

The Safety of First-Dose Home IV Antibiotic Therapy

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ABSTRACT

Background: The first dose of home IV antibiotic therapy is traditionally administered under a physician's supervision because of concerns about unpredictable immediate allergic reactions. In some jurisdictions, patients also have the added expense of purchasing epinephrine kits.

Objective: To evaluate the standard of care and to develop evidence-based guidelines for patients receiving IV antibiotics at home.

Methods: Information was gathered through a literature review, analysis of reports retrieved from the Canadian Adverse Drug Reaction Information System (CADRIS) database, a survey of the policies of Ontario Community Care Access Centres (CCACs), and opinion polls of pharmacists interested in parenteral antibiotic therapy and of infectious disease physicians.

Results: A literature search did not yield any reports on the incidence of adverse drug reactions with the first dose of IV antibiotics. About half of anaphylactic reactions reported to CADRIS during the past 8 years in which an IV antibiotic was the suspected drug occurred with initiation of therapy. Of the 29 CCACs that responded to the survey (67% response rate), 21 (72%) allowed the first dose of IV therapy to be given at home. Most of the specialists surveyed have protocols regarding home IV antibiotic therapy. In most cases, patients were not required to purchase epinephrine.

Conclusions: In certain situations, it should be possible to initiate home IV therapy with antibiotics under the supervision of a nurse, but in other situations (e.g., allergy to medications, patient preference), such therapy should be started under the supervision of a physician. A decision algorithm was developed.

Key words: IV antibiotics, home IV administration, first dose, guideline

RÉSUMÉ

Historique : La dose initiale d'antibiotique dans le cadre d'une antibiothérapie intraveineuse (IV) à domicile est habituellement administrée sous la supervision d'un médecin, à cause des risques de réactions allergiques immédiates imprévisibles. Dans certaines régions, les patients doivent en plus acheter des trousseaux d'épinéphrine.

Objectif : Évaluer le traitement standard et élaborer des lignes directrices fondées sur des données probantes à l'intention des patients sous antibiothérapie IV à domicile.

Méthodes : On a procédé à la collecte d'information à partir de l'examen de la littérature, de l'analyse de rapports tirés du système canadien d'information sur les effets indésirables des médicaments (Canadian Adverse Drug Reaction Information System—CADRIS), des résultats d'un sondage sur les politiques des Centres d'accès aux soins communautaires de l'Ontario (CASC), et de sondages d'opinion auprès de pharmaciens intéressés par l'antibiothérapie parentérale et de médecins infectiologistes.

Résultats : La recherche dans la littérature n'a pas permis de dégager de rapports sur l'incidence des effets indésirables suivant la dose initiale d'antibiotiques IV. Près de la moitié des réactions anaphylactiques consignées dans CADRIS au cours des 8 dernières années, dont on soupçonnait un antibiotique IV d'en être responsable, sont survenues au début du traitement. Des 29 (67 %) CASC qui ont répondu au sondage, 21 (72 %) ont permis l'administration à domicile de la dose initiale d'antibiotique IV. La majorité des spécialistes sondés avaient des protocoles d'antibiothérapie à domicile. Dans la plupart des cas, les patients n'avaient pas à acheter d'épinéphrine.

Conclusions : Dans certaines situations, il devrait être possible d'amorcer l'antibiothérapie IV à domicile sous la supervision d'une infirmière, mais dans d'autres cas (p. ex. allergie médicamenteuse, préférence du patient), l'antibiothérapie devrait être amorcée sous la supervision d'un médecin. Un algorithme de décision a été élaboré.

Mots clés : antibiotiques intraveineux, administration intraveineuse à domicile, dose initiale, lignes directrices

Can J Hosp Pharm 2006;60:106-113



INTRODUCTION

Home IV administration of antibiotics has evolved dramatically over the past 15 years, and this mode of therapy has become an important tool for the management of patients requiring long-term parenteral administration of antibiotics. Many models exist for outpatient delivery of antibiotic therapy, including home-based therapy administered by a visiting nurse, self-administration, and therapy in an infusion centre. Because of the greater risks of accelerated or immediate adverse reactions associated with IV as opposed to oral drug therapy,¹ administration of the first IV dose in a medically supervised setting is advocated by most health care professionals, as reflected in the 2004 practice guidelines of the Infectious Diseases Society of America.²

This requirement may be onerous for patients who need to travel a long distance to a health care facility or physician's office to receive the first dose, a situation that is likely to arise more frequently as fewer people are admitted to hospital and an increasing number of patients receive outpatient IV antibiotic therapy. In addition, some studies have shown that prompt administration of parenteral antimicrobial agents has improved patient outcomes,^{3,4} which suggests that the delay associated with obtaining physician supervision for the first dose may be detrimental to therapeutic outcomes.

