胸腔內科 EBM

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臨床場景(clinical scenario)分析

- 病人基本資料：
  - 65 y/o male
  - Underlying disease:
    - Intermittent fever
    - LMD: Cravit po
- 主訴/相關症狀/PE/Lab/image：
  - Intermittent fever and Cough for 1 week
  - yellowish sputum, general malaise
  - Leukocytosis , CRP↑
  - CXR: R't lower infilitration
  - Dx: CAP

臨床場景(clinical scenario)分析

- Day1: Levofloxacin
- Day7: Low grade fever + productive cough
  - CXR: right lower patch with cavity formation
  - AFS(+), TB-PCR(+)
  - Anti-TB: HERZ
- TB-Culture
  - Multiple drug resistant

提出foreground questions

問題描述： Controversies surrounding the empirical use of FQs to treat patient with CAP?	
P:	Community-acquired pneumonia
I:	Receive empirical FQs treatment
C:	Not receive FQs treatement
O:	Delay of TB diagnosis
T:	The median time between symptom onset and receipt of anti-TB medication

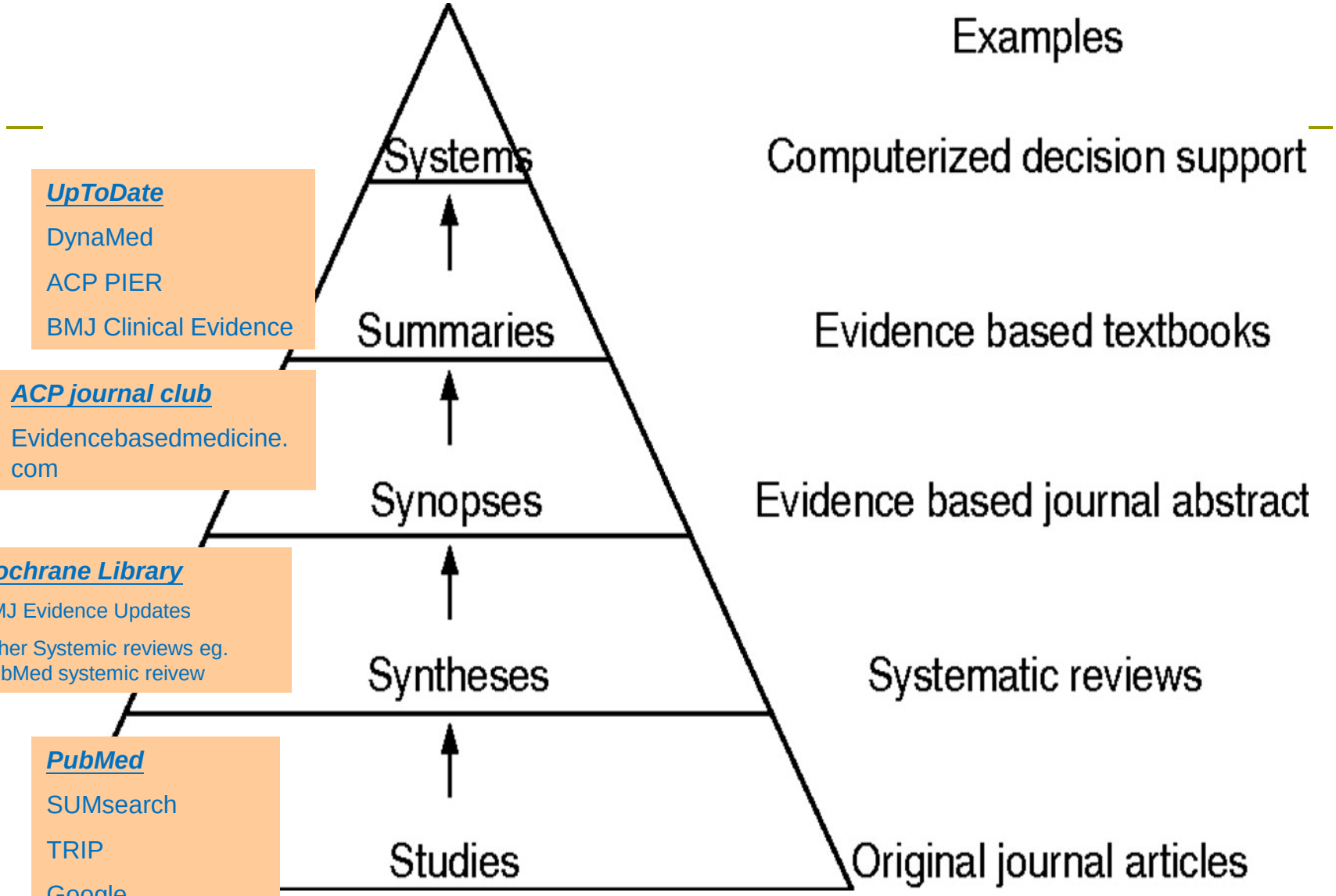
搜尋最有用的資料

Keywords :

- Community-acquired pneumonia
- Fluoroquinolones
- Tuberculosis
- Fluoroquinolone resistance
- Multidrug-resistant Mycobacterium tuberculosis

The "5S" levels of organisation of evidence from healthcare research

Brian Haynes, R Evid Based Med 2006;11:162-164



UpToDate

DynaMed

ACP PIER

BMJ Clinical Evidence

ACP journal club

Evidencebasedmedicine.com

Cochrane Library

BMJ Evidence Updates

Other Systemic reviews eg. PubMed systemic reivew

PubMed

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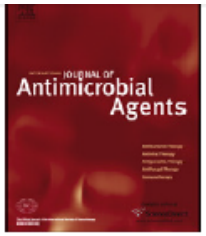
EBM ONLINE

搜尋到的文章標題

Contents lists available at SciVerse ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag



Review

Does empirical treatment of community-acquired pneumonia with fluoroquinolones delay tuberculosis treatment and result in fluoroquinolone resistance in *Mycobacterium tuberculosis*? Controversies and solutions

Gwan-Han Shen[a], Thomas Chang-Yao Tsao[b], Shang-Jyh Kao[c], Jen-Jyh Lee[d], Yen-Hsu Chen[e], Wei-Chung Hsieh[f], Gwo-Jong Hsu[g], Yen-Tao Hsu[h], Ching-Tai Huang[i], Yeu-Jun Lau[j], Shih-Ming Tsao[k], Po-Ren Hsueh[l,*]

