Adverse reactions to intravascular contrast agents

Routine prophylaxis is not supported by evidence

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Acute life threatening reactions to intravascular x ray contrast enhancing agents are often labelled “anaphylactoid” because they may have some or all the features of anaphylaxis—such as bronchospasm, airway obstruction, angio-oedema, or cardiovascular collapse—but are not truly anaphylactic. They are usually seen after direct intravascular administration but can also occur after intracavitary administration. Whether such reactions can be prevented is a subject of much debate among radiologists: in this week’s *BMJ* a systematic review by Tramèr and colleagues finds little evidence to support the use of drugs to prevent serious reactions to contrast media.¹

Iodinated contrast media can be categorised into ionic and non-ionic types. The main difference is that ionic media break down into charged particles when entering a solution such as blood. Since the introduction of non-ionic agents, which are now used almost exclusively in the United Kingdom,^{w1} adverse reactions have become less common. Two large studies in Japan and Australia found fewer severe reactions with use of non-ionic agents than with ionic agents,^{2,3} although “severity” is a difficult subjective judgment unless it is clearly defined. The authors concluded that non-ionic agents were some 6-10 times safer than ionic agents. Only two deaths were reported, but survival alone may not be the most robust outcome measure because it is influenced by the expertise of those attempting resuscitation.

Various factors increase the risk of adverse reactions—a history of adverse reaction increases the risk sixfold, asthma increases it 6-10-fold,^{w2} and a history of allergic reactions to other drugs increases it substantially.^{w2, w3} Incidence is also higher in people taking β adrenergic blockers and interleukin 2.^{w4, w5} Race may be an associated risk factor: in the UK people of Indian subcontinent and Mediterranean origin have a significantly higher risk than the native population.^{w6} Identification of risk factors is rarely helpful, however, since most reactions occur in people without them.

Prophylaxis against anaphylactoid reactions has long been a preoccupation of radiologists. Prophylaxis with corticosteroids has been frequently recommended for at risk patients.^{4w7-w9} However, the mechanism of action is unclear, its efficacy not firmly established, and its use has not received universal support.^{5, 6} It gained some credence with the publication of a multicentre randomised trial in the United States which indicated that two doses of oral corticosteroid (methylprednisolone 32 mg) taken about 48 and 12 hours before the injection of a contrast agent

significantly reduced the incidence of reactions of all types except hives.⁴ The biggest claim was a reduction in “grade III” (severe) reactions by 60%. However, the paper has been criticised for its statistical analysis,^{6, w10} on the variations in the numbers of people entered from the 27 participating hospitals (a range of 10-1888 patients during the four year intake), and because one person in the study may have died as a result of being given corticosteroids. If this death is included in the analysis the use of corticosteroids becomes more dangerous than the use of ionic contrast media alone.

Further evidence against the use of corticosteroids comes from a large randomised trial that compared ionic contrast agents alone, ionic contrast agents combined with corticosteroid prophylaxis (the regimen recommended by Lasser et al⁴), and non-ionic agents alone.⁵ This found dramatic differences in the incidence of severe reactions in the three groups—0.32% with an ionic agent alone, 0.25% with an ionic agent and corticosteroid prophylaxis, and 0.01% with a non-ionic agent alone. People with no definable risk factors who received the ionic agent plus corticosteroid prophylaxis had more reactions than those receiving the ionic agent alone.

Other approaches such as use of antihistamines and ephedrine have also been advocated, often in combination with corticosteroids,^{w11} but they are not evidence based and have gained little favour. Pretesting for adverse reactions by intravenous or subcutaneous injection of contrast agent is discredited and should not be performed.^{w12, w13}

Recent guidelines from the Royal College of Radiologists emphasise the lack of evidence to support prophylaxis. The present consensus among UK radiologists is that its efficacy is unproved and that the safety of non-ionic agents outweighs any gains provided by prophylaxis. The systematic review in this week’s *BMJ* is welcome support for this position¹ despite being open to criticisms itself, not least for the improper use of the term anaphylactic. The authors also consider arterial hypotension to be an “allergy related” syndrome that is “potentially life threatening”; but, if looked for, this is an extremely frequent event and is probably mediated by the effects of contrast agent on smooth muscle. Furthermore, they consider a broad range of adverse reactions in their review, including minor effects such as nausea which have, at

best, a tenuous relation to the more serious events of real interest.