In Ontario, home IV antibiotic therapy is coordinated by regional Community Care Access Centres (CCACs) and is provided by visiting nurses from agencies hired by the CCACs. Each CCAC has its own policy governing the administration of first-dose IV antibiotic therapy. For the Kingston, Frontenac, Lennox, and Addington CCAC, the contract with the nursing agency specifies that patients must have epinephrine available throughout the course of IV therapy, to be used by the visiting nurse in case of anaphylaxis. This requirement can be contentious, since the cost of this medication is often not covered by third-party insurance.

An adverse reaction to a drug, including drugs administered intravenously, can be categorized as an exaggerated therapeutic effect, a toxic effect, or a hypersensitivity (immunologic or allergic) response. Hypersensitivity reactions to drugs have been estimated to represent up to one-third of all drug reactions,⁵ and antibiotics constitute the class of medications most commonly associated with severe allergic reactions such as anaphylaxis.⁶ Therefore, this investigation into the safety of IV therapy focused on hypersensitivity reactions to antibiotics.

This study was undertaken to evaluate the need for physician supervision of first-dose IV therapy and the need for patients to purchase epinephrine kits.

METHODS

An evidence-based algorithm to determine location and level of supervision for the first dose of IV therapy and the need for patients meeting safety criteria for home IV antibiotic therapy to purchase epinephrine kits was formulated by author consensus. The algorithm was intended for potential use by organizations and health care workers involved in coordinating, prescribing, or administering outpatient IV antibiotic therapy. Evidence was gathered using a four-pronged approach: literature review, review of the Canadian Adverse Drug Reaction Information System (CADRIS) database, survey of CCACs, and survey of health care professionals.

Literature Review

Two literature searches were performed: one for the incidence of adverse reactions to first-dose IV antibiotics and one for occurrence of anaphylaxis with home IV therapy. For both searches, the databases were Ovid MEDLINE (January 1966 to week 1 of November 2006); Ovid MEDLINE in-process and other nonindexed citations (as of November 9, 2006); EMBASE (January 1980 to week 44 of 2006); all evidence-based reviews in the Cochrane Database of Systematic Reviews, the ACP Journal Club database, the Database of Abstracts of Reviews of Effects, and the Cochrane Controlled Trials Register; International Pharmaceutical Abstracts (January 1970 to October 2006); Ovid Healthstar (January 1966 to September 2006); CINAHL (January 1982 to week 1 of November 2006); and Web of Science (January 1900 to November 2006). Unpublished data sources were not searched. Articles in all languages and articles of all types (except case series) were included. References from all relevant articles were reviewed to identify additional sources.

For the incidence of adverse reactions to first-dose IV antibiotics, the search terms were "intravenous", "iv", "infusion", "antibiotic", "antibacterial", "anti-infective", "allergy", "anaphylaxis", "side-effect", "adverse effect", and "hypersensitivity", and permutations of these terms. Medical Subject Heading (MeSH) terms were {"antibacterial agents" or "anti-infective agent, local/urinary"} and {drug hypersensitivity} and {"infusions, intravenous" or "injections, intravenous"}. Similar MeSH terms were used when searching the other databases individually as appropriate. The titles of 55 human studies were retrieved, of which 15 were excluded because they did



not pertain to antibiotic treatment. Thirty-five abstracts were excluded as they did not pertain to IV therapy or to drug adverse effects, or because they were case reports. Of the remaining articles, 3 did not specify time to onset of adverse effect after start of infusion and were thus excluded. Two articles remained for analysis.

For anaphylaxis in home IV therapy, the terms (“home infusion therapy” or “home intravenous therapy”) and “anaphylaxis” were used. A total of 34 articles were identified, but 30 were excluded because they did not discuss antibiotic therapy, 2 did not pertain to anaphylaxis, and 1 was a case series. Only 1 article remained, and it had also been found in the other literature search.

