Review

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Teicoplanin in peritoneal dialysis: efficacy, safety, and pharmacological considerations

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Abstract

Peritoneal dialysis (PD) is a vital treatment modality for renal failure patients, facilitating the removal of excess fluid and unwanted substances. However, peritonitis, a significant complication experienced by PD patients, necessitates careful selection of antibiotics to ensure successful treatment. Commonly used antibiotics in PD patients, such as cephalosporins and glycopeptides like vancomycin, have been associated with undesirable side effects and high failure rates. In response to these challenges, teicoplanin, a novel glycopeptide antibiotic, has gained attention due to its similar range of activity to vancomycin, extended half-life, reduced side effects, and improved elimination. The objective of this study is to comprehensively review the efficacy, mechanism of action, adverse effects, and pharmacological benefits of teicoplanin in peritoneal dialysis patients. Our research involved an extensive review of 21 articles from reputable databases, including Google Scholar, PubMed, and ScienceDirect. The data extracted from these studies was meticulously evaluated to comprehensively understand teicoplanin's clinical profile in this specific patient population. Major findings of these studies are that glycopeptide-based regimens have higher cure rates over first-generation cephalosporins or fluoroquinolones, and teicoplanin demonstrated several advantages over vancomycin, such as a higher therapeutic index, good tolerance, longer half-life, lower rates of nephrotoxicity, improved elimination while being equally effective. Teicoplanin is typically administered to peritoneal dialysis patients with a loading dose of 400 mg, aiming to achieve a trough concentration of 10–15 mg/dl. Teicoplanin's improved tolerability and lack of regular serum level monitoring requirements make it a promising alternative to traditional antibiotics for clinical use.

Keywords: peritoneal dialysis, peritonitis, safety and efficacy, teicoplanin, vancomycin

Introduction

Peritoneal dialysis (PD) is a medical procedure employed in individuals with kidney failure to filter excess fluid, balance electrolytes, and eliminate toxins from the blood by utilising the peritoneum in the abdomen as a filtering membrane. In the early 2000s, ~275 053 patients in the US underwent PD, with 5.2% utilising continuous ambulatory peritoneal dialysis (CAPD) and 4% using automated peritoneal dialysis (APD)[1]. Globally, it was estimated that by the end of 1997, about 120 000 individuals, comprising roughly 15% of all dialysis patients worldwide, were undergoing PD[2].

HIGHLIGHTS

- Regrettably, peritonitis, an infection of the peritoneum, has been the leading cause of mortality among peritoneal dialysis (PD) patients since its introduction in clinical practice.
- Teicoplanin, a newer glycopeptide, belonging to the vancomycin-ristocetin family and possessing a glycopeptide core (a fused ring linked to two sugars, mannose and N-acetylglucosamine), is also employed in PD patients with peritonitis.
- Teicoplanin has a better efficiency and safety profile compared to vancomycin and exhibits partial cross-resistance with vancomycin.
- Most of the side effects caused are mild in severity and do not require treatment.

Regrettably, peritonitis, an infection of the peritoneum, has been the leading cause of mortality among PD patients since its introduction in clinical practice[3,4]. The appropriate selection of antimicrobial medication for early treatment is crucial in effectively managing peritonitis in PD[5]. Typically, initial empirical peritonitis antibiotic therapy includes cephalosporin, vancomycin, and an associated aminoglycoside until culture results are obtained[6,7].

Teicoplanin, a newer glycopeptide antibiotic belonging to the vancomycin-ristocetin family[8] and possessing a glycopeptide

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core (a fused ring linked to two sugars, mannose and N-acetylglucosamine), is also employed in PD patients with peritonitis[9]. This newer glycopeptide functions by inhibiting the production of bacterial cell walls, thus eliminating pathogens. It is equally effective as vancomycin in reducing mortality caused by methicillin-resistant S. aureus infections, with a 56% lower incidence of nephrotoxicity[10]. Teicoplanin's biological characteristics and activity spectrum are comparable to vancomycin's. It exhibits partial cross-resistance with vancomycin and exerts bactericidal effects on gram-positive pathogens[9].