These criticisms aside, however, this review is welcome as it provides further support for the contention that prophylactic treatments are unnecessary.

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Bullying and harassment in medical schools

Still rife and must be tackled

Recent changes in undergraduate medical education have been rapid and profound. Faced with the explosion of knowledge, ongoing technological advances, patients' changing expectations, the recognition of health inequalities worldwide, and better understanding of educational theory, medical educators have striven to provide undergraduate programmes that equip students with basic knowledge, skills, and attitudes that recognise their immediate progression into independent practice and their need to develop skills as lifelong learners.

What remains familiar at the core of medical education is exposure to patients with their multifaceted problems and the experience of health care at the point of delivery. Sadly, clinical practice also exposes medical students to some of the best recognised yet least easily solved problems in medical education: bullying and harassment. A study by Frank and colleagues in this week's *BMJ* reports the experiences of US medical students of this important but uncomfortable issue that needs to be tackled.¹

Bullying and harassment occur in all organisations, although rates seem to be higher in healthcare institutions,^{2,3} and such behaviour may be more common in medical faculties than in other higher education departments.⁴ Many definitions of bullying and harassment exist,^{5,6} and can be categorised into threats to professional status, threats to personal standing, isolation, overwork, and effects on self confidence. In all cases bullying behaviour is persistent, malicious, and undermining. It has important effects on the psychological wellbeing of the bullied and harassed person in terms of future performance, career choice, and retention within the profession.

Frank and colleagues describe the extent to which belittlement and harassment were reported by medical students in the United States in a large study of more than 2300 students from 16 medical schools at three different time points in their studies.¹ By the end of the course 85% of students reported having been harassed or belittled and 40% had experienced both. These findings were not influenced by ethnic origin or gender. The perpetrators included other students and patients, but residents and attending doctors or clinical professors were most often to blame. In all, 13% of respondents reported these incidents to be severe.

The authors asked about specific groups of medical staff and patients but not about other healthcare professionals. In a recent cross sectional survey by the British Medical Association of 297 UK medical students,⁷ bullying was reported, but UK students held nurses (a group not reported in the US study) to be the second most likely perpetrators. Interestingly, rates of bullying and harassment were much lower among UK students than US ones—83% reported no incidents through their entire medical school career.

These data and the results of numerous other studies should be interpreted with caution. Many studies are small, cross sectional, and conducted by faculty members of the students' institution; others ask for specific instances of abuse such as sexual harassment or racism. In general, bullying and harassment are more commonly reported by female students. However, the high rate of reported incidents of bullying in Frank and colleagues' study is striking.¹

Medical students in the US tend to be older than their UK counterparts and may have a greater awareness of unacceptable professional behaviour or a lower threshold of tolerance. Other cultural, educational, and contextual differences may underpin the results from the US. Given that the incidence of bullying and harassment in the United Kingdom's health service is high,² it is unlikely that UK medical students are not exposed to these behaviours. Most probably UK students develop coping strategies such as peer support, deliberate intervention in teaching sessions, or ignoring unwanted events as they arise.⁸

Not all students have the psychological characteristics to respond in this way, however, and those that do may perpetuate the problem as they qualify and move into the workforce. Other students may be reluctant to report incidents of harassment, may just regard it as normal behaviour, or may even think that harassment and humiliation are useful educational experiences.⁹ On the contrary, it is clear from the available evidence that bullying and harassment can have profoundly negative effects. Severe harassment and belittlement may be associated in students with higher rates of alcohol misuse, depression, and suicidal intent and with lower satisfaction with their chosen career as a doctor.¹

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