Search of CADRIS Database

The CADRIS database (http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/index_e.html) was searched for all adverse reactions reported between January 1, 1998, and March 31, 2006, and classified as “allergic”, “anaphylactic”, “anaphylactoid reaction”, “anaphylaxis”, or “anaphylactic shock”, where an IV antibiotic was identified as the suspected or a concomitant drug. Records for these adverse reactions were extracted and analyzed by one author (S.M.) to ascertain the details of drug administration and outcome.

Survey of CCACs

A voluntary survey (Appendix 1) of the policies and practices of CCACs in Ontario was administered by e-mail. The survey included questions about first-dose IV administration of medication and requirements for epinephrine availability. Follow-up to nonresponders was performed by e-mail and/or telephone calls 2 weeks after the initial request. This survey was not formally validated.

Survey of Health Care Professionals

A voluntary survey was administered by e-mail to physicians affiliated with the Canadian Infectious Disease Society (CIDS) (Appendix 2) and pharmacists registered with the Canadian Society of Hospital Pharmacists Professional Specialty Network (PSN) for those with an interest in infectious diseases and/or parenteral therapy (Appendix 3). The survey sought information about policies for first-dose outpatient IV administration of antibiotics and for epinephrine availability, as well as expert opinion regarding the safety of first-dose outpatient IV antibiotic therapy for certain patient groups and the need for epinephrine prescription. The survey was not formally validated and was sent only once.

RESULTS

Literature Review

No studies were found specifically examining rates of anaphylaxis or other adverse events with the first dose of IV antibiotic therapy.

In an Australian prospective study of 770 patients who received the first dose of home IV therapy under medical supervision, there were no cases of anaphylaxis or other life-threatening adverse reactions.⁷ A total of 1000 courses of home IV therapy were given, with 25 different antibiotics for 37 conditions. Three patients (0.4% of the cohort) experienced delayed angioedema (with flucloxacillin in 2 cases and ceftazidime in the third case). All patients responded rapidly to withdrawal of the drug, and none required epinephrine. There were 28 allergic reactions, with a mean time to reaction of 19.6 days (range 1 to 39 days) after commencement of treatment. Dobson and others⁷ suggested that routine supply of epinephrine for anaphylaxis is not warranted, given the cost of this drug and its instability at extreme temperatures. There were also concerns about administration of epinephrine: patients may not recognize the signs of anaphylaxis, may not administer the epinephrine in time, or may not prepare the epinephrine appropriately.

In a prospective, randomized, double-blinded, placebo-controlled study (with 19 patients in each arm), Renz and others⁸ examined the efficacy of antihistamine pretreatment in preventing “red man syndrome” in patients undergoing elective orthopedic surgery and receiving vancomycin by rapid infusion (1 g over 10 min). The exclusion criteria included a history of atopy and active asthma. Although 1 patient who received antihistamine pretreatment and 12 control patients experienced hypotension and other allergic symptoms, none of the patients experienced recurrence of their symptoms or rash after a switch to the standard infusion rate for vancomycin (1 g over 1 h).

Search of CADRIS Database

Among all reactions reported in Canada between January 1, 1998, and March 31, 2006, 386 reports were compatible with anaphylaxis. Only 27 of these reports identified an IV antibiotic as the suspected medication; an additional 6 reports listed at least one IV antibiotic as a concomitant medication. β -Lactams were the most commonly implicated (12 reports in total: cephalosporins in 8 cases, penicillins in 2, an aminoglycoside and penicillin in 1, and a cephalosporin and carbapenem in 1). Fluoroquinolones and macrolides were implicated in 4 reports each, vancomycin in 3 reports, and



amphotericin B, clindamycin, aztreonam, and imipenem–cilastatin in 1 report each. Overall, cefazolin was the most commonly implicated antimicrobial (total of 7 reports). All but 2 reports indicated that patients were receiving several other medications in addition to the suspected drug.

Fourteen of the 27 reports described the reaction as occurring on the first dose or day of IV administration of the suspected antimicrobial. In 3 cases, the patients died; 2 of the deaths were associated with anaphylactic reaction after a first dose of cefazolin. In 7 cases, the patient had not yet recovered or the outcome was unknown at the time of reporting. Recovery without sequelae was reported for the other cases.

