EBM report

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Case scenario

48 y/o, male with underlying type 2 DM, hypertension, and CKD, stage 3

Septic shock, left foot infection related

- Left foot necrotizing fasciitis
- post fasciotomy+sequestrectomy on 9/30
- post amputation of the left second and third toes, debridement on 10/12
- post below knee amputation on 10/18
- post below knee amputation wound closure on 10/26

Case scenario

Admitted on 11/27 due to swelling and redness over wound, suspected cellulitis

Treatment:

- Vancomycin 1gm, q12h
- Shifted to Linezolid 600mg, q12h on 12/2
    - Due to poor clinical improvement
- Debridement on 12/02

Clinical improved afterwards

Case scenario

- Wound culture results: Negative(on 11/30 and 12/02)
- Previous pus culture(11/18):Staphylococcus haemolyticus with multiple drug resistance(sensitive to Vancomycine, Tigycycline, Teicoplanin, Linezolid, Fusidic acid

Background question

- Risk factors of soft tissue infection/poor wound healing?
- Common pathogen of Skin and soft tissue infections?
- Empirical antibiotics choice?
- Role of surgical debridement?
- Risk factor of MRSA infection?

Foreground question

- Vancomycin versus linezolid, which one is better to treat my patient?

P	patients with complicated SSTI
I	Antibiotics treatment with linezolid
C	Antibiotics treatment with vancomycin
O	treatment response

Search for EBM

- Key words:
- Cellulitis / Skin and soft tissue infection
- Vancomycin
- Linezolid
- MRSA

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1. In Vivo Bioluminescence Imaging to Evaluate Systemic and Topical Antibiotics against Community-Acquired **Methicillin-Resistant Staphylococcus aureus**-Infected **Skin** Wounds in Mice.
   Guo Y, Ramos RI, Cho JS, Donegan NP, Cheung AL, Miller LS.
   Antimicrob Agents Chemother. 2012 Dec 3. [Epub ahead of print]
   PMID: 23208713 [PubMed - as supplied by publisher]
   Related citations

2. A 39-year-old man with a **skin infection**.
   Moellering RC Jr.
   JAMA. 2008 Jan 2;299(1):79-87. Epub 2007 Dec 4.
   PMID: 18056894 [PubMed - indexed for MEDLINE]
   Related citations

3. Children hospitalized with **skin** and **soft tissue infections**: a guide to antibacterial selection and treatment.
   Vayalumkal JV, Jadavji T.
   Paediatr Drugs. 2006;8(2):99-111. Review.
   PMID: 16608371 [PubMed - indexed for MEDLINE]
   Related citations

1 free full-text article in PubMed Central

Linezolid versus **vancomycin** trea [Antimicrob Agents Chemo

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Search details

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("cellulitis"[MeSH Ter
OR "cellulitis"[All
Fields]) AND ("skin"[Me
Terms] OR "skin"[All
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Search

Search results

- Linezolid versus Vancomycin in Treatment of Complicated Skin and Soft Tissue Infections (*Antimicrobial agents chemotherapy, June 2005, p.2260-2266*)
- Linezolid reduces length of stay and intravenous treatment compared with vancomycin for complicated skin and soft tissue infections due to suspected or proven methicillin-resistant Staphylococcus aureus(MRSA) (*International Journal of Antimicrobial Agents 26(2005)442-448*)

research result

- Linezolid versus Vancomycin in Treatment of Complicated Skin and Soft Tissue Infections (*Antimicrobial agents chemotherapy, June 2005, p.2260-2266*)
  - Randomized, open-label, comparator-controlled, multicenter, multinational study
  - Compare linezolid to vancomycin in the treatment of suspected or proven methicillin-resistant gram-positive complicated SSTIs (CSSTIs) requiring hospitalization

證據等級

Level	與[治療/預防/病因/危害]有關的文獻
1a	用多篇RCT所做成的綜合性分析(SR of RCTs)
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series(poor quality :cohort / case-control studies

Research result

- From October 2002 to March 2003
- Enroll 1200 patients with SSTI, suspected or proven MRSA related, required hospitalization with physical or symptoms finding
- Patients with gram negative infections, osteomyelitis, endocarditis, septic arhtritis, necrotizing fasciitis, gas gangrene were excluded
- Surgical intervention was allowed

Research result

- Patients enrolled were randomized to receive
  - Linezolid 600mg, q12h, i.v. or orally
  - Vancomycin, 1gm, q12h, i.v.
- Concomitant use of other Abx. for gram-negative organisms were permitted
- Minimal treatment period was 4 days, but no longer than 21 days

Research result

- Primary endpoint: clinical cure
  - EOT(end of treatment)
  - TOC(test of cure): 7 days after EOT
- Long-term follow-up: day 35

- ITT(intent-to-treat) population
- MITT(modified intent-to-treat) population:
  - ITT population with culture confirmed gram+ pathogen
- CE(clinically evaluable) population:
  - >4 days of therapy and returned to TOC visit
- ME(microbiologically evaluable) population:
  - CE patients with one or more gram+

