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Linezolid for the treatment of patients with endocarditis: a systematic review of the published evidence

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Background: Linezolid is a bacteriostatic oxazolidinone antibiotic that has been proven to be effective for the treatment of patients with pneumonia, skin and soft tissue infections, and possibly bacteraemia, due to Gram-positive cocci. However, the drug is sometimes used for the treatment of patients with endocarditis due to Gram-positive cocci resistant to other antibiotics.

Methods: We carried out a review of the available literature to evaluate whether linezolid is also effective for the treatment of patients with infective endocarditis.

Results: We identified 23 case reports and 3 case series reporting the experience with 56 patients with endocarditis treated with linezolid. Evaluable data for 33 patients who received linezolid and for whom individual patient data were reported were further analysed. Prosthetic valve infective endocarditis accounted for 25% of the reviewed cases. Methicillin-resistant *Staphylococcus aureus* and vancomycin-intermediate *S. aureus* were the most commonly isolated cocci (24.2% and 30.3% of cases, respectively). Linezolid alone was administered to 66.7% of patients while the rest received the antibiotic in combination with rifampicin, gentamicin, fusidic acid or amikacin. A total of 63.6% (21/33) of patients with endocarditis were cured after linezolid administration. The overall and endocarditis-related mortality was 33.3% (11/33) and 12.1% (4/33), respectively. Thrombocytopenia developed in 30.8% (8/26) of patients for whom relevant data were available.

Conclusions: The limited available evidence suggests that linezolid may be considered as a therapeutic option for the treatment of patients with endocarditis due to multidrug-resistant Gram-positive cocci. However, further published experience is needed to answer the question of whether a bacteriostatic antibiotic could be proven beneficial for patients with an infection for which bactericidal antibiotics have been traditionally used.

Keywords: oxazolidinones, prosthetic heart valves, *Staphylococcus*, *Streptococcus*, *Enterococcus*, Gram-positive

Introduction

Linezolid has been used for the treatment of patients with pneumonia, bacteraemia, and skin and soft tissue infections due to Gram-positive cocci. However, the gradually increasing frequency of infections caused by multidrug-resistant (MDR) microorganisms has led to the use of linezolid for the treatment of patients with infections in other body organs and tissues. Among these infections, endocarditis has a special clinical significance because it is associated with considerable morbidity (attributed mainly to its complications such as congestive heart failure, embolic episodes, mycotic aneurysms, and splenic abscesses) and mortality, which reaches 16–25% of the affected individuals even nowadays.[1–3]

Although antibiotics with bactericidal activity have been considered the gold standard for the treatment of patients with deep tissue infections such as endocarditis and osteomyelitis, the use of linezolid, a bacteriostatic antibiotic, sometimes becomes a necessity in patients with infections in these sites due to bacteria with *in vitro* resistance to other antimicrobial agents. Therefore, we sought to review and evaluate the available evidence regarding the effectiveness and safety of linezolid in patients with bacterial endocarditis.

Methods

Literature search

We carried out a systematic review of the current evidence for the effectiveness of linezolid in the treatment of endocarditis. Two independent reviewers (KGM and FN) searched PubMed (January 1995 to March 2006) in order to identify articles appropriate for inclusion

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in our review. We also searched reference lists of retrieved articles for other relevant papers. Search terms included 'endocarditis', 'linezolid', 'heart disease', 'bacteraemia', 'Gram-positive bacteria', '*Staphylococcus*', '*Enterococcus*' and '*Streptococcus*'.

Study selection and data extraction

A study was eligible for inclusion in the review if it assessed the effectiveness and safety of linezolid for the treatment of patients with infective endocarditis. Case series and case reports were eligible for inclusion. All patients receiving treatment with linezolid for infective endocarditis were evaluable for the analysis, if age, gender, medical history, reason for linezolid administration and/or outcome of the infection was available. All patients with endocarditis according to Duke's criteria who received linezolid as a monotherapy or as a part of the regimen are included. Studies evaluating animal models were not eligible for inclusion in this review.

