Cost-Effective Prophylaxis of Surgical Infections

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Contents

Summary .................................................. 129
1. Literature Retrieval .................................. 130
2. Pharmacokinetic Aspects .......................... 130
3. Microbiological Aspects ........................... 130
4. Prophylactic Regimens in Various Types of Surgery ............. 131
   4.1 Ophthalmic Surgery ............................... 131
   4.2 Neurosurgery ..................................... 131
   4.3 Head and Neck Surgery ......................... 132
   4.4 Breast Surgery .................................... 132
   4.5 Cardiovascular Surgery ......................... 133
   4.6 Pulmonary Surgery ............................... 133
   4.7 Abdominal Surgery ............................... 134
   4.8 Hernia Surgery .................................... 134
   4.9 Gynaecological and Obstetric Surgery .............. 134
   4.10 Urological Surgery .............................. 136
   4.11 Orthopaedic Surgery ......................... 137
5. Conclusion ............................................. 138

Summary

There are few formal pharmacoeconomic studies of antibacterial prophylaxis in surgery. An important reason for this is that such prophylaxis is difficult to study, because extremely large patient samples are needed to demonstrate differences or equalities with reasonable statistical power. When the cost effectiveness of various regimens is evaluated, indirect methods must often be used. Clearly, the ideal prophylactic regimen, both clinically and economically, is one that is easy to administer, has a low acquisition cost, can be given as a single dose and provides maximal protection against postoperative infections.

However, if and when such a regimen is identified, its universal acceptance and use might have negative ecological consequences (e.g. the selection of resistant organisms in the hospital environment). Thus, the search for the ideal prophylactic regimen must be a continuous process.

There is a paucity of pharmacoeconomic studies on the use of antibacterials or other procedures for preventing postoperative infections. However, one group has proposed a model for cost-effectiveness analyses of prophylactic therapy. The model offers the possibility of comparing outcomes with various regimens as well as the costs of preventing postoperative complications. It has been tested in
several studies of prophylactic regimens, with convincing results.\textsuperscript{[3-5]}

Because of the lack of high quality, prospective, controlled pharmacoeconomic trials evaluating antibacterial prophylaxis in surgery, this review takes other approaches to estimating the cost effectiveness of this intervention. First, if a short course of antibacterial treatment is demonstrated to have at least equivalent (with reasonable statistical power) prophylactic efficacy to a longer course of the same drug, the short course is to be preferred. Short course, especially single-dose, regimens are likely to cause minimal disturbances in normal gut flora and, hence, the selection of resistant bacteria is less likely to occur.

Secondly, prophylaxis should clearly be used if prospective, placebo-controlled trials demonstrate that it prevents clinically important infections. The problem in this context is to define 'clinically important'; that is, to find clinically relevant end-points.\textsuperscript{[6]} Since deep abscesses and/or systemic postoperative infections are rare in most types of surgery, even in placebo recipients, most studies fail to demonstrate benefits of active treatment if such infections are used as end-points. Thus, we must concentrate on other infections, such as wound infections. The consequences of such infections, for example prolonged hospitalisation times, additional antibacterial treatment and the need for additional surgical procedures, should be measured.

Thirdly, if 2 drugs are comparable in terms of their efficacy, safety and ecological pressure (selection of pathogenic and/or antibacterial resistant microorganisms), the least costly drug should be preferred.

1. Literature Retrieval

For the purposes of this article, ‘prophylaxis’ is defined as the perioperative administration of antibacterial(s) to a patient who, before surgery, did not have an infection at the site of the surgery. Published studies of prophylaxis in surgery were identified in literature searches performed in September 1995 of \textit{Current Contents} and ‘Medline’ for the period from January 1990. The searches were performed using the keywords ‘surgery’ and ‘prophylaxis’, or both of these plus ‘cost’ or ‘cost effectiveness’. Studies were selected if they were prospective and controlled, and studied only one type of surgical procedure. Articles that pooled results from several studies were included only to the extent that they provided original data or if they presented data from correctly performed meta-analyses.

2. Pharmacokinetic Aspects

The main purpose of antibacterial prophylaxis is either to reduce the size of the bacterial inoculum when ‘spillage’ occurs during surgery or, more commonly, to deliver the antibacterial to tissues and tissue fluids in concentrations sufficiently high to prevent the establishment of an infection. In both of these situations, the antibacterial regimen should be considered as an aid to physiological host defences, particularly phagocytosis.

It is very important to remember that in healthy tissues antibacterial concentrations similar to those in plasma are achieved 30 minutes after intravenous administration.\textsuperscript{[7,8]} This is particularly important when antibacterials that are rapidly eliminated (e.g. most penicillins and cephalosporins) are used prophylactically. If, for example, an antibacterial with a plasma half-life of 1 hour is given intravenously 2 hours before the start of surgery, only low antibacterial concentrations will remain in the tissues when intraoperative ‘spillage’ may occur.

Against this background, it is important to optimise prophylactic regimens with respect to the route of administration, time of administration and time, relative to the surgical procedure, when treatment is started and finished.\textsuperscript{[9-11]}

3. Microbiological Aspects

Antibacterial prophylaxis should cover the bacterial pathogens most likely to cause postoperative infections. This can only be assessed from published reports of the aetiology of postoperative infections. As noted by Ridgway et al.,\textsuperscript{[12]} preoperative screening of cultures is poorly predictive of the