This review evaluated the efficacy of teicoplanin in treating peritonitis in CAPD patients. Since 1986, intraperitoneal vancomycin and netilmicin have been employed as primary antibiotics, while cefotaxime was previously used but discontinued due to increased methicillin resistance (from 46 to 75%) and treatment failure[11]. Recently, teicoplanin has been utilised in CAPD treatment due to its structural and activity similarities to vancomycin and minimal risk of causing hearing loss[11].

Literature assessment

An extensive literature review was conducted based on a systematic and comprehensive search of the related articles from databases, Google Scholar, PubMed, and ScienceDirect. Search terms used to find relevant articles are Teicoplanin, Peritoneal dialysis, Vancomycin and infections in peritoneal dialysis.

Inclusion criteria for the selection of articles consist of studies from 1990 to 2023, published in the English language, human studies, meta-analysis, systemic review, randomized control trial (RCT), case series, case reports, and patients of 18 years or above age. Exclusion criteria include in vitro and animal studies, review articles, letters to editors, studies conducted before 1990, and studies in languages other than English. After applying the criteria, 12 articles were extensively reviewed for data: sample size, loading dose, outcomes, and results. The efficacy and pharmacokinetics of teicoplanin in peritoneal dialysis patients were significantly discussed along with adverse effects: nephrotoxicity and transiently elevated liver enzymes, thrombocytopenia, and allergic sensitivity. Also, teicoplanin, in comparison with vancomycin, was weighed up. Data from 12 articles are tabulated in Table 1 and Table 2 below..

Barretti *et al.*[3]. observed that Glycopeptides with aminoglycosides were found to have significantly better outcomes than ceftazidime plus glycopeptide as a first treatment, indicating higher cure rates for glycopeptide-based regimens, including teicoplanin and vancomycin, compared to first-generation cephalosporins and fluoroquinolones. Teicoplanin also demonstrated several advantages over vancomycin, such as a higher therapeutic index, good tolerance of rapid intravenous injection, longer half-life, post-antibiotic effect, lower rates of nephrotoxicity, and improved elimination[1,8]. Wood *et al.*[12]. suggest that teicoplanin is equally effective as vancomycin and holds greater potential for clinical utilisation due to its improved tolerability and the absence of a need for regular monitoring of serum levels. Lupo *et al.*[6]. state that the combination therapy of teicoplanin and tobramycin exhibits high efficacy and good tolerability in the treatment of PD-related peritonitis, surpassing the effectiveness of cephalothin and tobramycin, thus suggesting its potential as a first-line treatment option for PD peritonitis. Bowley *et al.*[9]. also highlight that teicoplanin is a suitable alternative to vancomycin in treating peritonitis in PD patients without the associated risk of ototoxicity. Additionally, when teicoplanin is combined with aminoglycosides, the incidence of nephrotoxicity is significantly lower than when vancomycin and aminoglycosides are used in combination[15]. Moreover, teicoplanin exhibits a lower rate of primary treatment failure compared to vancomycin[3].

Limitations of reviewed studies

There is insufficient data to determine the most effective treatment methods, including combining teicoplanin and cephalosporins,