Survey of CCACs

Ontario's 43 CCACs have various policies and practices regarding the location of and extent of physician supervision during administration of the first dose of home IV therapy. Of the 29 CCACs that responded to the survey (67% response rate), 21 (72%) indicated that they allow the first dose of IV therapy to be given at home on a case-by-case basis; only 11 (52%) of these 21 CCACs had specific inclusion or exclusion criteria for initiation of home IV therapy. Inclusion criteria for administering the first dose at home under a nurse's supervision included recent use of the drug without complications, referrals from the community, and indications specific to the type of drug given and concurrent medications. For example, patients are not approved for home IV therapy if they are receiving β -blockers or anti-adrenergics, as these medications can attenuate the therapeutic effects of epinephrine administered for anaphylaxis.

In some jurisdictions, the contracted nursing agencies dictate the eligibility criteria for patients to receive the first dose at home. These policies give consideration to safety issues for both the patient (e.g., adverse drug reactions) and the nurse involved (e.g., remoteness of the client's home and travel restrictions imposed by adverse weather conditions). At least 3 CCAC respondents commented that most contracted nursing agencies are reluctant to administer the first dose at home because of the potential legal implications of assuming full responsibility for the patient's safety.

Surveys of Health Care Professionals

Different versions of the survey were sent to the 2 groups of health care professionals (physicians and pharmacists), so the responses were not combined. The

response rate was low: 18/254 (7%) and 10/220 (5%) for the CIDS and PSN surveys, respectively. Most respondents in both groups had policies specifying that the first dose of IV antibiotic be administered in hospital. One policy waived the requirement that the first dose be given under direct medical supervision for patients who had previously received the same antibiotic class from home care. Another policy allowed first-dose IV administration without direct medical supervision for clients receiving palliative care who had "do not resuscitate" orders and who had given informed consent after being advised of the risks of a severe reaction. Most pharmacist respondents who had policies regarding epinephrine availability required visiting nurses to carry epinephrine at all times.

DISCUSSION

The search of the published literature yielded no cases of anaphylaxis in patients receiving standard doses of IV antibiotics at standard rates of administration in hospital or as outpatients, and no allergic reactions to medications within a day of initiation of IV antibiotic therapy. Still, the results of the vancomycin study were limited by small sample size.⁸ However, no studies specifically designed to determine the incidence of adverse effects with the first dose of IV antibiotics were identified.

The overall incidence of anaphylactic events with the first dose of IV antibiotics in Canada could not be determined from the CADRIS database alone, as information for this database is collected primarily through voluntary reporting, which results in underestimation of adverse reaction rates. In many cases, the database information is also incomplete, without consistent specification of the route of drug administration or timing of adverse reactions with respect to the first dose. However, the 14 reports of anaphylaxis in association with first doses of IV antimicrobials, 2 of which resulted in death, are cause for serious consideration. A key factor missing from these reports is information about patient susceptibility to hypersensitivity reactions (e.g., history of previous reactions to drugs of the same class or any other drug).

The results of the literature and CADRIS searches highlight the need for more standardized data collection and interpretation of drug-related adverse effects. Particularly important would be data about the timing of these events with respect to initiation of therapy for patients receiving IV antibiotics.

Although the incidence of hypersensitivity reactions to any agent is difficult to determine because the clinical manifestations are often indistinct, with severity ranging

from a mild rash to shock and death,⁹ β -lactams (such as penicillins and cephalosporins) and sulfonamides are known as the most likely to induce an immunologic reaction.¹⁰ Penicillins are the most common therapeutic drugs causing anaphylaxis. Allergy to penicillin is estimated to exist in 0.7% to 10% of the population, causing approximately 75% of fatal anaphylaxis cases in the United States⁶ and an incidence of anaphylaxis of 32 cases per 100 000 exposures.¹¹

Nevertheless, the overall incidence of anaphylaxis due to medications is reportedly low. In an international multicentre study, the prevalence of severe anaphylaxis to drugs was 135 per million hospital inpatients. Of these reactions, 57% occurred within the first 2 days of drug administration and 75% occurred within the first 5 days.¹² The in-hospital mortality rate has been estimated at 5% in cases of severe anaphylaxis. In a 20-year Dutch retrospective cohort study, the estimated annual incidence of drug-induced anaphylaxis was approximately 3 to 4 events per million people.¹³ Fatal drug-related anaphylactic shock was very rare in Denmark, with an estimated rate of 0.3 per million inhabitants per year.¹⁴ In a 5-year retrospective international study, the estimated incidence of drug-induced anaphylaxis was 5 to 15 per 100 000 exposures.¹¹

The CCAC, CIDS, and PSN surveys were created to compare existing policies of infectious disease specialists and other health care professionals involved in IV antibiotic therapy. The results indicate that the majority of hospitals and practices require the first dose of IV antibiotics to be administered in hospital, despite a lack of substantive evidence that this is the best practice in terms of efficiency, patient satisfaction, and resource management.

