Survival Time of HIV-Infected Patients with Cryptococcal Meningitis

Suthat Chottanapund MD*,***,
Pratap Singhasivanon MD*, Jaranit Kaewkungwal PhD*,
Kanittha Chamroonswasdi PhD**, Weerawat Manosuthi MD***

** Faculty of Tropical Medicine, Mahidol University, Bangkok*
*** Faculty of Public Health, Mahidol University, Bangkok*
**** Bamrasnaradura Infectious Diseases Institute, Ministry of Public Health, Bangkok*

Objective: *To study survival time and risk factors of mortality among HIV-infected patients who had cryptococcal meningitis.*
Design: *Retrospective cohort study.*
Material and Method: *Patients' medical records of those who had HIV-infection with newly diagnosed cryptoccocal meningitis between January 2002 and December 2004 were reviewed. Each patient was classified into one of two groups, according to their anti-retroviral status (ART).*
Results: *Five hundred and forty nine patients enrolled in the present study: 281 (51.2%) in the ART+ group and 268 (48.8%) in the ART-group. The mean age was 33.4 $\pm$ 6.9 years old in the ART + group and 33.6 $\pm$ 7.0 years old in the ART-group. There were more male in both groups: 207 males and 74 females in the ART+ group, and 195 males and 73 females in the ART-group. Baseline CD4 cell count of both groups was 20 (6-74) cells/ mL and 24 (9-72) cells/ ml. About 30% of both groups of patients experienced major opportunistic infection before cryptococcal meningitis. All patients were treated by standard amphotericin B for a 2-week duration followed by fluconazole for an additional 8 weeks. There were no differences of baseline characteristics between the two groups ($p > 0.05$). The survival rates at 12, 24, and 36 months were 92.8%, 87.4%, and 85.4% in the ART+ group and 55.3%, 42.2%, and 36.8% in the ART– group, respectively ($p < 0.01$). The median survival time in the ART- group was 15 months. From the Cox regression model, the hazard ratio for "not received ART" was 4.87 (95%CI = 2.48-9.44, $p < 0.01$).*
Conclusion: *The present study demonstrated the substantial increasing of survival time of HIV-infected patients with cryptococcal meningitis by initiated ART, even in a resource limited setting (no flucytosine, local combined antiretroviral drugs with NVP based regimens).*

Keywords: *HIV/AIDS, Cryptococcal meningitis, Survival time, Antiretroviral therapy, GPO-VIR*

J Med Assoc Thai 2007; 90 (10): 2104-11
Full text. e-Journal: *http://www.medassocthai.org/journal*

Opportunistic infections (OIs) are common causes of death in HIV-infected patients. Antiretroviral therapy (ART) has reduced the incidence of opportunistic infections for certain patients with access to care. However, opportunistic infections will continue to cause substantial morbidity and mortality in patients with HIV infection[1,2]. In Thailand, the most common opportunistic infections were *Mycobacterium tuberculosis* (81,955 cases/year, 29.74%), pulmonary or extrapulmonary, *Pneumocystis Carinii* (58,433 cases/year, 21.21%), cryptococcosis (44,061 cases/year, 15.99%), candidiasis of trachea and bronchi (14,568 cases/year, 5.29%), and recurrent bacterial pneumonia (10,251 cases/year, 3.72%)[3,4].

As the above number, cryptococcal meningitis is one of the leading causes of mortality and morbidity

Correspondence to : Chottanapund S, Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Rd, Ratchadawee, Bangkok 10400, Thailand. Phone: 086-300-6645, E-mail: suthat_97@yahoo.com

among patients with AIDS. Before the ART era, approximately 5%-8% of HIV-infected patients in developed countries acquired disseminated cryptococcosis, especially those who had CD4 count < 100 cells/mL[5,6]. Untreated cryptococcal meningitis is uniformly fatal. The median survival time is about nine months.