Research result

1. Summary of baseline demographics and clinical characteristics of ITT population

cteristic	No. (%) of patients treated with: Linezolid (*N* = 592)	Vancomycin[a] (*N* = 588)
	375 (63.3)	363 (61.7)
	217 (36.7)	225 (38.3)
	295 (49.8)	299 (50.9)
	76 (12.8)	67 (11.4)
	138 (23.3)	136 (23.1)
ed	162 (27.4)	172 (29.2)
	282 (47.6)	266 (45.2)
abscess	158 (26.7)	146 (24.8)
gical incision	63 (10.6)	65 (11.1)
ated		
	142 (41.3)	146 (44.1)
	106 (30.8)	95 (28.7)
± SD)	52 ± 18	52 ± 18

TABLE 2. Clinical outcomes at TOC visit[a]

Population	% of patients (no. cured/total) after treatment with: Linezolid	Vancomycin[b]	95% CI
ITT	92.2 (439/476)	88.5 (402/454)	−0.11, 7.4
MITT	92.9 (314/338)	88.0 (287/326)	0.40, 9.3
CE	94.4 (436/462)	90.4 (394/436)	0.53, 7.4
ME	94.5 (312/330)	89.7 (278/310)	0.69, 9.0

[a] Results do not include indeterminate outcomes. TOC visits occ after the end of treatment. CI, confidence interval.

[b] Patients could be switched to nafcillin, oxacillin, dicloxacillin, or f based on culture results.

Research result

3. Clinical success at TOC visit of CE and ME patients by baseline diagnosis[a]

is and type	% of patients (no. cured/total) after treatment with: Linezolid	Vancomycin[b]	95% CI	*P* value
abscess				
ents	98.3 (116/118)	91.1 (92/101)	1.19, 13.24	0.026
ents	98.0 (97/99)	90.1 (82/91)	1.14, 14.6	0.028
ents	91.5 (205/224)	91.5 (184/201)	−5.33, 5.28	0.993
ents	91.6 (120/131)	91.7 (99/108)	−7.12, 6.99	>0.999
rgical on				
ents	98.0 (50/51)	88.2 (45/51)	0.18, 19.43	0.112
ents	97.7 (43/44)	88.1 (37/42)	−1.11, 20.37	0.106

s do not include indeterminate outcomes. TOC visits occured 7 days nd of treatment. CI, confidence interval.
s could be switched to nafcillin, oxacillin, dicloxacillin, or flucloxacillin ulture results.

TABLE 4. Microbiological outcomes at TOC visit by pathogen in ME and MITT patient populations treat linezolid or comparator drugs[a]

Organism and patient population	% of patients cured (no. cured/total) after treatment with: Linezolid	Vancomycin[b]	95% CI
MRSA			
ME	88.6 (124/140)	66.9 (97/145)	12.38, 30.9
MITT	71.0 (125/176)	55.1 (102/185)	6.08, 25.7
MSSA			
ME	84.9 (90/106)	75.3 (70/93)	−1.47, 20.7
MITT	73.0 (92/126)	66.4 (75/113)	−5.02, 18.3
Streptococcus pyogenes			
ME	86.7 (13/15)	94.4 (17/18)	−27.97, 12.4
MITT	68.4 (13/19)	65.4 (17/26)	−24.73, 30.8

[a] TOC visits occured 7 days after the end of treatment. CI, confid
[b] Patients could be switched to nafcillin, oxacillin, dicloxacillin, o based on culture results.

Conclusion

- The results indicate that the two drugs are equivalent for the ITT population.
- Linezolid superior to the comparative regimen in the per-protocol analysis and to vancomycin in the MRSA subset.
- The difference between linezolid and vancomycin results was most dramatic in patients with abscesses and surgical-site infections

Appraisal

Item		comments
Answer	此文獻有沒有回答我的問題？	部分
Authors	作者是否為experts?有沒有利益衝突？	是/有
Method	此文獻設計是哪一種類型？	RCT
Population	取樣是否隨機？其特性是否接近我的病人？分組是否採盲法？	病人特性應屬接近
Intervention	給予實驗組的處置是否描述清楚，並且是臨床可行的？	V
Comparison	給予對照組的處置是否描述清楚，並且是臨床可行的？各種可能比較皆有了？	V
Outcome	測量了那些結果？是否用客觀的方式測量？是否有統計學上的意義？	V
	測量結果的時間點是否合宜？追蹤的	

audit

- 提出臨床問題
- 搜尋最佳證據
- 評讀文獻
- 應用到臨床病人身上
- 改變醫療行為

Apply to the Patient

- Linezolid didn’t be superior choice according to the final culture pathogen.
- Surgical site infection
- Sensitivity result
- Drug level, renal insufficiency

Thanks for your attention!