Investigation of the various CCAC policies for first-dose administration of home IV therapy uncovered a lack of consensus about the standard of care and what constitutes acceptable risk. Without consensus, it is foreseeable that policies may progress toward an American-style "avoid-litigation-at-any-cost" approach, which evades safety assessment and may limit the best use of health care dollars. As seen in the results from the CCAC survey, private for-profit nursing agencies are already more resistant to giving the first dose of therapy at home than are nonprofit agencies. Contextual factors play a role in policy, with some jurisdictions accommodating issues such as physician shortages and problems related to access to care in rural settings.

Certain concerns are especially pertinent for rural regions with a paucity of physicians. One CCAC respondent commented that physicians in the region overwhelmingly chose to have the patient sent to

hospital rather than travelling to the patient's home. The benefit derived from the presence of a physician instead of a trained nurse during an anaphylactic reaction is debatable. Hence, it could be more efficient and convenient for all parties involved if the constraint for physician supervision were waived.

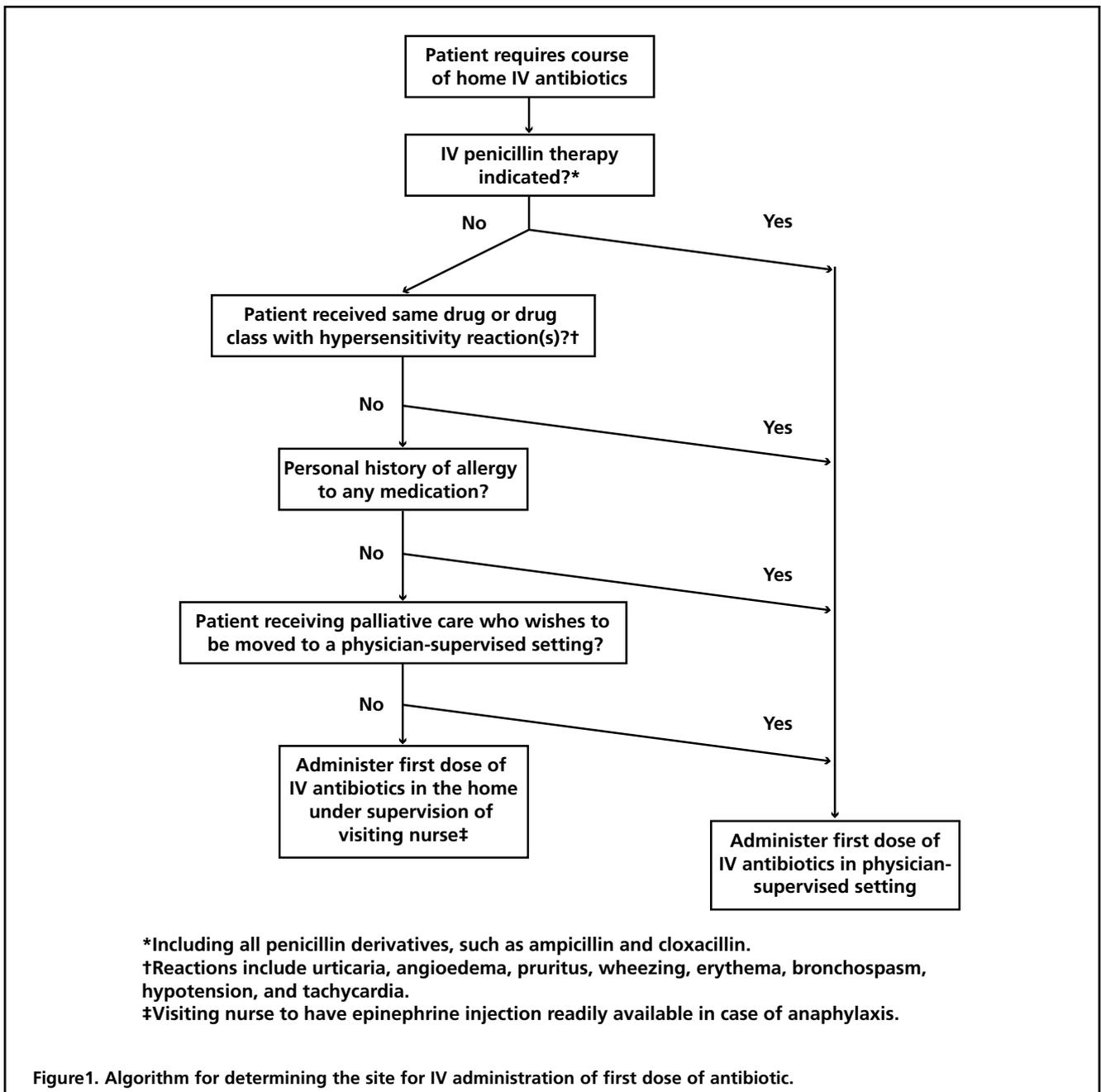
Even if this change were made, a number of hurdles remain. Nursing agencies have their own stringent criteria for deciding whether to administer the first dose without medical supervision, and such criteria could override patient preferences by giving more weight to the potential for adverse medical and legal consequences. However, if standard policies were adopted, nursing agencies might be more willing to have nurses administer the first dose in the home. This conjecture lends support to the need for revisions to policies for home IV antibiotic therapy, as many existing CCAC policies date back to the early 1990s, when home IV programs were established.

