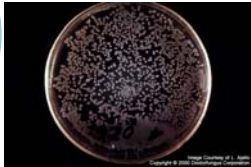


Fungal Peritonitis... easier to prevent than to treat?

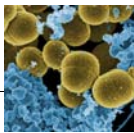


Judith Marin, PharmD
Fraser Health Authority, BC
March 2012

Outline

- Review complications related to fungal peritonitis
- Evaluate literature around fungal peritonitis prophylaxis
- Discuss FHA PD program experience

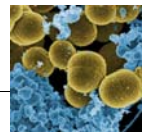
Fungal Peritonitis



- 3 to 6% of all peritonitis episodes
- Mortality rate between 15 to 50%
- 70 to 90% caused by *Candida species*
 - Predominantly *C. albican*

Matuszkiewicz-Rowinska J. *Perit Dial Int* 2009; 29 (S2): S161-5.

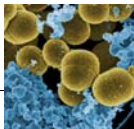
Fungal Peritonitis



- Complications
 - High mortality risk
 - 40% unable to resume PD
 - Sclerosing peritonitis
 - Bowel obstruction
 - Abscess formation

Matuszkiewicz-Rowinska J. *Perit Dial Int* 2009; 29 (S2): S161-5.

Fungal Peritonitis



- Risk factors
 - Immunosuppression
 - Malnutrition
 - Bowel perforation
 - Diverticulitis
 - DM
 - Neoplasm
 - Vaginal candidiasis
 - **50 to 80% received broad spectrum ATB in last 3 months**
 - Gram neg peritonitis might have greater risk

Matuszkiewicz-Rowinska J. *Perit Dial Int* 2009; 29 (S2): S161-5.

Fungal peritonitis



- Why is antibiotic exposure associated with fungal peritonitis?
 - Antibiotic kills normal flora and promotes yeast colonization and proliferation in GI tract
 - *Candida sp.* found in stool sample of pts treated with antibiotics
 - Fungi invade across intestinal mucosal barrier and reach peritoneal cavity
 - Inflammation during peritonitis may enhanced susceptibility of peritoneum to fungal infection

Moreiras-Plaza M et al. *Perit Dial Int* 2007; 27: 460-2.

Prophylaxis... what do we know about it?



Ideal Prophylactic Agent

- Good oral bioavailability and penetration in PD fluid
- Active against putative pathogens
- High safety profile
- Minimum risk for inducing resistance or selecting resistant organism
- Inexpensive

ISPD Guidelines: “Reducing the risks of PD-related infections”

- Most episodes of fungal peritonitis are preceded by courses of antibiotics
- Fungal prophylaxis during antibiotic therapy may prevent some cases of *Candida* peritonitis in programs that have high rates of fungal peritonitis
 - ... particularly for patients taking prolonged or frequent courses of antibiotics (such as those with foot ulcer and osteomyelitis).

Piraino B, et al. Perit Dial Int 2011; 31: 614-30.

Observational studies

- 9 observational studies published
 - 1 study with ketoconazole/nystatin (peds)
 - 1 study on fluconazole/nystatin
 - 4 studies on nystatin
 - 3 studies on fluconazole
- 7/9 studies showed benefits with prophylaxis
 - 2 negative studies with nystatin
 - Both negative studies had low baseline incidence of fungal peritonitis => limited study power

Nystatin prophylaxis

Lo W.K. et al. Am J Kidney Dis 1996; 28: 549-52.

Design	Randomized control trial
Intervention	Nystatin 500,000 units PO QID during antibiotic therapy vs. control x 24 months Antibiotics ordered for any indications
Population	397 CAPD pts in 2 centres

Nystatin prophylaxis

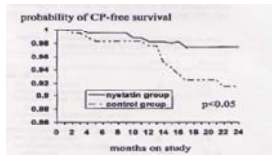
Lo W.K. et al. Am J Kidney Dis 1996; 28: 549-52.

	Nystatin group n=199	Control group n=198
No. pts with peritonitis	103	103
Peritonitis rate (pt-mo/episode)	16.6	17.5
No. antibiotic prescriptions	452	420

Nystatin prophylaxis

Lo W.K. et al. *Am J Kidney Dis* 1996; 28: 549-52.

- 4 vs. 12 episodes of *Candida* peritonitis in nystatin vs. control group



- Rate of antibiotic related *Candida* peritonitis 1.39 vs. 3.10 per 100 peritonitis episodes (p=NS)
- No difference in probability of antibiotics-related CP-free survival
- No ADRs reported

Nystatin prophylaxis

Lo W.K. et al. *Am J Kidney Dis* 1996; 28: 549-52.

- Author's conclusion

" We conclude that oral nystatin prophylaxis with each antibiotic prescription reduced the rate of *Candida* peritonitis in patients on CAPD irrespective of its apparent temporal relationship to antibiotic prescription."

Nystatin prophylaxis

Lo W.K. et al. *Am J Kidney Dis* 1996; 28: 549-52.

○ Limitations

- Methodology
- Only antibiotics ordered by renal unit were accounted for
- Patient compliance to prophylaxis treatment was not evaluated
- Evaluation on ADRs
- Resistance rate not reported

Fluconazole prophylaxis

Restrepo et al. *Perit Dial Int* 2010; 30: 619-25.

