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Efficacy and Tolerability of Linezolid for Treatment of Infectious Spondylitis

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Introduction

- Infectious spondylitis requires long-term antibiotic treatment for 6 weeks or more, and the use of intravenous antibiotics during this period has high social and monetary costs due to hospitalization.
- Linezolid has high oral bioavailability and is not affected by changes in renal or hepatic function.
- We investigated the clinical and microbiological effects of linezolid in infectious spondylitis caused by beta-lactam resistant gram positive bacteria.

Methods

- Clinical data from patients who were diagnosed infectious spondylitis and treated with linezolid for at least four weeks were collected retrospectively from electronic medical records at 3 tertiary hospitals from 2006 to 2016.

Results

- Twenty Korean patients were treated with linezolid at least four weeks during the study period(Table 1). Of these, 14 patients were cured, four failed and two cases of mortality occurred due to other causes than infectious spondylitis. Ten of 13 patients who had previously been assessed as vancomycin treatment failure were cured by linezolid. Median duration of linezolid treatment was 40.5 days.
- Major causative organism was methicillin-resistant *Staphylococcus aureus* (n=15), followed by methicillin-resistant coagulase-negative *Staphylococcus* (n=3).
- Bacteremia occurred in 14 patients, and 10 of these showed persistent bacteremia at the time of linezolid administration. Eight of these cases of persistent bacteremia were cured by linezolid.
- In 10 of 20 patients treated with linezolid, antibiotics were changed for side effects or de-escalation of antibiotics(Table 2). The most common reason for discontinuation of linezolid was thrombocytopenia(n=6).
- Cytopenia was most common drug adverse reaction, and severe cytopenia (grade II or more of National Cancer Institute criteria) was 11.11% for neutropenia, 12.96% for anemia and 20.37% for thrombocytopenia(Table 3).

Table 1. Baseline characteristics of patients with infectious spondylitis treated by linezolid

No.	Age (yr)	Sex	Underlying diseases	Post-operative spondylitis	Organism	Bacteremia	Persistent bacteremia	Previous antibiotics	Salvage	Linezolid duration (oral, days)	Surgery (Initial)	Surgery (Salvage)	Cure	Follow up (days)
1	69	M	HT, Spinal stenosis	No	MRSA	Yes	No	Vancomycin, Ciprofloxacin, Rifampin	Yes	77(32)	No	Yes	Yes	392
2	63	F	SLE	No	MRSA	Yes	Yes	Vancomycin	Yes	30(0)	No	Yes	Yes	1171
3	61	M	RA	No	MRSA	Yes	Yes	Vancomycin	Yes	90(7)	No	Yes	Yes	2045
4	75	M	None	No	MRSA	Yes	No	Vancomycin	No	50(5)	No	Yes	Relapse/Yes	388
5	77	M	DM	No	MRSA	Yes	Yes	Vancomycin, Amikacin	No	30(0)	No	Yes	No	Death
6	65	M	DM, ESRD, Pulmonary Tb	No	MRSA	Yes	No	Vancomycin	No	35(13)	Yes	No	No	Death
7	81	M	ASO, HT	No	MRSA	Yes	Yes	Vancomycin, Arbekacin	Yes	65(0)	No	No	No	Death
8	79	F	HT, DM	No	MRSA	Yes	Yes	Vancomycin, TMP/SMX, Rifampin	No	38(0)	No	Yes	Yes	1696
9	59	M	HT	No	MRCNS	No	No	Vancomycin	No	60(14)	No	No	Yes	75
10	55	M	TB spondylitis	No	VISA	No	No	None	No	48(14)	Yes	No	Yes	1116
11	80	M	MM, HT, DM, BPH	No	MRSA	Yes	Yes	Vancomycin	Yes	28(0)	No	Yes	Yes	77
12	73	M	Spinal stenosis	Yes (prosthesis)	MRCNS	No	No	None	No	50(35)	Yes	No	Yes	575
13	73	F	HT, DM, HIVD	No	MRCNS	No	No	Vancomycin, Teicoplanin	Yes	30(14)	No	Yes	Yes	461
14	78	F	None	No	MRSA	No	No	Vancomycin	Yes	40(0)	Yes	No	Yes	1000
15	69	F	HT, DM, ESRD, Colon ca, Stroke, CVD	No	MRSA	Yes	Yes	Vancomycin	Yes	32(0)	No	No	Yes	539
16	69	F	HT, DM, Spinal stenosis	Yes (prosthesis)	MRSA	Yes	Yes	Vancomycin	Yes	41(0)	Yes	No	Yes	1276
17	66	M	CVD, COPD	No	MRSA	Yes	Yes	Vancomycin	Yes	71(50)	No	No	Yes	756
18	79	M	DM, CKD	No	VSE	No	No	Teicoplanin, Vancomycin	Yes	46(0)	No	No	Yes	249
19	63	M	No	No	MRSA	Yes	Yes	Vancomycin	Yes	28(0)	Yes	No	Relapse/Yes	157
20	68	M	HT, DM, CKD, SDH	No	MRSA	Yes	No	Vancomycin	Yes	36(0)	No	Yes	Relapse/Yes	339