As seen in the study by Dobson and others,⁷ the acquisition of epinephrine by patients can be problematic. In the study reported here, only one CCAC required the purchase of epinephrine as mandatory for patients receiving home IV antibiotic therapy. In both the CCAC and PSN surveys, the majority of respondents had a policy requiring the visiting nurse to carry epinephrine at all times. Such a policy avoids the inconvenience of patients acquiring their own supply. It is also a more logical choice, as the intent is for the visiting nurse to administer the epinephrine, if it is required. The proposed policy revision does not preclude prescribing epinephrine for patients if the physician deems it necessary.

The problems related to the safe administration of first-dose IV antibiotic therapy in the outpatient setting could be addressed by different strategies. Infusion centres constitute a medically supervised setting for outpatient administration of antibiotics to patients who are physically able to attend such clinics. Maintenance of a home-based model for administration of IV antibiotic therapy requires an algorithm for determining the appropriateness of administering the first dose at home.

Such an algorithm was developed on the basis of the evidence gathered in this study. The proposed guideline (Figure 1) reflects the authors' interpretation of current data and is in keeping with McNutty's 1993 conclusion that "first-dose antimicrobial therapy can be administered safely in the home"¹⁵ with approval by the patient's physician and appropriate planning. McNutty also recommended that drugs with a high frequency of allergic reactions, such as penicillin, be first administered





in hospital, at a slow infusion rate for the first 5 to 10 minutes, and that complete anaphylaxis kits be carried by the nurses. Before the algorithm developed in the current study is applied to any patient population, it should be piloted by the home care agencies and physicians to determine its practicability and compliance and to address any concerns that arise. As with any medical treatment, IV antibiotic therapy carries inherent risk. Informed consent should be obtained before administration of the first dose of IV antibiotics in the home.

Although the response rate to the CCAC survey was fair, it was far from ideal, as the survey was intended to gather statistics on CCAC policies (i.e., not an opinion poll). Another approach to gathering these data would be to ask all CCAC managers to submit their respective policies regarding home IV therapy, if such documents exist. It is unclear whether the CCACs that failed to respond did not provide outpatient antibiotic therapy or did not have formal policies on home IV therapy, or whether the lack of response was due to lack of time or availability to find and provide the necessary information.



Although limited by low response rates, the CIDS and PSN surveys collated information on policies for first dosing of IV antibiotics on a national basis. The low response rate may be attributed to the surveys being sent by e-mail to listservs, where messages may be numerous, read infrequently, or even treated as junk mail. These surveys were not resent, as they were entirely voluntary, and respondents who were interested in replying would probably have responded to the first request. In certain regions, there may be a small number of infectious disease specialists serving a large population; even if they responded, the results might not be representative. Use of a formal survey with validated questions may increase response rates. A validated survey could also delineate the current standard of care in Canada, for example, to answer whether there are differences between provinces or between rural and urban centres.