Table 1

Studies focused on the efficacy of Teicoplanin

References	Type of study	No. studies	Outcome	Results	Comments
Barretti *et al.*[3]	Meta-analysis	64 studies + 21 RCTs	Glycopeptide + ceftazidime is stronger	resolution rate is 86% compared to Cef + Ag 66% and glycopeptide + Ag 75%	Rx was not statistically significant for Gram-positive or negative rods.
Lupo *et al.*[6]	RCT	68 patients	Teicoplanin + tobramycin is superior to cephalothin + tobramycin	Failure rates were 4.5× higher in the cephalothin + tobramycin group	Good systemic and local tolerability was observed
Stille *et al.*[8]	Case study	310 patients	Teicoplanin is effective in the Rx of various infections	79% treated with teicoplanin showed elimination of causative pathogens.	This case study showed that teicoplanin is an effective antibiotic.
Bowley *et al.*[9]	RCT	1	Response to vancomycin or teicoplanin did not significantly differ from one another	improvement with intervention within 24–48 h.	Teicoplanin can be a substitute for vancomycin as it is less ototoxic.
Neville *et al.*[11]	Pilot study	11 patients	In all patients, the bacteriological cure was accomplished	teicoplanin can be alternative to vancomycin	No adverse effects were noted
Wood[12]	Meta-analysis	1276 patients from 11 RCTs	Response rates varied for teicoplanin from 54 to 92%	Successful Rx rates were 78.8% with teicoplanin compared to 77.2% with vancomycin	Teicoplanin has a good success rate in eliminating pathogens.
Wiggins *et al.*[13]	Systematic Review of RCTs	36 trials	no class of improved antibiotics was found.	Intermittent and continuous antibiotic dosing are equivalent treatment strategies.	In one trial, Intraperitoneal (IP) antibiotics outperformed IV Rx.
Ballinger *et al.*[14]	Review of RCTs and quasi-RCTs	42 studies	IP glycopeptides had a greater chance of achieving a complete cure	RR is 1.66	Compared to Cef, glycopeptides showed ambiguous results with Rx response and relapse rates.

Ag, aminoglycoside; Cef, cephalosporin; RCT, randomized control trials; RR, risk ratio; Rx, treatment.

Table 2

Studies focused on the adverse events of Teicoplanin

References	Type of study	No. studies	Result	Adverse event
Hirai *et al.*[10]	Meta-analysis	Eight articles-634 patients	Teicoplanin nephrotoxicity was observed in 11.0% of patients.	Teicoplanin nephrotoxicity is increased by hypoalbuminemia.
Wilson[15]	Retrospective observational study.	482 patients	TIT incidence was low overall in the study cohort.	TIT incidence was 4.6%.
Qi *et al.*[16]	Pharmacokinetic study	8 patients	The mean dose of teicoplanin was 7.02 ± 0.75 mg/kg.	Employ a modified regimen that reduces the time between doses.
Tobudic *et al.*[17]	Case study	9 isolates	Teicoplanin's efficacy against MRSA biofilm has been reduced.	Teicoplanin has no effect on MRSA peritonitis when the infection is associated with a biofilm.

MRSA, methicillin-resistant staphylococcus aureus; TIT, teicoplanin-induced thrombocytopenia.

which may be effective due to better coverage against gram-negative organisms[3]. Other than Tobudic *et al.*[7]. no research has looked into the usage of teicoplanin in biofilm-related Methicillin-resistant Staphylococcus aureus (MRSA) infections. Tobudic *et al.*[17]. discovered that teicoplanin had no noticeable effect on biofilm-related MRSA peritonitis associated with biofilms. While studies have provided valuable insights, certain aspects remain inadequately explored, such as drug interactions, dosage adjustments for patients with hepatic and renal disorders, and long-term treatment outcomes.

Discussion

Teicoplanin exerts its action similarly to vancomycin by interacting with the terminal D-alanyl-D-alanine on peptidoglycan precursors, thus hindering peptidoglycan formation and exhibiting inhibitory effects against most gram-positive bacteria[18]. Both glycopeptides are primarily eliminated renally, without significant oral absorption or metabolism. Despite their similarities, there are notable pharmacokinetic differences in teicoplanin[15]. Teicoplanin exhibits a comparable unbound clearance to vancomycin but demonstrates substantially higher tissue binding, resulting in a prolonged half-life and a longer time required to reach steady-state concentrations[19]. Most teicoplanin binding occurs with plasma proteins, and the binding appears linear as concentrations increase up to 300 mg/l[15], with higher unbound concentrations observed in individuals with hypoalbuminemia[10].

In addition to serum albumin, factors such as age, body weight, and creatinine clearance influence the pharmacokinetics of teicoplanin and consequently impact trough concentrations[20]. An optimal trough concentration of greater than 13 mg/l (range 10–15 mg/l) is recommended for teicoplanin[21]. To achieve this target trough concentration, an initial loading dose of 400 mg followed by adjusted maintenance doses is recommended[19]. Failure to administer the appropriate loading dose (400 mg) may be a significant factor in the early treatment phase of critically ill patients, resulting in inadequate exposure to teicoplanin (trough concentration <10 mg/l), which has been suggested as a cause of clinical treatment failure with teicoplanin[20]. The appropriate loading dose required for individuals with varying renal functions remains uncertain[21].