No., Number; M, Men; F, Women; HT, Hypertension; SLE, Systemic lupus erythematosus; RA, Rheumatoid arthritis; DM, Diabetes mellitus; ASO, Atherosclerosis obliterans; TB spondylitis, tuberculous spondylitis; MM, Multiple myeloma; BPH, Benign prostatic hyperplasia; HIVD, Herniated intervertebral disc; ESRD, End stage renal disease; Pulmonary Tb, Pulmonary tuberculosis; CVD, Coronary vascular disease; COPD, Chronic obstructive pulmonary disease; CKD, Chronic kidney disease; SDH, Subdural hemorrhage; MRSA, Methicillin resistant *Staphylococcus aureus*; MRCNS, Methicillin resistant coagulase negative *Staphylococcus*; VISA, Vancomycin intermediate *Staphylococcus aureus*; VSE, Vancomycin sensitive *Enterococcus(E.faecium)*

Table 2. Reasons for discontinuation of linezolid during the treatment of infectious spondylitis

No.	Reason for Discontinuation	Duration of linezolid (days)	Subsequent antibiotic agents
2	Thrombocytopenia, GI disturbance	28	Levofloxacin, RFP
3	Neutropenia, Anemia	43	Vancomycin, RFP
4	Thrombocytopenia	25	TMP-SMX, RFP
5	Thrombocytopenia	22	Levofloxacin, RFP
8	Thrombocytopenia	32	TMP-SMX, RFP
11	De-escalation	28	Vancomycin
14	Change to oral agent	40	Levofloxacin, RFP
15	Thrombocytopenia	32	Ciprofloxacin, RFP
16	De-escalation	41	Vancomycin, RFP
19	Thrombocytopenia	28	Vancomycin

No., number; GI, Gastrointestinal; RFP, Rifampin; TMP-SMX, Trimethoprim-sulfamethoxazole

Table 3. Adverse reactions of linezolid during the treatment of infectious spondylitis (N=54)

		All events	Severe events[a]
Cytopenia	Neutropenia	6 (11.11)	6 (11.11)
	Anemia	9 (16.67)	7 (12.96)
	Thrombocytopenia	15 (27.78)	11 (20.37)
Fever		1 (1.85)	
Rash		3 (5.56)	
GI disturbance		3 (5.56)	

Values are presented as number (%).
[a]Severe cytopenia was defined as Grade II or more of National Cancer Institute criteria.

Conclusion

- Linezolid can be used as an effective antibiotic agent in patients with infectious spondylitis, especially when treatment failure of the first-line treatment is expected.
- Linezolid can be administered orally in outpatient clinic, reducing health care cost.
- Since cytopenia (especially thrombocytopenia) are common, a regular follow up of complete blood cell count is needed.