Design	Randomized control trial
Intervention	Fluconazole 200 mg PO Q48hours during ATB treatment vs. control group x 150 days post ATB PO/IV/IP ATBs ordered for BP, TI or ESI
Population	410 CAPD and APD pts in 1 centre Exclusion: allergy to fluconazole, liver failure, < 18 y/o or > 70 y/o, recurrent peritonitis

Fluconazole prophylaxis

Restrepo et al. *Perit Dial Int* 2010; 30: 619-25.

	Fluconazole group n=210	Control group n=210
Frequency of bacterial peritonitis	210	210
Frequency of ESI or TI	26	26
Frequency of secondary fungal peritonitis	3	15

Fluconazole prophylaxis

Restrepo et al. *Perit Dial Int* 2010; 30: 619-25.



- For ESI and TI, no difference in FP with prophylactic fluconazole.
- 2 patients died from fungal peritonitis
- Sensitivity for fluconazole was available in 10 cases
 - 4/10 were sensitive culture to fluconazole
 - Of the resistant cases, 2/6 were secondary peritonitis
- No ADR (↑AST/ALT) reported

Fluconazole prophylaxis

Restrepo et al. Perit Dial Int 2010; 30: 619-25.

○ Author’s conclusion:

“In patients with bacterial peritonitis, administration of prophylactic oral fluconazole throughout the time they received antibiotics significantly prevented the appearance of secondary fungal peritonitis.”

Fluconazole prophylaxis

Restrepo et al. Perit Dial Int 2010; 30: 619-25.

○ Limitations:

- Methodology
- Numbers given didn’t match
- Not all antibiotic orders received taken into account
- No data on compliance and minimal data on ADRs

Comparison of Prophylactic Agents

Fluconazole	Nystatin
<ul style="list-style-type: none"> ○ ADRs: Headaches; ↑ QTc; N/V/D; ↑ AST/ALT/ Alk phos; rash ○ Prevents systemic fungal overgrowth ○ Good penetration in PD fluid ○ Cost: \$45 (100 mg po Q2days x 14 d) 	<ul style="list-style-type: none"> ○ ADRs: N/V/D; taste ○ Prevents GI fungal overgrowth ○ No systemic effect ○ Cost: \$29 (500,000 units po QID x 14 d)

Lexicomp 2012.

Ideal Prophylactic Agent

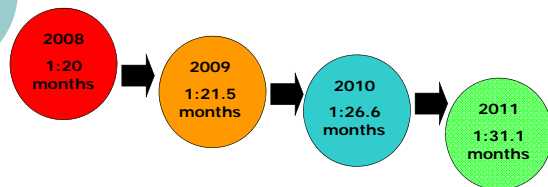
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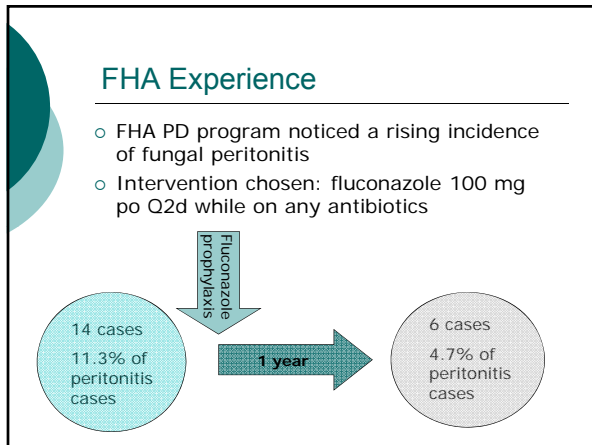
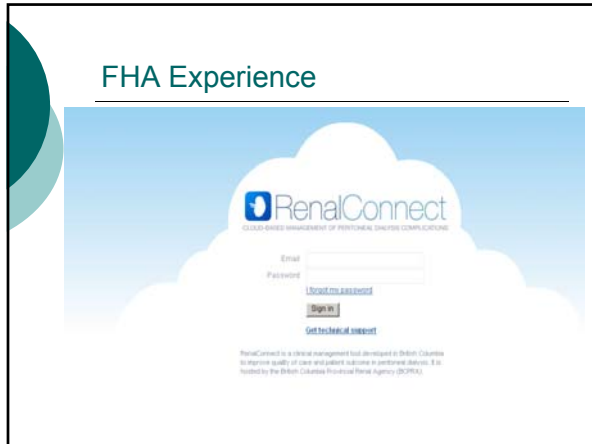
FHA Experience

- Currently about 250 PD pts
 - 2 centres
 - 375 pts-year
 - ~ 90% pts doing APD
 - Bedside insertion of PD catheter done by 5 nephrologists
- Follow-up q2 to 3 months
- 1 RNs doing home visit post-training or post-peritonitis
- 12 PD pts receiving care in nursing home

FHA Experience

Peritonitis Rate





- ## Summary
- Prognosis for fungal peritonitis is poor with high risk of complications.
 - Studies have been published on use of nystatin or fluconazole for fungal peritonitis prophylaxis.
 - Studies supporting fluconazole use might have more consistent data.
 - In PD programs with high fungal peritonitis rates, fungal peritonitis prophylaxis should be considered.