The recommended initial treatment for acute disease is amphotericin B, usually combined with flucytosine, for a 2-week duration followed by fluconazole alone for an additional 8 weeks. After completion of induction treatment, fluconazole 200 mg/day has been used for standard secondary prophylaxis until immune reconstitution occurs because of ART[7]. In Thailand, flucytosine is not available. Amphotericin B for two weeks plus fluconazole for 8 weeks is a treatment for cryptococcal meningitis. There is a report showing that for serious cryptococcal infection, such as cryptococcal meningitis, a combination of amphotericin B with flucytosine would sterilize patients' cerebrospinal fluid faster than amphotericin B alone[8]. Furthermore, there is a study showing that amphotericin B was not as effective, cumulative mortality at 2 weeks, 4 weeks, and 1 year were 16%, 24%, and 76%, respectively[9-11]. The lack of flucytosine administration during the initial two weeks of therapy is also one of the predictive factors for relapse of the disease[12].

Due to few clinical data regarding survival rates among HIV-infected patients who had cryptococcal meningitis as co-infection in a resource limited setting; no flucytosine, using locally made antiretroviral therapy (GPO-VIR, local combined Navirapine (NVP) based regimen antiretroviral drugs, provides by Thai Government Pharmaceutical Company)[3,4]. The objective of the present study was to determine the survival time among HIV-infected patients with cryptococcal meningitis who received and did not receive antiretroviral therapy in a resource limiting setting situation. The second objective was to identify possible risk factors that may relate to death among these patients.

Material and Method

A retrospective cohort study was conducted by reviewing patients' medical records of those who had HIV-infection with newly diagnosed cryptoccocal meningitis between January 2002 and December 2004 in Bamrasnaradura Infectious Diseases Institute, Ministry of Public Health, Thailand. Patients' identification numbers were identified by annual database of the Institute. Inclusion criteria were HIV-infected patients, whose age was above 15 years old, newly diagnosed cryptococcal meningitis during the studied period. Cryptococcal meningitis was diagnosed by a) presumptive criteria; Histopathology or India ink stain of cerebrospinal fluid demonstrated typical encapsulated yeasts or b) definitive criteria; culture positive for *Cryptococcus neoformans* or presence of cryptococcal capsular polysaccharide in serum or cerebrospinal fluid demonstrated by agglutination of antibody-coated latex beads or reactivity with specific DNA probes (rDNA)[5,13]. Exclusion criteria were as follows: 1) Patients who had diagnosed cryptoccocal meningitis from other hospitals. 2) Patients who initiated antiretroviral therapy before diagnosed cryptococcal meningitis. All patients were followed until the end of the present study (1 October 2006) or death. Each patient was classified into two groups during the follow-up period: received antiretroviral therapy (ART+ group) and did not receive antiretroviral therapy (ART– group). A patient who was eligible to ART+ group defined as a patient who received antiretroviral therapy for at least two visits.

The primary outcome of interest was duration of time from diagnosed cryptoccocal meningitis to death. Patients were censored at the date of last visit if they were lost to follow-up or censored at the date of referral. The last event responsible for the patients' death was defined as the cause of death.

Statistical analysis

Data was analyzed as follows: 1) Patients' baseline characteristics were described by descriptive statistics. Continuous variables were described by mean $\pm$ SD. Categorical variables were described by proportion and percentage. 2) Survival time after cryptococcal meningitis was treated as continuous variable. Due to distribution free survival time with unknown baseline hazard ratio, the present research used Kaplan-Meier method for survival analysis. 3) Possible risk factors were used for univariate analysis. For variable that had more than one group, Log rank test was used for comparison. The significant level was set at 0.05 ($p < 0.05$). 4) Significant variables from univariate analysis were further fitted into Cox's proportional hazard model for multivariate analysis[14-18].

Ethical consideration

Case record forms were treated anonymously and the present study was approved by The Ethical Committee for Research in Human Subjects, Department of Diseases Control, Ministry of Public Health, Thailand.

