



NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Pneumocystis Pneumonia (PCP): Part 2

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Last Updated: 1/24/13

Pneumocystis Pneumonia (PCP): Part 2

- Prevention
 - Initiating Prophylaxis
 - Discontinuing Prophylaxis
 - Other Considerations
- Treatment
 - Recommended Agents
 - Managing Side Effects/Treatment Failure
 - Drug Resistance

Prevention

Initiating Prophylaxis

- Indications for prophylaxis:
 - **CD4 count <200 cells/mm³ (AI)**
 - **Oral thrush (AII)**
 - CD4% <14 or other AIDS-defining illness (BII)
 - Following PCP treatment (secondary prophylaxis)



Options for Prophylaxis

Trimethoprim-Sulfamethoxazole (TMP-SMX)

- DS or SS tab daily recommended (AI)
- DS tab 3x/week an alternative (BI)

Dapsone

- Check G6PD level
- 100 mg daily

Atovaquone

- Liquid, expensive
- 1500 mg daily

Inhaled Pentamidine

- Several limitations
- 300 mg monthly

Discontinuation of Prophylaxis

- **CD4 count >200 cells/mm³ for at least 3 months**
- Systematic review of early discontinuation:
 - CD4 <200 cells/mm³ and suppressed viral load
 - Overall rate of PCP: 0.48/100 person-years
 - Inadequate data for CD4 \leq 100

1) Kaplan JE, Benson C, Holmes KK et al. CDC MWR 2009;58(RR-4):1-207.

2) Costinuk CT, Fergusson DA, Doucette S, Angel JB. PLoS One 2011;6(12): doi: 10.1371/journal.pone.0028570

Early Discontinuation of Prophylaxis

Study	Site	Type	# Subjects	Criteria	PCP Rate
Soriano et al (AIDS 2000)	Madrid, Spain	Retrospective	29 (secondary prophylaxis only)	VL <500 after 3 months ART	1/522 patient months
D'Egidio et al (AIDS 2007)	Ottawa, Canada	Prospective	19	VL <50 for ≥ 3 months	0/261 patient months
COHERE (CID 2010)	29 European cities	Prospective	23,412 (primary prophylaxis only)	VL <400	0/1000 patient years
Cheng et al (BMC ID 2010)	Thailand	Retrospective	215	VL <400	0.31/100 patient years

Prevention of Exposure

- Difficult because ubiquitous organism
- Should infected hospitalized patients be isolated?
 - 1) Study in France and Switzerland:
 - % with DHPS mutation who had never been exposed to sulfa: 29.7% in Lyon, France vs. 3% in Switzerland
 - Lyon did not have policy of isolating/separating PCP patients
 - 2) Outbreak among renal transplant recipients

1) Hauser PM, et al. Clin Infect Dis 2010;15;51(4):e28-33. doi: 10.1086/655145

2) Rabodonirina M et al. Emerg Infect Dis 2004;10:1766-73

Treatment

Treatment Options

- Outpatient
- No significant hypoxia
- Able to take PO
- Adherent to meds

Mild Disease

Oral TMP-SMX

Clindamycin-primaquine

TMP-Dapsone

Atovaquone

Severe Disease

IV TMP-SMX

IV Pentamidine

Clindamycin-primaquine

- Inpatient
- Significant hypoxia
- Unable to take PO
- Comorbidities
- Need pentamidine

Key Treatment Considerations

- Empiric treatment ok? **Yes**
- Standard course: **21 days**
- Corticosteroids if: **PaO₂ <70 or A-a gradient >35**
- Pregnancy: **TMP-SMX**
- Treatment based on prophylaxis? **No**

Managing Side Effects

TMP-SMX	*Dapsone	Atovaquone	Clindamycin	*Primaquine	Pentamidine
Rash	Rash	Rash	Rash	Agranulocytosis	Electrolyte changes
Renal/ hepatic dysfunction	Hemolytic anemia	Hepatic dysfunction	C. diff	Hemolytic anemia	Renal / hepatic dysfunction
HyperK	Cytopenias	GI symptoms	GI symptoms	Cytopenias	Arrhythmias
GI symptoms	Methemoglobinemia				Hypotension
Cytopenias					Hypoglycemia
					Pancreatitis
					Cytopenias

*Remember to check G6PD level

Treatment Failure

- May worsen in first **2-3** days but should improve by days **5-7**; if not, consider the following:
 - Rule out concomitant infection
 - Switch oral meds to IV? IV med to alternate agent?
 - Add additional agent?
 - Increase steroid dose?
 - Extend duration?
 - Add an echinocandin?

Prognosis

- Factors associated with poor outcome in PCP:
 - **Severe disease:**
 - Hypoxia, ICU admission, mechanical ventilation
 - **Advanced immunosuppression**
 - Older age
 - Higher LDH
 - Prior episodes of PCP
 - Low albumin

Drug Resistance

- DHFR gene mutation (from TMP)
- DHPS gene mutation (from SMX or dapsone)
 - More Common
- Some association with treatment failure, not always
 - Other factors likely more important
- Bottom line: **TMP-SMX** always first line

Summary

- Prophylaxis indicated if CD4 <200, thrush, prior PCP
- Stop if CD4 >200 for 3 months, though likely safe if CD4 100-200 and VL undetectable
- Should likely separate patients with PCP from other immunosuppressed patients
- First-line for prophylaxis and treatment: TMP-SMX
- Many possible drug side effects and no clear guidelines for managing treatment failure