The treatment outcome was defined as cure when patient's general status had improved, the blood cultures were negative and trans-thoracic echocardiograph (TTE) or transoesophageal echocardiograph (TEE) revealed no evidence of persistent vegetations on the infected valve according to the information provided by the authors of each case report. In addition, an adequate follow-up period (at least 1 month) was necessary. Treatment outcome was defined as improvement when there were no signs of persistent infection (negative blood cultures, no evidence of persistent vegetations) but the duration of the follow-up period was not adequate (less than 1 month) or the patient died due to other reasons during the same hospitalization. Treatment failure was defined as persistence of signs, symptoms, and laboratory or imaging findings of infective endocarditis despite appropriate antibiotic treatment with linezolid, relapse of the infection or death due to infective endocarditis or its complications.

Results

Case reports

A summary of the evidence from published case reports to date with use of linezolid with bacterial endocarditis is shown in Table 1.[4–27] A total of 33 cases were retrieved. Information regarding the demographics, clinical data, type of heart valve and other variables were not reported in a few cases, thus the denominator varies in the following proportion of cases. Of the affected individuals 62.5% (20/32) were men. The median age of patients was 66 years (range 0.5–80). Prosthetic valve infective endocarditis accounted for 25% (8/32) of cases.

Chronic renal failure (27.3%, 9/33), immunosuppression due to steroid therapy (24.2%, 8/33) and diabetes mellitus (24.2%, 8/33) were the most common comorbidities. Other diseases reported in the reviewed cases were coronary artery disease (12.1%, 4/33) and asthma or chronic obstructive pulmonary disease (9.1%, 3/33). Only one of the reported patients had a positive history of rheumatic disease. One more patient was human immunodeficiency virus (HIV) seropositive. None of the reported patients with infective endocarditis had history of intravenous drug abuse.

Blood cultures were performed and proven positive for all reviewed patients; the identity of one isolate was not available. Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-intermediate resistant *S. aureus* (VISA) or *S. aureus* with reduced susceptibility to vancomycin were the predominant isolated pathogens [24.2% (8/33) and 30.3% (10/33), respectively]. Other commonly isolated pathogens included vancomycin-resistant *Enterococcus* (VRE) *faecalis* (6.1%, two

isolates) and *faecium* (12.1%, four isolates), vancomycin-susceptible *E. faecalis* (6.1%, two isolates) and coagulase-negative staphylococci (15.2%, five isolates). None of the blood cultures yielded more than one microorganism.

Ultrasound techniques were applied to detect valve vegetations. The echocardiogram method used for the diagnosis of nine cases (28.1%) of endocarditis was not specified. TEE was used in 50% (12/24) of the cases reporting the echocardiogram method used, while TTE was used in the remaining cases.

The reason for administration of linezolid varied between cases. No reason was reported for one case. Failure of previously administered treatment was the most common reason for administration of linezolid (34.4%, 11/32). In seven additional patients, the authors considered the administration of vancomycin for 7 days without clinical or microbiological improvement as treatment failure. Other reasons for administration of linezolid included history or development of allergic reactions to vancomycin or teicoplanin (21.9%, 7/32), development of other adverse effects with the antibiotics administered prior to linezolid (12.5%, 4/32), refusal or inability of patients to receive intravenous antibiotics (9.4%, 3/32) and isolation of MDR bacteria (1 patient).

The median duration of linezolid administration was 42 days (range 7–148). Linezolid was administered at the same dosage in all case reports (600 mg every 12 h), except for a neonate who received a dosage of 15 mg/kg every 8 h. Linezolid was administered either alone (66.7%, 22/33) or in combination with rifampicin (5 cases), gentamicin (4 cases), fusidic acid (3 cases) or amikacin (1 case). A total of 16 out of 24 (66%) patients for whom the method of administration was specified in the reviewed articles received oral linezolid. In 9 of these 16 patients oral linezolid was used after intravenous administration of the drug (the 7 remaining patients were primarily treated with oral linezolid). Eight out of 33 (24%) patients had a surgical intervention; operation for replacement of a prosthetic and natural valve was performed in 3 and 5 patients, respectively.

The outcome at the end of the follow-up period (median 6 months, range 1 week to 52 months) was good for the majority of patients with endocarditis treated with linezolid (63.6%, 21/33 cases). Three out of these 21 patients who were treated successfully with linezolid for endocarditis died of other comorbidity during the follow-up period. Of note, the follow-up period was ≥6 months for 12 out of 21 patients with complete resolution of their infection. Failure of treatment with linezolid was documented in 7 cases (21.2%). Of these 7 patients with documented failure of linezolid treatment 4 died of endocarditis whereas the remaining 3 patients had persisting positive blood cultures that became negative after the administration of other antibiotics. In addition to these 7 patients, the results were considered indeterminate for 5 patients even though their laboratory and/or imaging findings improved after the administration of linezolid. Four of these 5 patients died (2 of them due to a new infection other than endocarditis and 2 due to other comorbidity). The overall and endocarditis-related mortality was 33.3% (11/33) and 12.1% (4/33), respectively.

