4]

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