Teicoplanin can be administered via intravenous (IV) or intramuscular (IM) routes. The systemic availability of the IM route is close to 100% and comparable to the clearance observed with the IV route. In individuals undergoing CAPD, teicoplanin can be administered intraperitoneally[15]. A suggested regimen for CAPD patients is intraperitoneal administration of teicoplanin at 10 mg/kg every 24 h. However, no reports discuss the pharmacokinetics of multiple-dose administration in CAPD patients[22].

Fever, rash, allergic reactions, diarrhoea, bronchospasm, mild tremors, nephrotoxicity, the temporary elevation of liver enzymes, and thrombocytopenia are among the adverse effects observed in a minority of individuals receiving teicoplanin. Most of these side effects are minor and do not require treatment[8,15]. The elevation of liver enzymes is independent of trough concentrations and shows prompt improvement following teicoplanin therapy[20]. In patients commencing teicoplanin, the median time for the initial decrease in platelet count to 100 000/microliter was 5 days, while it took 8 days for the highest platelet count to decline[23]. Nephrotoxicity, trough concentration, and the initial daily dose did not exhibit a significant correlation, but patients over 65 have a higher risk of experiencing nephrotoxicity[10]. According to the findings of a meta-analysis, patients receiving teicoplanin reported significantly fewer adverse events, including kidney toxicity, compared to those receiving vancomycin. This is particularly relevant in cases of severe infections where concomitant use of nephrotoxic medications is anticipated[12].

Furthermore, patients treated with teicoplanin did not experience red man syndrome or changes in audiometry results[8]. Serial audiometry assessments conducted on individuals with previously normal hearing showed no evidence of sensorineural toxicity, and patients with pre-existing bilateral sensorineural hearing loss did not experience further deterioration[11]. Although teicoplanin is not orally absorbed, it does reach modest levels in breast milk. It can also cross the placenta, although the clinical implications of this are not yet clear[15].

Teicoplanin exhibits partial cross-resistance with vancomycin[9]; thus, caution is advised to avoid therapy with teicoplanin or other alternative glycopeptides, as such strains may develop cross-resistance[18]. Additionally, the effectiveness of teicoplanin may be influenced by local microbial resistance, which should be considered when selecting a treatment plan. While this review provides valuable information, certain aspects remain insufficiently explored, such as the optimal duration of therapy, treatment modifications for patients with comorbidities, appropriate follow-up periods, and long-term outcomes. Furthermore, there are variations among research studies in terms of patient selection, admission criteria, underlying renal conditions, sample sizes, methods of antibiotic administration, and related factors[5]. Teicoplanin is considered a safer medication compared to vancomycin, but further research is warranted to determine the most effective therapeutic protocols for teicoplanin use in PD-related peritonitis.

Conclusion

The introduction of peritoneal dialysis as a standard clinical procedure has highlighted the significant impact of peritonitis on patient mortality. Consequently, there is an increased emphasis on the prompt and targeted use of antimicrobial medications. Teicoplanin, a replacement for vancomycin and other antimicrobials in treating peritonitis, has demonstrated superior efficacy and lower toxicity. Extensive studies have been conducted to investigate the pharmacokinetics and pharmacodynamics of teicoplanin. Although a few uncommon side effects are associated with this drug, they generally do not require treatment.

Ethical approval

Not applicable.

Consent

Informed consent was not required for this review.

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Author contribution

P.K.R.K. suggested the idea first. P.K.R.K., S.G., M.M., S.G.R.Y. further developed the idea, searched the databases, went through the articles and screened them. S.D., S.T.L., Sushmitha contributing by extracting and compiling the data. K.N.G., M.G., P.K.T. contributed by structuring the article, checking the references, verifying the data. All the authors contributed to the writing and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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