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搜尋到的文章內容

- Fluoroquinolone resistance amongst Mycobacterium tuberculosis isolates in Taiwan.

- Empirical use of fluoroquinolones amogst community-acquired pneumonia patients and delayed tuberculosis diagnosis and treatment.

Fluoroquinolone resistance amongst Mycobacterium tuberculosis isolates in Taiwan

- Reference
- Keywords: M. tuberculosis, TB, multidrug resistance, gyrA, gyrB

Journal of Antimicrobial Chemotherapy (2007) **59**, 860–865
doi:10.1093/jac/dkm061
Advance Access publication 5 April 2007

JAC

Fluoroquinolone resistance in *Mycobacterium tuberculosis* isolates: associated genetic mutations and relationship to antimicrobial exposure

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Received 30 November 2006; returned 20 December 2006; revised 31 January 2007; accepted 5 February 2007

搜尋到的文章內容 Summary

- **Methods:**
  - 420 M. tuberculosis isolates during 2004/1~2005/12, randomly selected.
  - The MICs of ofloxacin, ciprofloxacin, levofloxacin and moxifloxacin were determined.
  - Spoligotyping and sequencing of the gyrA and gyrB genes were performed for all isolates resistant to any tested FQ.

搜尋到的文章內容 Summary

- **Results:**
  - 52 (12.4%), 26 (6.2%), 26 (6.2%) and 30 (7.1%) were resistant to isoniazid, rifampicin, ethambutol and streptomycin, respectively.
  - Multidrug resistance was found in 5.0% of isolates.
  - For all tested FQs, the susceptibility rate was higher than 97%.
  - Resistance to any first-line drug and isolation from a patient with prior anti-tuberculous treatment were correlated with FQ resistance.
  - **Multidrug resistance had the strongest correlation with FQ resistance (19% of isolates).**
  - Of the 14 FQ-resistant isolates, five (35.7%) had **gyrA mutations** (four D94G and one A90V) and another one (7.1%) had a **gyrB mutation** (N538D).