The results of this study emphasize not only the need for revisions to current policies governing home IV antibiotic therapy, but also the utility of developing standard protocols that balance available evidence with best practice. Further investigations such as a formal survey to demarcate standard of care will help to develop standard protocols. The proposed algorithm for first-dose home IV antibiotic treatment is a first step toward addressing 2 pertinent issues that have both clinical and economic impact: the location of first-dose administration and the prescription of epinephrine for each patient. Although the algorithm should be piloted before it is implemented as standard practice, the proposed guideline may allow for more efficient delivery of home IV antibiotic therapy and reduce patient inconvenience and costs associated with visits to clinics and physicians' offices, while maintaining patient safety as the priority.

References

1. Kishiyama JL, Tevrizian AT, Avila PC. Drug allergy. In: Parslow TC, Stites DP, Terr AI, Imboden JB, editors. *Medical immunology*. 10th ed. New York (NY): Lange Medical Books/McGraw-Hill; 2001.
2. Tice AD, Rehm SJ, Dalovisio JR, Bradley JS, Martinelli LP, Graham DR, et al. Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. *Clin Infect Dis* 2004;38(12):1651-1672.
3. Meehan TP, Fine MJ, Krumholz HM, Scinto JD, Galusha DH, Mockalis JT, et al. Quality of care, process, and outcomes in elderly patients with pneumonia. *JAMA* 1997;278(23):2080-2084.
4. Norgard B, Sorensen HT, Jensen ES, Faber T, Schonheyder HC, Nielsen GL. Pre-hospital parenteral antibiotic treatment of meningococcal disease and case fatality: a Danish population-based cohort study. *J Infect* 2002;45(3):144-151.
5. Demoly P, Bousquet J. Epidemiology of drug allergy. *Curr Opin Allergy Clin Immunol* 2001;1(4):305-310.
6. Neugut AI, Ghatak AT, Miller RL. Anaphylaxis in the United States: an investigation into its epidemiology. *Arch Intern Med* 2001;161(1):15-21.

7. Dobson PM, Boyle M, Loewenthal M. Home intravenous antibiotic therapy and allergic drug reactions: is there a case for routine supply of anaphylaxis kits? *J Infus Nurs* 200;27(6):425-430.
8. Renz CL, Thurn JD, Finn HA, Lynch JP, Moss J. Antihistamine prophylaxis permits rapid vancomycin infusion. *Crit Care Med* 1999;27(9):1732-1737.
9. Matasar MJ, Neugut AI. Epidemiology of anaphylaxis in the United States. *Curr Allergy Asthma Rep* 2003;3(1):30-35.
10. Peebles RS Jr, Adkinson NF Jr. Hypersensitivity to antibiotics. In: Schlossberg D, editor. *Current therapy of infectious disease*. St Louis (MO): Mosby; 2000. p 740-744.
11. Risk of anaphylaxis in a hospital population in relation to the use of various drugs: an international study. The International Collaborative Study of Severe Anaphylaxis. *Pharmacoeconomol Drug Saf* 2003;12(3):195-202.
12. An epidemiologic study of severe anaphylactic and anaphylactoid reactions among hospital patients: methods and overall risks. The International Collaborative Study of Severe Anaphylaxis. *Epidemiology* 1998;9(2):141-6.
13. Van der Klauw MM, Wilson JH, Stricker BH. Drug-associated anaphylaxis: 20 years of reporting in the Netherlands (1974-1994) and review of the literature. *Clin Exp Allergy* 1996;26(12):1355-1363.
14. Lenler-Petersen P, Hansen D, Andersen M, Sorensen H, Bille H. Drug-related fatal anaphylactic shock in Denmark 1968-1990. A study based on notifications to the Committee on Adverse Drug Reactions. *J Clin Epidemiol* 1995;48(9):1185-1188.
15. McNutty TJ Jr. Initiation of antimicrobial therapy in the home. *Am J Hosp Pharm* 1993;50(4):773-774.

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Appendix 1. Survey Questions for Ontario Community Care Access Centres (CCAC)

Location:

Your name, position, and contact information

1. Do you have a policy stipulating location of first-dose IV antibiotic administration?

If yes, approximately how long has this policy been in effect?