Information regarding the possible adverse effects associated to linezolid administration was available in 26 case reports. Adverse effects developed in 9 of these patients (34.6%). Thrombocytopenia developed in 30.8% (8/26) of patients. Seven of these patients had platelet counts <100 000/μL; the platelet count of one patient was not reported. Two patients discontinued treatment with linezolid and one of them also received platelet

Table 1. Characteristics and outcome of patients in the reviewed case reports

First author, year of publication (ref)	Sex and age	Comorbidities	Infected valve	Isolated pathogens	Previous antibiotic treatment (duration, days)	Reason for linezolid administration	Duration of linezolid treatment (days)	Outcome	Follow-up duration (months)	Adverse effects
Hill et al., 2006 (4)	M 46	RA, AV and MV replacement	possible abscess in the mitral-aortic area	CoNS	VAN, RIF (15), TEC, FUS (8)	allergic reaction to VAN, thrombocytopenia due to TEC	18	cure	6	none
Corne et al., 2005 (5)	M 62	asthma	native MV	MRSA	VAN (13), SXT (10)	refused to continue hospitalization	29	Improvement—relapse—died	2	anaemia, thrombocytopenia
De Feiter et al., 2005 (6)	M 49	Marfan disease, HoE, MV, AV replacement, CAD, AA	prosthetic MV	Staphylococcus epidermidis, developing MRSE	OXA (11), GEN, RIF (43), VAN (40), FUS (NA)	treatment failure	148	improvement—died of septic due to Klebsiella pneumoniae	1.5	none
Nathani et al., 2005 (7)	F 28	asthma, history of MRSA infections	native TV, PV	MRSA	VAN (NA)	no iv access	28	cure	NA	none
Ng et al., 2005 (8)	M 37	RHD, HoE, allergy to β-lactams	native MV	Streptococcus mitis	VAN, GEN (5)	development of rash	43	cure	1	none
Shah and Murillo, 2005 (9)	F 46	CRF, arterial graft of left iliac artery, allergy to VAN and PEN	native TV with cerebral emboli	Corynebacterium striatum	none	allergy to AMP,VAN	7	failure	NA	NA
Souli et al., 2005 (10)	M 67	HoE	prosthetic TV	MRSA	VAN then TEC, RIF, GEN, SXT (20)	ARF	42	cure	12	NA
Wareham et al., 2005 (11)	F 61	MV replacement, repeated bacteraemias	prosthetic MV	S. epidermidis	VAN, RIF, FUS (NA)	treatment failure	14	cure	12	thrombocytopenia
	F 79	MV replacement, allergy to PEN	prosthetic MV	VRE faecalis	Q/D, DOX (NA)	treatment failure	98	cure	52	NA
Archuleta et al., 2004 (12)	M 64	HIV (+), Hep C, RT, parathyroidectomy	native MV	VRE faecium	Q/D (21), SAM (4), DOX (17)	treatment failure	42	cure	6	thrombocytopenia
Bassetti et al., 2004 (13)	F 77	CVD	native MV, AV	MRSA	TEC, RIF (NA)	development of rash and wheezing	42	cure	12	none
Hamza et al., 2004 (14)	M 64	CAD, HT, HPT, CRF, renal Ca	native PV	VRE faecalis	VAN (14), GEN	development of resistance to VAN	42	improvement—died	0.25[a]	NA