搜尋到的文章內容 Summary

- **Conclusions:**
  - This study found FQ resistance in 3.3% of all clinical isolates of M. tuberculosis.
  - FQ resistance was correlated with first-line drug resistance and prior anti-tuberculous treatment

Empirical use of fluoroquinolones amogst community-acquired pneumonia patients and delayed tuberculosis diagnosis and treatment

- Reference 1

MAJOR ARTICLE

Empiric Treatment of Community-Acquired Pneumonia with Fluoroquinolones, and Delays in the Treatment of Tuberculosis

Kelly E. Dooley,[1] Jonathan Golub,[2,5] Fernando S. Goes,[1] William G. Merz,[3] and Timothy R. Sterling[2,4,6]

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搜尋到的文章內容 Summary

- **Methods:**
  - A retrospective cohort study was conducted among adults with culture-confirmed tuberculosis to assess the effect of empiric fluoroquinolone therapy on delays in the treatment of tuberculosis.
  - Sixteen (48%) of 33 patients received fluoroquinolones for presumed bacterial pneumonia before tuberculosis was diagnosed and treated.

搜尋到的文章內容 Summary

- **Results:**
  - Among patients treated empirically with fluoroquinolones, the median time between presentation to the hospital and initiation of antituberculosis treatment was **21 days** (interquartile range, 5–32 days).
  - Among those who were not, it was **5 days** (interquartile range, 1–16 days; Pp.04).

搜尋到的文章內容 Summary

- **Conclusions:**
  - Initial empiric therapy with a fluoroquinolone was associated with a delay in the initiation of appropriate antituberculosis treatment.

Empirical use of fluoroquinolones amogst community-acquired pneumonia patients and delayed tuberculosis diagnosis and treatment

- Reference 2
- Keywords:Tuberculosis, Fluoroquinolone Resistance, Meta-analysis

International Journal of Infectious Diseases 15 (2011) e211–e216

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Fluoroquinolones are associated with delayed treatment and resistance in tuberculosis: a systematic review and meta-analysis

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搜尋到的文章內容 Summary

- **Methods:**
  - systematic review and meta-analysis
  - searched through September 30, 2010: PubMed, EMBASE, CINAHL, Cochrane Library, Web of Science, BIOSIS Previews, and the ACP Journal Club.

搜尋到的文章內容 Summary

- **Results:**
  - Nine eligible studies (four for delays and five for resistance issues) were included in the metaanalysis from the 770 articles originally identified in the database search.
  - The mean duration of delayed diagnosis and treatment of pulmonary TB in the fluoroquinolone prescription group was **19.03 days**, significantly longer than that in the non-fluoroquinolone group (95% confidence interval (CI) 10.87 to 27.18, $p < 0.001$).

搜尋到的文章內容 Summary

- **Conclusions:**
  - Empirical fluoroquinolone prescriptions for pneumonia are associated with longer delays in diagnosis and treatment of pulmonary TB and a higher risk of developing fluoroquinolone-resistant M. tuberculosis.

Empirical use of fluoroquinolones amogst community-acquired pneumonia patients and delayed tuberculosis diagnosis and treatment

- Reference 3
- Keywords: tuberculosis; fluoroquinolone; diagnosis

INT J TUBERC LUNG DIS 9(11):1215–1219

Impact of fluoroquinolones on the diagnosis of pulmonary tuberculosis initially treated as bacterial pneumonia

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SUMMARY

搜尋到的文章內容 Summary

- **Methods:**
  - 9 patients with PTB initially treated as having community-acquired pneumonia and treated with fluoroquinolones for more than 5 consecutive days, from 2000/1~2004/12 as a control group.
  - 19 patients TB patients initially treated with non-fluoroquinolone antibiotics were enrolled.
  - Reviewed the clinical data and compared treatment responses between the two groups.

搜尋到的文章內容 Summary

- **Results:**
  - In the fluoroquinolone group, eight patients (89%) improved clinically or radiographically.
  - whereas only eight patients (42%) in the non-fluoroquinolone group improved (P=0.04).
  - The delay in initiation of anti-tuberculosis medication was longer in the fluoroquinolone group than in the non-fluoroquinolone group (**43.1**±40.0 vs. **18.7**±16.9 days, P=0.04).