Results

Five hundred and forty nine patients were enrolled in the present study. The mean (± SD) age was 33.5 ± 6.9 years old. The patients were classified into two groups according to antiretroviral therapy status: ART+ and ART–. The mean age was 33.4 □ 6.9 years old in the ART+ group and 33.6 □ 7.0 years old in the ART-group. There were more male in both groups: 207 males and 74 females in the ART+ group, and 195 males and 73 females in the ART– group. Baseline CD4 cell count were 20 (6 -74) cells/ mL. and 24 (9 -72) cells/ mL, respectively. About 30% of patients experienced major opportunistic infection before cryptococcal meningitis. All patents were treated by standard amphotericin B for a 2-week duration followed by fluconazole for an additional 8 weeks. There was no significant difference in the baseline characteristics of patients in both groups. All p-values were greater than 0.05 (Table 1). The distribution of ART (281 cases) were NVP based regimens 209 cases (74.4%; GPO-VIR 172 cases, 61.2%), EFV based regimens 48 cases(17%), PI based regimens 18 cases (6.5%), and other 6 cases (2.1%). For baseline viral load, in the ART+ group, most patients had baseline viral load < 100,000 copies/mL. However, only eight patients in the ART-group had baseline viral load testing due to financial constraints.

By stratified patients according to their ART status, univariate analysis for the following possible risk factors were performed: history of previous major opportunistic infections, site of cryptococcal infection, complication of cryptococcal meningitis (blindness, deafness, hydrocephalus), baseline level of CD4+, white blood cells in first diagnosed cerebrospinal fluid of patients, and opening pressure of patients' cerebrospinal fluid. In ART– group, not all factors related to the death of HIV-infected patients who had cryptococcal meningitis (all $p > 0.05$). For the ART+ group, the analysis included baseline plasma level of HIV RNA. The only risk factor for death found significant was baseline level of CD4 ($p < 0.01$) (Table 2).

One hundred and seventy nine patients died in the ART– group, 160 (89.3%) of cryptococcal meningitis and 19 (24%) of other causes. Fifty-two patients died in the ART+group, 44 (84.6%) of cryptococcal meningitis and eight (15.38%) of other causes. The Cox regression analysis was used in multivariate analysis. "Not received ART" gave the highest possibility of death in HIV infected patients with cryptococcal meningitis. The hazard ratio was 4.87 (95%CI = 2.48-9.44, $p < 0.01$). That means patients who did not receive ART had a 4.87 times higher chance to die of cryptococcal meningitis compared to patients who received ART (Table 3).

The possibility of survival time after being diagnosed with cryptococcal meningitis estimated by the Kaplan-Meier survival analysis compared the ART+ group and the ART– group. The survival rate at 12, 24, and 36 months was 92.8%, 87.4%, and 85.4% in the ART+ group, and 55.3%, 42.2%, and 36.8% in the ART– group, respectively (Log-rank, $p < 0.01$). The median survival time in the ART– group was 15 months (Fig. 1).

The possibility of survival time after being diagnosed with cryptococcal meningitis estimated by the Kaplan-Meier survival analysis after stratified by types of ART, also showed that local combined antiretroviral drugs, GPO-VIR, had a higher possibility of survival than the ART– group (Log-rank, $p < 0.01$).

Table 1. Baseline characteristics of the patients (n = 549)

Characteristic	ART+ group (n = 281)	ART– group (n = 268)	p-value
Mean age (years), ± SD	33.4 ± 6.9	33.6 ± 7.0	0.80
Gender			
Male	207 (74%)	195 (73%)	0.499
Female	74	73	
Baseline CD4 cell count, cells/mL, median (IQR) (n = 316)	20 (6-74)	24 (9-72)	0.639
Baseline CD4 percentage, %, median (IQR) (n = 316)	2 (1-6)	3 (1-6)	0.636
Previous major OIs	85 (30%)	70 (26%)	0.177
Sites of infection			
Meningitis	273 (97%)	250 (93%)	0.174
Meningitis with extra-neural sites	9	17	

Table 2. Univariate analysis for possible risks of mortality in HIV infected patients with cryptococcal meningitis according to ART status (n = 549)

