The Evidence for and Against Corticosteroid Prophylaxis in At-Risk Patients

Matthew S. Davenport, MD, FSAR, FSCBTMR[a,*],
Richard H. Cohan, MD, FSAR[b]

KEYWORDS

• Corticosteroid prophylaxis • Steroid preparation • Allergiclike reaction • Anaphylaxis
• Contrast material • Premedication • Pretreatment

KEY POINTS

- Corticosteroid prophylaxis is commonly used in the United States for the prevention of allergiclike reactions to iodinated and gadolinium-based contrast material in patients at highest risk of an allergiclike reaction.
- Corticosteroid prophylaxis causes short-term (24–48 h) hyperglycemia that is on average 40 to 150 mg/dL higher than a patient's baseline and is greatest in diabetics and rarely, if ever, causes hyperglycemia-related complications.
- Corticosteroid prophylaxis has a weak mitigating effect on allergiclike reactions, is unlikely to affect the severity of subsequent reactions, and does not prevent all reactions.
- The number needed to treat with corticosteroid prophylaxis to prevent 1 allergiclike reaction-related death in high-risk patients receiving low-osmolality iodinated contrast material is approximately 50,000.
- In the inpatient population, corticosteroid prophylaxis is likely associated with substantial cost and indirect harm related to length-of-stay prolongation that may exceed the benefits premedication is intended to provide in this population.

INTRODUCTION

Allergiclike reactions to modern low-osmolality iodinated contrast media (LOCM) and iso-osmolality iodinated contrast media (IOCM) are uncommon, occurring after approximately 0.6% of intravenous administrations in the general population.[1,2] Although most are mild[1,2] and consist of limited urticaria, moderate (eg, bronchospasm) and severe (eg, anaphylactic shock) reactions can occur.[1,2] The estimated risk of a severe reaction to LOCM or IOCM is approximately 4 in 10,000,[1] and the risk of death is estimated to be less than 1 in 170,000.[1] These risks are even less for gadolinium-based contrast material (GBCM), in which the reaction rate is approximately 0.05% to 0.33%[3–5] and the risk of death is 0.1 to 2.7 per million.[5]

In the United States, patients who are considered at highest risk of an allergiclike reaction to contrast material are often given corticosteroid prophylaxis. This prophylaxis usually consists of a 12- or

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[a] Department of Radiology and Urology, Michigan Radiology Quality Collaborative, University of Michigan Health System, 1500 East Medical Center Drive, B2-A209P, Ann Arbor, MI 48109, USA; [b] Department of Radiology, University of Michigan Health System, 1500 East Medical Center Drive, B2-A209P, Ann Arbor, MI 48109, USA
* Department of Radiology, University of Michigan Health System, 1500 East Medical Center Drive, B2-A209P, Ann Arbor, MI 48109, USA
E-mail address: matdaven@med.umich.edu

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13-hour multidose regimen with or without diphenhydramine. Prophylaxis is given before contrast material administration because (1) it is considered the standard of care in the United States for patients at highest risk (eg, prior moderate or severe allergiclike reaction), (2) there may not be an adequate imaging alternative (ie, contrast material for a particular examination is deemed necessary), (3) switching contrast agents within a class of substances (eg, from one LOCM or IOCM to another, or from one GBCM to another) has been incompletely studied, and (4) corticosteroid prophylaxis is considered a low-risk intervention.[6,7]

In other countries, corticosteroid prophylaxis is not commonly administered because (1) there is no level I evidence that prophylaxis reduces mortality, (2) there is no level I evidence that prophylaxis reduces the incidence of moderate or severe reactions to LOCM or IOCM, and (3) there is no level I evidence that prophylaxis reduces the reaction rate in high-risk patients.[8–10] This lack of an international standard highlights differences in how national guidelines are developed, differences in the priorities of national health care systems, and differences in how data supporting and opposing prophylaxis are interpreted. This review summarizes the literature supporting and opposing the use of corticosteroid prophylaxis, describes the evidence base behind different premedication regimens, reviews national guidelines and standards of practice, and compares the known benefits with the potential harms of prophylaxis.

HISTORICAL PERSPECTIVE

Corticosteroid prophylaxis was popularized in the 1980s for the prevention of contrast reactions related to intravenous urography, angiography, and contrast-enhanced computed tomography (CT).[8,11,12] At that time, most intravascular administrations were with high-osmolality iodinated contrast material (HOCM), which had an adverse event rate 4- to 10-fold higher than LOCM and IOCM.[1] Because of the commonality (overall rate, 12.7%) and seriousness (severe reaction rate, 0.22%) of these reactions in the general population[1] and the necessity of iodinated contrast material for diagnosis, determining a way to reduce the incidence of contrast reactions was considered important. Therefore, early experiments with prophylaxis were conducted in the general population and in high-risk cohorts.[8–11]

Premedication of Average-Risk Patients

The 2 trials with the greatest level of evidence supporting prophylaxis for the prevention of contrast reactions were performed in average-risk patients.[8,9] This design decision was presumably made for the first HOCM trial[8] because there was a strong interest in reducing the reaction rate in all patients. When a second trial was conducted with LOCM in the early 1990s by the same group,[9] average-risk patients were used again despite the lower reaction rate of LOCM compared with HOCM. This second study included a much smaller number of patients. Therefore, these 2 trials, although blinded and randomized, do not directly inform the effect size of prophylaxis in high-risk patients receiving modern LOCM or IOCM.

The first of these 2 trials, published in 1987,[8] randomly assigned 6763 average-risk patients to 1 of 3 arms: 32 mg oral methylprednisolone 12 and 2 hours before HOCM, 32 mg oral methylprednisolone 2 hours before HOCM, or placebo. Since that time, the 12-hour and 2-hour methylprednisolone premedication regimen used in these studies has been termed the *Lasser prep* after the first author of these trials (**Box 1**). This study found that the 2-hour regimen did not reduce reaction rates but that the 12-hour regimen significantly did—reducing the rate of aggregate reactions (9.0% vs 6.4%), reactions necessitating therapy (2.2% vs 1.2%), and grade III reactions (0.7% vs 0.2%; eg, shock, bronchospasm, laryngospasm or edema, loss of consciousness, convulsions, lowering of blood pressure, cardiac arrhythmia, angina, angioedema, pulmonary edema). This trial

Box 1
Common premedication regimens

Lasser 12-hour regimen[8,9]

- 32 mg oral methylprednisolone 12 h prior
- 32 mg oral methylprednisolone 2 h prior

Greenberger 13-hour regimen[11,12]

- 50 mg oral prednisone 13 h prior
- 50 mg oral prednisone 7 h prior
- 50 mg oral prednisone 1 h prior
- 50 mg oral diphenhydramine 1 h prior

Emergent/rapid regimen[15]

- 200 mg IV hydrocortisone immediately
- 200 mg IV hydrocortisone every 4 h prior
- 50 mg IV diphenhydramine 1 h prior

Data from O'Malley RB, Cohan RH, Ellis JH, et al. A survey on the use of premedication prior to iodinated and gadolinium-based contrast material administration. J Am Coll Radiol 2011;8:345–54.