搜尋到的文章內容 Summary

- **Conclusions:**
  - Delay in the initiation of anti-tuberculosis treatment is possible in patients administered fluoroquinolone and initially misdiagnosed as having bacterial pneumonia.

Empirical use of fluoroquinolones amogst community-acquired pneumonia patients and delayed tuberculosis diagnosis and treatment

- Reference 4

TUBERCULOSIS

Empirical treatment with a fluoroquinolone delays the treatment for tuberculosis and is associated with a poor prognosis in endemic areas

J-Y Wang, P-R Hsueh, I-S Jan, L-N Lee, Y-S Liaw, P-C Yang, K-T Luh

Thorax 2006;**61**:903–908. doi: 10.1136/thx.2005.056887

搜尋到的文章內容 Summary

- **Methods:**
  - 548 patients with culture confirmed tuberculosis aged >14 years diagnosed 2002/7~2003/12 were included and their medical records were reviewed.
  - 79 (14.4%) received a fluoroquinolone. (FQ group)
  - 218 received a non-fluoroquinolone. (AB group)
  - 251 received no antibiotics before antituberculous treatment.

搜尋到的文章內容 Summary

- **Results:**
  - In the FQ group the median interval from the initial visit to starting antituberculous treatment was longer than in the AB group and in those who received no antibiotics (**41** v 16 v **7** days), and the prognosis was worse (hazard ratio 6.88 (95% CI 1.84 to 25.72)).
  - Of the 9 mycobacterial isolates obtained after fluoroquinolone use whose initial isolates were susceptible to ofloxacin, one (11.1%) was resistant to ofloxacin **(after fluoroquinolone use for 7 days).**
  - Independent factors for a poor prognosis included empirical fluoroquinolone use, age>65, underlying disease, hypoalbuminaemia, and lack of early antituberculous treatment.

搜尋到的文章內容 Summary

- **Conclusions:**
  - 14.4% of our patients with tuberculosis received a fluoroquinolone before the diagnosis.
  - With a **34 day delay** in antituberculous treatment and more frequent coexistence of underlying disease and hypoalbuminaemia, empirical fluoroquinolone treatment was associated with a poor outcome.
  - Mycobacterium tuberculosis isolates could obtain **ofloxacin resistance within 1 week**.

Conclusions

- Empirical treatment of CAP with a FQ might mask active TB, delay treatment and contribute to the development of FQ resistance.
- FQ resistance is less likely to occur amongst M. tuberculosis strains isolated from patients with short-term exposure (<7 days) to FQ.
- in Taiwan as well as in other countries with endemicity of TB, a short-course (5-day) regimen of a FQ (levofloxacin, moxifloxacin and gemifloxacin) is still recommended for empirical therapy for CAP patients if the patient is at **low risk** for TB.

Appraisal

Answer	文獻試圖回答什麼問？	是否回答我的問題？
Author	作者是誰，是否爲這方面專家?	有無利益衝突?
Method	RCT	
Patient	是否隨機取樣 (randomization)	取樣是否具代表性 (representative)
Intervention	是否有清楚的描述(Ascertain)是否實際可行	
Comparasion		
Outcome	是否有客觀雙盲的測量 (MBO)	是否有統計學或臨床上的意義？
Time	是否清楚描述研究取樣、操作、結果測量的時間點，追蹤時間是否夠長	

Evidence appraisal

- Was the assignment of patients to treatments randomised? **Yes**
- Were the groups similar at the start of the trial? **Yes**
- Aside from the allocated treatment, were groups treated equally? **Yes**

External Validity / Applicability

- Is my patient so different to those in the study that the results cannot apply? **No**
- Is the treatment feasible in my setting? **Yes**

Audit（自我評估）

- 「提出臨床問題」方面：
  - 我提出的問題是否具有臨床重要性？**Yes**
- 「搜尋最佳證據」方面：
  - 我是否知道我的問題的最佳證據來源？ **Yes**
  - 我是否從大量的資料庫來搜尋答案？ **Yes**
- 「嚴格評讀文獻」方面：
  - 我是否盡全力做評讀了？ **Yes**
- 「應用到病人身上」方面：
  - 我是否將搜尋到的最佳證據應用到我的臨床工作中？ **Yes**

Thanks for your attention~~