Risk factors	ART– group (n = 268)			ART+ group (n = 281)		
	No. of death by crypto.	Total	p-value	No. of death by crypto.	Total	p-value
History of previous major OIs						
No	116	199	0.56	30	195	0.90
Yes	44	69		14	86	
Sites of infection						
Meningitis	152	251	0.50	43	272	0.63
Meningitis with extra-neural sites	8	17		1	9	
Complication from crypto.						
No	149	250	0.93	43	274	0.95
Yes	11	18		1	7	
Baseline level of CD4						
CD4 ≤ 50 cells/mL	14	37	0.46	30	175	0.007
CD4 ≥ 51 cells/mL	10	21		4	84	
Baseline plasma level of HIV RNA						
≤ 100,000 copies/mL	N/A	N/A	N/A	8	140	0.33
> 100,000 copies/mL	N/A	N/A		6	62	
CSF WBC						
< 20 cell/mL	101	167	0.55	25	156	0.79
≥ 21 cell/mL	46	77		13	88	
High opening CSF pressure						
CSF pressure < 25 mmHg	38	70	0.60	10	74	0.88
CSF pressure ≥ 25 mmHg	91	149		22	153	

Table 3. Multivariate analysis (Cox regression) for possible risks of mortality in HIV infected patients with cryptococcal meningitis (n = 549)

Risk factors	HR	95% CI	p-value
Not received ART	4.87	2.48-9.44	<0.01
Extra neural infection	1.90	0.44-8.13	0.39
Complication from crypto.	1.75	0.50-6.11	0.37
High opening CSF pressure	1.26	0.61-2.61	0.54
Baseline level of CD4 < 50 cells/mL	1.16	0.57-2.37	0.69
Low WBC count in CSF (< 20 cells/mL)	1.13	0.56-2.27	0.73
History of previous major OIs	1.00	0.48-2.10	0.99

Discussion

In the present study, most of the HIV-infected patients with cryptococcal meningitis usually presented at a stage of profound immunodeficiency. Most of them had low baseline CD4 cells (< 50 cells/mL). Mean baseline CD4 cells were 20 cells/mL in the ART+ group and 24 cells/ml in the ART- group. This finding corresponded with previous studies in many countries[13,19-24]. About half of the patients in the present study had not received ART, even although the cost of ART was only 1 US$ per day (about 40 Baht). In Thailand, average personnel income per month was 3,844 baht at the study time (year 2002). The national universal coverage ART program was implemented on a later year due to the benefits of ART.

A previous study showed that early death of HIV-infected patients with cryptococcal meningitis was associated significantly with low CSF white blood

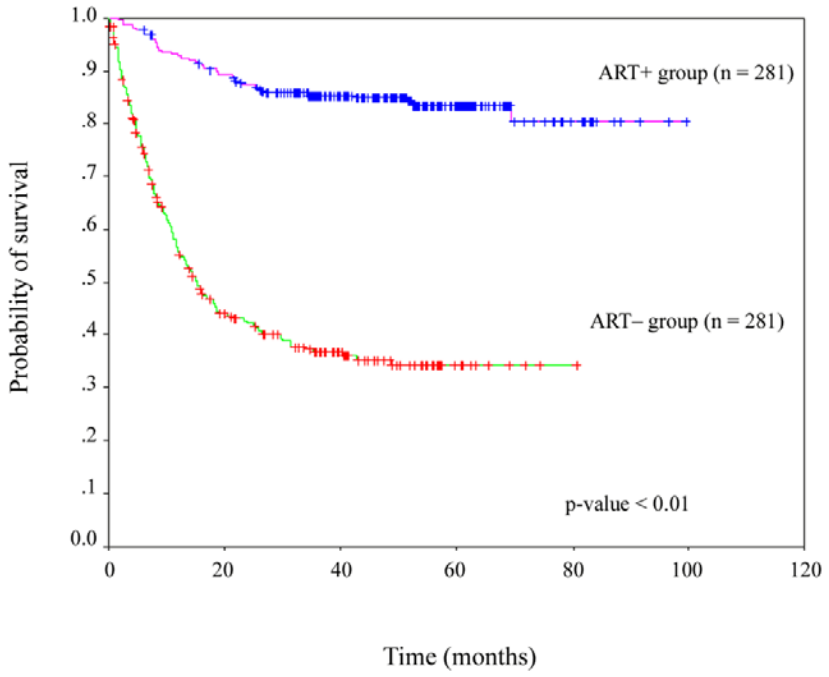

Fig. 1 Survival curves of HIV infected patients with cryptococcal meningitis according to ART status

