

## A Meta-Analysis of Randomized Controlled Trials Assessing the Prophylactic Use of Ceftriaxone. A Study of Wound, Chest and Urinary Infections

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The use of prophylactic antibiotics has been nowadays generally accepted as an important precaution to prevent infectious complications following surgery. Surgeons may sometimes lack the required infectiological knowledge, and to keep an up-dated overview of the extensive literature remains difficult, hence we have to rely on meta-analysis and to benefit from collating information from different meta-analysis [1]. In this article, Woodfield et al. have shown with their meticulously performed meta-analysis of 90 publications that ceftriaxone is more effective than most other prophylactic antibiotics to reduce surgical site infections, urinary tract infections and postoperative pneumonia in patients at risk [2].

Ceftriaxone is a third generation cephalosporin that covers a wide range of gram negative and gram positive bacteria. It has bactericidal effects by inhibiting the synthesis of the cell wall. Ceftriaxone has a high stability against the vast majority of beta-lactamases (i.e. penicillinases and cephalosporinases), which remained unchanged during the last 40 years. Already 30 min after intravenous injection, serum levels far above the minimal inhibitory concentration (MIC) for most organisms are achieved. Due its excellent penetration into different tissues and fluids (e.g. bone, lung, liver, heart, skin, bile, cerebrovascular fluid) as well as the prolonged half-life of 8 h, a sustained concentration well above the MIC for most bacteria has been observed for 24 h after single-shot application.

The chemical and pharmacokinetical properties of ceftriaxone have contributed to the rather unique clinical characteristics, which almost fulfil every criteria for an “ideal” prophylactic antibiotics. First, despite ceftriaxone is widely used for more than four decades, no relevant resistance formation could have been observed. Second, the capacity to nearly penetrate in every tissue and fluid compartment, and the long half-life of 8 h provide a high ceftriaxone concentration with a long-lasting protective effect. Thus, ceftriaxone successfully prevents both, surgical site infections (local action) and remote infections, away from the surgical site (systemic action). Not surprisingly, it reveals its best effects for clean-contaminated and contaminated surgical interventions. Third, since generic products are now available, cost for ceftriaxone has been decreased in many countries.

The main goal of prophylactic antibiotics in surgery is still to prevent infections directly related to the intervention, e.g. surgical site infections, but also remote infectious complications, e.g. respiratory tract in case of abdominal surgery [3]. In order to achieve those goals, a responsible use of antibiotics is pivotal to achieve low infection rates, to prevent resistance formation, and to keep a good cost-effectiveness. There is a broad range of antibiotics that are available for prophylaxis. Numerous antibiotic regimens have been proposed for many different indications and surgical specialities, respectively. Surgeon’s choice for one particular antibiotic is influenced by various factors. Among those, institutional traditions, personal experience, and last but not least, strong economical interests of the pharmaceutical industry often play a key role, while evidence is often of subordinate importance.

We should keep in mind that the number of newly released antimicrobial drugs has steadily decreased over the last 30 years, while the number of multiresistant organisms has

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rapidly increased (e.g. MRSA, ESBL bacteria). Therefore, a careful selection of the respective antibiotics for prophylaxis is of utmost importance. The pharmaceutical companies may suggest new antibiotics with “better” mode of actions, although there is no real need to change current antibiotic prophylaxis. Epidemiological aspects weigh harder in this setting than individual considerations. According to this meta-analysis, ceftriaxone has kept its excellent profile, and its use is still safe and effective.

Despite all the beneficial effects, we should not forget that prevention of infectious complications related to surgery is not solely based on antibiotic prophylaxis. Local bacterial contamination and systemic spillage are also dependent on the surgical technique. Prevention of inadvertent opening of the respiratory, gastrointestinal and

genitourinary tract, minimizing blood loss, preoperative correction of malnutrition and other co-morbidities remain crucial.

## References

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