Antibiotic prophylaxis for cardiac surgery

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Antibiotic prophylaxis for cardiac surgery is a controversial area. Recent systematic reviews and meta-analyses of randomized controlled trials have concluded that surgical site infection can be reduced by prolonging prophylaxis for 24–48 h. Also, post-operative pneumonia and all-cause mortality can be reduced by giving agents with both anti-Gram-negative and anti-Gram-positive activity. The choice of the most appropriate regimen remains open to debate.

Keywords: surgical site infection surveillance, antibiotic stewardship, cephalosporins

Introduction

In this issue of JAC, Lador et al.1 report a systematic review and meta-analysis of randomized controlled trials (RCTs) evaluating the use of antibiotic prophylaxis in cardiac surgery. The authors performed a review of such trials published between 1968 and 2010. They selected 59 trials out of a total of 962 on the basis of relevance to pre-defined criteria, including the type of surgery, the timing and duration of antibiotic prophylaxis, methods of surveillance of surgical site infection (SSI) (such as duration of follow-up) and mortality. The primary outcome measure was deep sternal wound infection. The authors concluded that evidence supports the use of second- or third-generation cephalosporins as prophylaxis for cardiac surgery and administration of prophylactic antibiotics for >24 h, but no longer than 48 h.

This conclusion by the authors contrasts with general antibiotic stewardship advice in many countries, including the UK, where single-dose surgical prophylaxis regimens and avoidance of cephalosporin use are encouraged.3 Is an exception to these general principles justified in cardiac surgery?

Prevention of SSIs

Although antibiotic prophylaxis is important to reduce the incidence of SSI, it is just one of many preventative measures. These include meticulous aseptic surgical technique and local policies or care bundles for pre-operative screening for carriage of resistant organisms together with decolonization, pre-operative showering and hair removal, perioperative skin preparation, temperature and blood glucose control, maintenance of adequate haemoglobin saturation, and post-operative wound management.3 The timing of prophylactic doses of antibiotics is also crucial. To be effective the pre-operative dose should be given either 30 min (for β-lactams) or 60 min (for glycopeptides) prior to the start of surgery.4 In practice it may often be difficult to achieve this window, particularly in emergency cases. Furthermore, additional intra-operative doses (if surgery is prolonged) and post-operative doses are sometimes omitted or delayed. Therefore comparison of studies where different preventative measures, duration of antibiotics and antibiotic regimens were given in each arm of a trial is difficult because the outcome of reduction in SSI will depend on all of these factors, not just the prophylaxis regimen.

In addition, Lador et al.1 recognize that a potential limitation of their analysis was the long period over which studies were included (1968–2010), since surgical techniques and measures taken to prevent infection changed significantly over this time. Nevertheless, they report that there was no impact of study year on the risk ratios for the outcomes given in their results.

Duration of prophylactic antibiotics

Prophylactic antibiotics are recommended for certain types of surgeries to reduce the incidence of SSI. There has been a general move towards the use of shorter courses of antibiotics for surgical prophylaxis in order to reduce toxicity, selection of resistant organisms, Clostridium difficile infection and cost.5 In most surgeries other than cardiac surgery, a single pre-operative antibiotic dose is recommended.6

Lador et al.1 report that prolonging the duration of antibiotic prophylaxis to up to 48 h was associated with a significant reduction in deep SSI. So what are the features related to cardiac surgery that might warrant prolonged prophylactic antibiotic regimens? Coronary artery bypass graft surgery often involves the use of a saphenous vein autograft. Such tissue can carry bacteria from the harvest site deep into the cardiac operative site. If SSI does occur, then organ space infection (e.g. mediastinitis) and endocarditis have considerable morbidity and high mortality rates. Furthermore, the use of prosthetic implants is widespread in cardiac surgery, particularly valve surgery and aortic surgery. The effects of infection related to implanted intracardiac or aortic graft prosthetic material can be catastrophic.
Other features that increase the risk of infection in cardiac surgery include cardiopulmonary bypass and systemic cooling for myocardial protection, invasive devices remaining after surgery (chest drains, pacing wires, intravenous catheters), high risk of bleeding requiring blood transfusion and re-exploration, and delayed extubation after surgery. There are few data on the pharmacokinetics of antibiotics during cardiopulmonary bypass, and therefore dosing regimens are often based on historical practice. Taking all of this into account, further evidence for the use of prolonged prophylactic regimens in cardiac surgery comes from another systematic review published recently by Mertz et al. They concluded that perioperative prophylactic regimens of at least 24 h duration are more effective in preventing SSI in cardiac surgery. However, the 2011 American College of Cardiology Foundation/American Heart Association guideline for coronary artery bypass graft surgery still only gives recommendations for pre-operative antibiotic prophylaxis, with further intra-operative doses for prolonged surgery. No specific recommendation is made with regard to subsequent duration of prophylaxis.

Conclusions

Although the reduction in SSI in cardiac surgery is multifactorial, the use of prophylactic antibiotics plays an important part. There are several reasons why prolonged (24–48 h) prophylactic regimens should be used in cardiac surgery. This is evidenced by the two recent systematic reviews, which conclude that SSIs are prevented by antibiotic prophylactic regimens of at least 24 h. The issue of which antibiotic regimen to use is unresolved. The majority of UK cardiothoracic hospitals use alternative regimens to cephalosporins. Further RCT evidence is therefore needed to compare these cephalosporin regimens with alternative regimens providing equivalent Gram-positive and Gram-negative cover with regard to reduction in SSI, potential toxic effects (including nephrotoxicity and ototoxicity) and incidence of C. difficile infection. The appropriate regimen must also take into account the antimicrobial susceptibilities of Gram-negative organisms found in individual hospitals.

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References


Use of cephalosporins

The data presented by Lador et al. indicate that second- and third-generation cephalosporins are superior to first-generation cephalosporins or to regimens containing penicillin or glycopeptides with no added Gram-negative cover. However, the benefit is not related to a reduction in deep sternal wound infection or other categories of SSI, but, perhaps surprisingly, to a significantly lower rate of post-operative pneumonia and all-cause mortality. Prevention of post-operative pneumonia is not normally a primary aim of surgical prophylaxis, and perhaps the use of antibiotics in such a way should be considered early empirical therapy rather than prophylaxis. Nevertheless, the findings provide evidence that both Gram-positive and Gram-negative coverage is optimal for prophylaxis in this setting.

The overall use of cephalosporins in the UK has decreased significantly in the past 5 years due to the association of these agents with C. difficile infection. The majority of the RCTs mentioned in the systematic review by Lador et al. were published at a time when cephalosporins were more widely used. Therefore it is not unexpected that the authors conclude that the evidence supports their use. However, with the decreasing popularity of cephalosporins in the UK, the recommendations for cephalosporin use from the systematic review are to be noted with caution. The majority (87%) of cardiothoracic surgery units in the UK currently use alternatives to cephalosporins in prophylactic regimens for cardiac surgery. A combination of fluoroquinolone and gentamicin is the most common regimen. In the analysis of different antibiotic combinations including Gram-negative cover, only three studies were included that used an aminoglycoside. Therefore, although there was a trend favouring the use of aminoglycosides compared with no Gram-negative cover, this was not statistically significant and no definitive conclusions can be made about whether or not cephalosporins are superior to aminoglycoside-containing regimens. This is not discussed in the review. Furthermore, Lador et al. were unable to comment on the incidence of C. difficile infection in cephalosporin regimens, as the information was lacking.