cells < 20 cells/mL, extra-neural site of infection, raised opening pressure of CSF > 25 cmH_2O, persistence lower CSF sugar and initial serum cryptococcal titer > 1:32. The late mortality was associated with delayed cerebrospinal fluid (CSF) yeast clearance and relapse[9,25,26]. Not all the previously mentioned risk factors were found to have statistical significance in the present study. The only factor demonstrated to be an important risk factor of survival in HIV-infected patients with cryptococcal meningitis was "not received ART" ($p < 0.01$). In the present study, most of the patients died early within the first year after being diagnosed with cryptococcal meningitis[27]. This reason may explain why there were no risk factors found to be significant. By stratifying patients according to their ART status, the authors found that in the ART+ group, baseline level of CD4 $\leq$ 50 cells/mL was found significantly to be the risk of death in HIV-infected patients who had cryptococcal meningitis ($p < 0.01$). From the results of the present study, baseline CD4 cells $\geq$ 50 cells/mL and initiation of ART may be the most important two factors to improve survival in HIV-infected patients who had cryptococcal meningitis.

The median survival time of patients in the ART- group was about one year, which is the same as a previous study by Powderly[5]. In addition, in the present study, the authors found that, in HIV-infected patients, amphotericin-B alone might not be effective enough. The survival rate at one year was about 50%, which is the same as the study by Pitisuttithum[9].

There were limitations in the present study. First, the present study was a retrospective research by using secondary data source (patients' medical records). There usually is missing data in this kind of study. In the present study, some risk factors were not completely recorded such as socioeconomic status, serum cryptococcal titer, CD4 cells count, viral load, results of CSF culture. This limitation may lead to information bias. Second, the ART statuses were not well randomized; in the present study, the group who had ART was assigned by their own financial status. To solve this problem, a French study group conducted two historical cohorts which compared patients in the pre-ART era with those in the ART era[27]. Third, the authors did not study either drugs safety or side effects of ART, which may effect the survival time. Finally, the data on immune reconstitution syndromes will be further explored. The authors did not show the data here due to limitation of some missing data.

In conclusion, the present study demonstrated the substantial increase of survival time of HIV-infected patients with cryptococcal meningitis by initiated ART,

even in a resource limited setting (no flu-cytosine, local combined antiretroviral drugs with NVP based regimens). The ART proved to be the only modifiable risk factor that could prolong survival time in the present study. Further prospective study for HIV-infected patients with cryptococcal meningitis regarding timing of ART initiation, immuno-reconstitution syndrome, and ART side effects would be beneficial for improving care in HIV-infected patients with cryptococcal meningitis.