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Table 1. *(continued)*

First author, year of publication (ref)	Sex and age	Comorbidities	Infected valve	Isolated pathogens	Previous antibiotic treatment (duration, days)	Reason for linezolid administration	Duration of linezolid treatment (days)	Outcome	Follow-up duration (months)	Adverse effects
	M 47	CRF, CVD, HPT, DM, allergy to VAN	native PV	MR CoNS	none	allergy to VAN	NA	improvement	NA	NA
Howden *et al.*, 2004 (15)	M 80	DM, Wegener granulomatosis, CRF, STI, IVCF	native TV	VISA	VAN (29)	NA	40	cure	10	thrombocytopenia, discontinued linezolid
	F 66	DM, CAD, PPM, IVCF	native TV	VISA	VAN (19), RIF, FUS (11)	NA	38	cure	2.5	thrombocytopenia
	M 73	RF, STI, laparotomy	native MV	VISA	VAN (8)	NA	49	cure	3	none
	F 73	bowel Ca, STI	native TV	VISA	VAN (8)	NA	42	improvement—died of comorbidities	NA	thrombocytopenia
	F 66	DM, cervical Ca, STI, aortic stenosis	native MV	VISA	VAN (13)	NA	12	died	NA	none
	F 77	DM	native AV	VISA	VAN (20), RIF (9)	NA	7	died	NA	none
Leung *et al.*, 2004 (16)	M 67	DM	prosthetic AV	VISA	VAN (32)	NA	42	died	NA	none
	M 60	HL, HPT, CAD, CRF	prosthetic AV	VISA	VAN (77) and AMK	emergence of VISA	84	cure	12	none
Pistella *et al.*, 2004 (17)	M 47	none	native MV and cerebritis	MRSA	AMP, GEN, VAN (8)	dissemination of cerebral infection	56	cure	6	NA
Woods *et al.*, 2004 (18)	M 63	AICD, non-Hodgkin lymphoma	native AV and MV	SARV	VAN (23)	treatment failure	67	cure— died from respiratory failure	4.5	none
Andrade-Baiocchi *et al.*, 2003 (19)	F 52	multiple myeloma	native MV	VISA	VAN (90), RIF (14)	treatment failure	21	cure	6	NA
Ang *et al.*, 2003 (20)	M 4 month	preterm infant, RDS, bronchopulmonary dysplasia, atrial septal defect	native TV	VRE *faecium*	none	VRE resistant also to Q/D	63	cure—died from respiratory failure	6	none

Reference				Organism	Antibiotics	Reason	Duration	Outcome		Side effects
Ravindran et al., 2003 (21)	F 74	MV prolapse, VT, HT, small bowel obstruction, IPA, laparotomy	native MV	S. epidermidis	GEN, FCX, RIF (28)	treatment failure	62	cure—died after operation for mitral valve replacement	NA	thrombocytopenia
Zimmer et al., 2003 (22)	M 40	Hep C, CRF, HPT, HoE	native TV, AV	E. faecalis	none	allergy to AMP, VAN	18	failure	NA	NA
Rao and White, 2002 (23)	M 78	DM, CAD, AV replacement	prosthetic AV	E. faecalis	AMP, GEN (4)	development of renal failure	42	cure	4	decrease in WBC, thrombocytopenia
Ruiz et al., 2002 (24)	M 75	lung, larynx Ca, CRF	native AV	MRSA	none	history of CRF	19	improvement—failure	3	NA
	M 77	COPD	native MV	MRSA	VAN (22)	renal insufficiency and rash	33	improvement—died due to septic shock from Morganella morganii	NA	NA
Viale et al., 2002 (25)	F 80	PPM, mitral annuloplasty	native MV	MRSA	VAN, SXT, CLI (28), VAN, AMK, RIF (14), Q/D (28)	need for oral antibiotic	28	cure	2	vomiting, alopecia
Babcock et al., 2001 (26)	F 34	Down syndrome, CRF, HT, CCD, common atrium, history of Ash catheter-related VREF infection	native AV, TV	VRE faecium	Q/D (12)	treatment failure	47	cure	9	NA
Chien et al., 2000 (27)	NA	abdominal aortic repair, DM, ARF	NA	VRE	VAN, ALF (NA)	NA	42	cure	1	none