Does it reflect a change to a previous policy?

2. Are some clients permitted to have the first dose at home?

If yes, are there inclusion/exclusion criteria for deciding which clients may receive the first dose at home?

3. Do you require the presence of a physician during administration of the first dose?

If no, are inclusion/exclusion criteria enumerated in your policy to decide which clients may receive the first dose without a physician present?

4. Do you require all patients on home IV antibiotic therapy to purchase epinephrine kits?

5. Please add comments.

Appendix 2. Survey Questions for Physicians Affiliated with the Canadian Infectious Disease Society

Your name:

Location of your practice (city, country):

Your type of practice (e.g., hospital, infusion centre):

Number of years you have been in this practice:

1. In my experience, I have seen approximately (*fill in blank*) anaphylactic reactions to IV antibiotics in the last (*fill in blank*) years.
2. I would estimate (*fill in blank*)% of the reactions were on the first dose and (*fill in blank*)% were during home IV therapy.
3. Do you think administering the first dose of antibiotics at home by a nurse is a safe practice in the following situations:
 - (a) If the patient has no history of allergic reactions?
 - (b) If the patient has a family history of allergic reactions?
 - (d) If the patient has had a minor allergic reaction to another drug?
 - (e) If the patient has had a distant past allergic reaction (e.g., to bee sting as a child)?

4. Do you have a policy stipulating location of first dose IV antibiotic administration?

If yes, how long has this policy been in effect?

Does it reflect a change to a previous policy?

5. Please describe your policy, or choose one of the following:
 - (a) first dose in hospital for all cases
 - (b) first dose at home/office/clinic for all cases, in the presence of a physician
 - (c) first dose at home, by a community nurse or health care practitioner other than a physician
 - (d) first dose at home or hospital/office/clinic, based on inclusion/exclusion criteria

6. Do you have specific inclusion/exclusion criteria that designate which patients should receive first dose IV antibiotics in hospital versus home?

If yes, please elaborate briefly/list criteria.

7. Do you have a policy with regard to epinephrine availability for patients receiving home IV antibiotic therapy?

8. Please describe your policy or choose one of the following:
 - (a) All patients must have epinephrine available.
 - (b) It is highly recommended that patients purchase an epinephrine kit, but not mandatory.
 - (c) Only some patients are required to purchase an epinephrine kit, based on certain criteria.
 - (d) Visiting nurses carry epinephrine with them at all times, for use in patients who may require it.
9. In your own opinion, for patients receiving home IV antibiotic therapy, the purchase of epinephrine (choose one of the following):
 - (a) should be mandatory for all
 - (b) should be mandatory for some based on certain criteria
 - (c) should be recommended, but not mandatory
 - (d) should not be recommended, as it is an unnecessary expense to patients
 - (e) epinephrine should be carried by the visiting nurses
10. Please add any further comments.

Appendix 3. Survey questions for participants in the Professional Specialty Network of the Canadian Society of Hospital Pharmacists

Your name:

Are you an infectious disease specialist?

Location of your practice (city, country):

Your type of practice (e.g., hospital, infusion centre):

Number of years you have been in this practice:

1. Do you have a policy stipulating location of first dose IV antibiotic administration?

If yes, how long has this policy been in effect?

2. Please describe your policy, or choose one of the following:
 - (a) first dose in hospital for all cases
 - (b) first dose at home/office/clinic for all cases, in the presence of a physician
 - (c) first dose at home, by a community nurse or health care practitioner other than a physician
 - (d) first dose at home or hospital/office/clinic, based on inclusion/exclusion criteria

3. Do you have specific inclusion/exclusion criteria that designate which patients should receive first dose IV antibiotics in hospital versus home?

If yes, please elaborate briefly/list criteria.

4. Do you have a policy with regard to epinephrine availability for patients receiving home IV antibiotic therapy?

5. Please describe your policy or choose one of the following:
 - (a) All patients must have epinephrine available.
 - (b) It is highly recommended that patients purchase an epinephrine kit, but not mandatory.
 - (c) Only some patients are required to purchase an epinephrine kit, based on certain criteria.
 - (d) Visiting nurses carry epinephrine with them at all times, for use in patients who may require it.

6. Please add any further comments.

