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REVIEW ARTICLE

Application of vancomycin powder into the wound during spine surgery: Systematic review and meta-analysis☆

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Abstract
Objective: To determine the effects of applying vancomycin powder within the surgical wound on the risk of surgical infections, pseudo-arthrosis and adverse events, in patients undergoing spinal surgery.
Material and methods: A meta-analysis was carried out, including controlled studies that evaluated the risk of postoperative infections and/or pseudo-arthrosis in patients undergoing spinal surgery in which vancomycin powder was applied within the surgical wound.

Results were presented as pooled relative risks, with its 95% confidence intervals. Additionally, the frequency of complications attributable to vancomycin was also assessed.
Results: A total of six controlled studies (3379 subjects) were included. Pooled relative risks were: surgical site infection, 0.11 (95% CI: 0.05–0.25; $P < .00001$), and pseudo-arthrosis, 0.87 (95% CI; 0.34–2.21; $P = .77$). No statistically significant heterogeneity was found in both analyses. In 1437 patients treated with vancomycin, there were no recorded vancomycin-related adverse events.
Conclusions: Application of vancomycin powder into the wound was associated with a significantly reduced risk of surgical site infections, without increasing pseudo-arthrosis or adverse events. However, randomized controlled trials are needed, in order to confirm the present results and make recommendations with more certainty.

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PALABRAS CLAVE
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Aplicación de vancomicina en polvo dentro de la herida quirúrgica durante cirugías de columna: revisión sistemática y metaanálisis

Resumen
Objetivo: Determinar los efectos de la aplicación de la vancomicina en polvo dentro de la herida quirúrgica, sobre el riesgo de infecciones postoperatorias, pseudoartrosis y efectos adversos en pacientes sometidos a cirugías de columna.
Material y métodos: Se realizó un metaanálisis incluyendo los estudios controlados que evaluaron el riesgo de infecciones postoperatorias y/o pseudoartrosis en pacientes sometidos a cirugía de columna a quienes les fue aplicada vancomicina en polvo en la herida quirúrgica.

Los resultados se presentaron como riesgos relativos combinados, con sus intervalos de confianza del 95%. Adicionalmente, se evaluó la frecuencia de complicaciones atribuibles al tratamiento.
Resultados: Se incluyeron 6 estudios controlados (3.379 sujetos). Los riesgos relativos combinados fueron: infección del sitio quirúrgico, 0,11 (IC 95%: 0,05-0,25; p < 0,00001), y pseudoartrosis, 0,87 (IC 95%: 0,34-2,21; p = 0,77). No se encontró heterogeneidad estadísticamente significativa en ninguno de los análisis. En 1.437 pacientes tratados no se reportaron complicaciones asociadas al uso de la vancomicina.
Conclusión: La aplicación de vancomicina en polvo dentro de la herida se asoció con una reducción significativa del riesgo de infecciones del sitio quirúrgico, sin incrementar el de pseudoartrosis o de efectos adversos. Sin embargo, se requieren estudios controlados y aleatorizados, con el fin de confirmar los presentes resultados y realizar recomendaciones más certeras.

Introduction

Surgical site infections (SSI) are one of the most common and devastating complications in spinal surgery. Their incidence varies according to several factors and it is estimated that between 2.8% and 11.9% of patients undergoing spinal surgery will suffer SSI, despite the application of conventional prevention strategies.[1,2]

Patients affected by these infections present prolonged hospitalization times and incapacity for work, reduced quality of life indices and, in general, notably unfavorable outcomes compared to patients who do not suffer these complications.[1] Additionally, the treatment of SSI requires considerable expenditure stemming from the prolonged hospitalization time, the use of diagnostic aids, reinterventions and intravenous antibiotic therapy, among others.[2,3] For these reasons, several measures focused on reducing their incidence to the minimum level possible have been investigated.[1,4]

The administration of intravenous antibiotics is perhaps the most widely used strategy for the prophylaxis of SSI. The most recent clinical guidelines from the Antibiotic Prophylaxis Work Group of the North American Spine Society[5] promote the systematic administration of intravenous prophylaxis. However, it has been demonstrated that the magnitude of SSI reduction is relatively low, thus leading to the search for other alternatives.[6]

The application of vancomycin in the form of unreconstituted powder within the surgical site represents an innovative trend for the prevention of SSI and is increasingly gaining supporters among spinal surgeons due to its low cost, extensive availability, ease of application, good safety profile and perception of effectiveness.[7–9] Sweet et al.[10] determined that the application of vancomycin under the muscle fascia can lead to concentrations within the surgical site up to 1000 times greater than the mean inhibitory concentration required to destroy methicillin-resistant *Staphylococcus aureus*, one of the most frequently isolated germs in spinal surgery infections. Moreover, its microbicide spectrum also includes other Gram-positive bacteria, such as *Staphylococcus epidermidis* and *Enterococcus* spp., which can also cause postoperative spinal infections.[3,11]

Although the pharmacokinetic properties of vancomycin applied within the surgical site make it a very attractive method for prophylaxis, its potential adverse effects represent a significant drawback. Intravenous administration has been associated with anaphylactic reactions, arterial hypotension, renal toxicity, otological toxicity and induction of antibiotic resistance. Nevertheless, its safety profile when applied topically is still not fully known.[12,13]

Furthermore, some studies describe mechanisms through which vancomycin could interfere with the maturation and functioning of osteoblasts, which would alter the biological pathways involved in bone fusion. For this reason, several authors maintain that high local vancomycin concentrations within the surgical site could be associated to a higher risk of pseudoarthrosis (or nonunion).[14–16]

Due to its recent use in clinical practice, several studies examining the effects of powdered vancomycin within the surgical site during spinal surgery have been published in the last decade. However, these studies have not been previously assessed through a metaanalysis.

The objective of the current metaanalysis is to determine the effects of applying vancomycin within the surgical site on SSI and pseudoarthrosis among patients undergoing