CoNS, coagulase-negative *Staphylococcus*; MRSA, methicillin-resistant *S. aureus*; MRSE, methicillin-resistant *S. epidermidis*; VISA, vancomycin-intermediate resistant *S. aureus*; SARV, *S. aureus* with reduced susceptibility to vancomycin; VRE, vancomycin-resistant *Enterococcus*; AV, aortic valve; MV, mitral valve; PV, pulmonic valve; TV, tricuspid valve; AA, aortic aneurysm; AICD, automated implantable cardiac defibrillator; ARF, acute renal failure; AS, aortic stenosis; Ca, cancer; CAD, coronary artery disease; CCD, congenital cyanotic disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CVD, cerebrovascular disease; DM, diabetes mellitus; Hep C, hepatitis C; HoE, history of endocarditis; HL, hyperlipidaemia; HPT, hypertension; HT, hypothyroidism; IPA, intraperitoneal adhesions; IVCF, inferior venacava filter; MVP, mitral valve prolapse; PPM, permanent pacemaker; RA, rheumatoid arthritis; RDS, respiratory distress syndrome; RHD, rheumatic heart disease; RF, retroperitoneal fibrosis; RT, renal transplantation; STI, steroid therapy immunosuppression; AICD automated implantable cardiac defibrillator; ALF, alatrofloxacin; SAM, ampicillin/subactam; AMK, amikacin; CLI, clindamycin; SXT, co-trimoxazole; DOX, doxycycline; FUS, fusidic acid; FCX, flucloxacillin; GEN, gentamicin; OXA, oxacillin; PEN, penicillins; Q/D, quinupristin/dalfopristin; RIF, rifampicin; TEC, teicoplanin; VAN, vancomycin; iv, intravenous; NA not applicable/available.
[a] For Hamza *et al*. the duration mentioned refers to 1 week.

transfusion. Anaemia and decrease of the white blood cells were reported for one patient each. One case each of nausea, vomiting and mild alopecia was also reported.

Case series

There are two published case series to date regarding the use of linezolid in patients with endocarditis, from which the data could not be extracted individually for each patient. In a compassionate-use programme, Birmingham *et al.* reported their experience in 40 patients with infective endocarditis.[28] The characteristics of 32 of these patients and the outcomes of 19 clinically evaluable patients were further reported in a conference abstract.[29] The mean duration (±standard deviation) of linezolid treatment was 36 (±33) days. Most cases involved native mitral and aortic valves (78.1%, 25/32). Vancomycin-resistant *Enterococcus faecium*, MRSA and *Staphylococcus haemolyticus* were the most commonly isolated bacteria. Of these patients 78% received linezolid because previous antibiotic treatment failed. Rifampicin and gentamicin were the antibiotics most commonly combined with linezolid (42% each). Treatment with linezolid was successful in 89.5% (17/19) and 71% (10/14) of patients at the end-of-treatment and test-of-cure (7–30 days after the end of treatment) assessment, respectively. Only six patients were evaluated 6 months after the end of treatment; treatment had failed in 50% of these patients. Overall, 41.1% of patients reported an adverse effect possibly or probably related to linezolid administration. Thrombocytopenia occurred in 15.1% of patients.

The second case series reported outcomes in patients undergoing cardiovascular surgery who developed nosocomial infective endocarditis due to methicillin-resistant staphylococci. Linezolid was administrated due to lack of effective antibiotic treatment, renal failure and/or intolerance to vancomycin. Four cases of endocarditis were reported; all of them were successfully treated with linezolid. No adverse effects were reported.[30]

Discussion

Very few data are currently available for the effectiveness of linezolid for the treatment of patients with infective endocarditis. The published case reports and case series are the main sources of relevant information. It is noteworthy that all randomized controlled trials that studied the effectiveness of linezolid for the treatment of patients with infections of various sites due to Gram-positive cocci excluded patients with endocarditis. In the majority of the reviewed cases the use of linezolid was considered only when other treatment options had failed or could not have been used for various reasons.

Although most of the reported patients with infective endocarditis treated with linezolid were cured or improved, we should emphasize the possible bias for publication of case reports with successful treatment. The low mortality attributed to endocarditis in these case reports (12.1%) may support this limitation. However, the overall mortality in the reviewed case reports was 33.3%. Thus, the overall mortality was comparable with that of patients with endocarditis treated with other antibiotics. These data suggest that innovative management strategies are needed to further reduce the considerable mortality of patients with infective endocarditis.

A considerable difference was noticed in the reported treatment failures between case reports and the case series when a 6 months interval was used as the follow-up period. A difference in treatment failures was also noticed between the different times of assessment in the case series reported by Dresser *et al.* (end of therapy 89%, test-of-cure visit 70% and 6 months follow-up 50%). The small number of the treated patients and the fact that most of the patients were lost to follow-up are the most probable reasons leading to these differences. In addition, some authors suggest that in cases of patients with infections caused by resistant Gram-positive cocci the serum levels of linezolid should be monitored in order to avoid suboptimal concentrations and the dosage should be increased accordingly, if the drug is well tolerated.[31] However, none of the identified case reports reported dose adjustments for linezolid according to its serum levels. Therefore, whether low inhibitory concentrations could be responsible for the observed treatment failures cannot be addressed.

From the reviewed patients who received linezolid for a prolonged period, 30.8% developed thrombocytopenia. Our team conducted a meta-analysis of randomized controlled trials that included 5470 patients and studied the effectiveness and safety of linezolid for the treatment of skin and soft tissue infections, pneumonia and bacteraemia (in peer review). Only 2% of patients developed a blood abnormality that was described by the authors as thrombocytopenia. Other reports also suggest that thrombocytopenia is even less common in patients who receive linezolid for a shorter period.[32–35] On the other hand, in a review of data regarding patients treated with linezolid for osteomyelitis, we found that 7% of patients developed thrombocytopenia (in peer review).

Although no study has been performed so far to evaluate the penetration of linezolid in human heart valves, several experimental models have been employed to study the effectiveness of linezolid for the treatment of infective endocarditis. One of these models showed that linezolid demonstrates synergic bactericidal effect with gentamicin against MRSA strains.[36] On the contrary, the combination of linezolid with rifampicin was not more effective than linezolid alone.[37] In addition, controversial results were reported from three experimental endocarditis models in rabbits that compared vancomycin with linezolid. Ghiang and Climo reported that vancomycin was more effective than linezolid plus vancomycin ($P < 0.05$) and linezolid alone ($P < 0.05$) in reducing the mean valvular vegetation bacterial count.[38] On the other hand, Jacqueline *et al.*[39] reported that continuous linezolid infusion resulted in the same reduction of bacterial counts of three MRSA strains as that of vancomycin. Finally, Dailey *et al.*[40] reported that high-dose oral linezolid (50 or 75 mg/kg) had the same effectiveness as vancomycin in reducing bacterial counts on rabbit heart valves and concluded that the effectiveness of linezolid in the treatment of experimental endocarditis is related to trough levels in plasma above the MICs for MRSA strains.

Vancomycin is the recommended antibiotic according to the scientific statement of the relevant committee of the American Heart Association (AHA) for patients with infective endocarditis due to Gram-positive cocci with intrinsic penicillin resistance and is the second-line therapy for patients who cannot tolerate penicillins.[41] The AHA committee members emphasize that evidence for the use of vancomycin in the treatment of patients with infective endocarditis (on which the recommendations were based) is conflicting and comes from consensus opinion of experts in the field. Some may contend that the same level of

evidence is available for the use of linezolid for the treatment of patients with infective endocarditis. Moreover, linezolid has been barely used as first-line treatment, and therefore the AHA committee members recommend its use only for the treatment of patients who cannot tolerate vancomycin or whose treatment with other antibiotics had failed. Subsequently, randomized controlled trials are needed to provide a definitive answer to the question of which of the aforementioned antibiotics is more effective for the treatment of patients with infective endocarditis due to MDR Gram-positive cocci.

Although the purpose of this review was not to address all the available antibiotics for the treatment of patients with infective endocarditis, it should be mentioned that several other antibiotics are available and can be used for the treatment of patients with infective endocarditis due to resistant Gram-positive cocci. Evidence regarding the use of these antibiotics such as daptomycin, quinupristin/dalfopristin, trimethoprim/sulfamethoxazole, rifampicin and fusidic acid is scarce. However, in some of the case reports in which linezolid administration resulted in treatment failure, the use of these antibiotics resulted in resolution of the infective endocarditis.

In conclusion, we reviewed the limited information regarding the use of linezolid, a newly marketed antibiotic, for the treatment of patients with bacterial endocarditis, a devastating infection. The published experience suggests that linezolid should be considered for the treatment of patients with infective endocarditis for whom limited treatment options are available. The antibiotic has an excellent pharmacokinetic profile; with an oral bioavailability of ∼100%, linezolid challenges the need for intravenous antibiotics for the treatment of patients with endocarditis. However, it remains to be evaluated in randomized controlled trials whether a bacteriostatic antibiotic could be proven beneficial for an infection for which bactericidal antibiotics have been traditionally used.

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