References

1. Holmes CB, Losina E, Walensky RP, Yazdanpanah Y, Freedberg KA. Review of human immunodeficiency virus type 1-related opportunistic infections in sub-Saharan Africa. Clin Infect Dis 2003; 36: 652-62.
2. Chariyalertsak S, Sirisanthana T, Saengwonloey O, Nelson KE. Clinical presentation and risk behaviors of patients with acquired immunodeficiency syndrome in Thailand, 1994-1998: regional variation and temporal trends. Clin Infect Dis 2001; 32: 955-62.
3. HIV/AIDS situation in Thailand by August 2003. Bangkok: AIDS Cluster, Bureau of AIDS, TB and STIs, Department of Diseases Control, Ministry of Public Health; 2006.
4. HIV/AIDS situation in Thailand. Bangkok: Bureau of epidemiology, Department of Diseases Control, Ministry of Public Health; 2006.
5. Powderly W. Cryptococcosis. New York: Churchill Livingstone; 1999.
6. Mirza SA, Phelan M, Rimland D, Graviss E, Hamill R, Brandt ME, et al. The changing epidemiology of cryptococcosis: an update from population-based active surveillance in 2 large metropolitan areas, 1992-2000. Clin Infect Dis 2003; 36: 789-94.
7. Saag MS, Graybill RJ, Larsen RA, Pappas PG, Perfect JR, Powderly WG, et al. Practice guidelines for the management of cryptococcal disease. Infectious Diseases Society of America. Clin Infect Dis 2000; 30: 710-8.
8. van der Horst CM, Saag MS, Cloud GA, Hamill RJ, Graybill JR, Sobel JD, et al. Treatment of cryptococcal meningitis associated with the acquired immunodeficiency syndrome. National Institute of Allergy and Infectious Diseases Mycoses Study Group and AIDS Clinical Trials Group. N Engl J Med 1997; 337: 15-21.
9. Pitisuttithum P, Tansuphasawadikul S, Simpson AJ, Howe PA, White NJ. A prospective study of AIDS-associated cryptococcal meningitis in Thailand treated with high-dose amphotericin B. J Infect 2001; 43: 226-33.
10. Larsen RA, Leal MA, Chan LS. Fluconazole compared with amphotericin B plus flucytosine for cryptococcal meningitis in AIDS. A randomized trial. Ann Intern Med. 1990; 113: 183-7.
11. Robinson PA, Bauer M, Leal MA, Evans SG, Holtom PD, Diamond DA, et al. Early mycological treatment failure in AIDS-associated cryptococcal meningitis. Clin Infect Dis 1999; 28: 82-92.
12. Saag MS, Cloud GA, Graybill JR, Sobel JD, Tuazon CU, Johnson PC, et al. A comparison of itraconazole versus fluconazole as maintenance therapy for AIDS-associated cryptococcal meningitis. National Institute of Allergy and Infectious Diseases Mycoses Study Group. Clin Infect Dis 1999; 28: 291-6.
13. Imwidthaya P, Poungvarin N. Cryptococcosis in AIDS. Postgrad Med J 2000; 76: 85-8.
14. Jenkins P. Survival analysis [Unpublished manuscript]. Colchester, UK: Institute for Social and Economic Research, University of Essex; 2005.
15. Kleinbaum D. Survival analysis: a self-learning text. New York: Springer; 1996.
16. Miller RG Jr. Survival analysis. New York: Wiley; 1981.
17. Klein JP, Moeschberger ML. Survival analysis. Techniques for censored & truncated data. New York: Springer-Verlag; 1997.
18. Stata Statistical Software: Release 7.0. Collage Station, TX: Stata Corporation; 2001.
19. Carretero G, Aguado G, Llano A. Cryptococcosis in AIDS patients: a study of 19 cases. Rev Clin Esp 1992; 190: 450-4.
20. Darras-Joly C, Chevret S, Wolff M, Matheron S, Longuet P, Casalino E, et al. Cryptococcus neoformans infection in France: epidemiologic features of and early prognostic parameters for 76 patients who were infected with human immunodeficiency virus. Clin Infect Dis 1996; 23: 369-76.
21. Knudsen JD, Jensen L, Sorensen TL, Jensen T, Kjersem H, Stenderup J, et al. Cryptococcosis in Denmark: an analysis of 28 cases in 1988-1993. Scand J Infect Dis 1997; 29: 51-5.
22. Mwaba P, Mwansa J, Chintu C, Pobee J, Scarborough M, Portsmouth S, et al. Clinical presentation, natural history, and cumulative death rates of 230 adults with primary cryptococcal meningitis in Zambian AIDS patients treated under local conditions. Postgrad Med J 2001; 77: 769-73.
23. Oursler KA, Moore RD, Chaisson RE. Risk factors for cryptococcal meningitis in HIV-infected

patients. AIDS Res Hum Retroviruses 1999; 15: 625-31.
24. Graybill JR, Sobel J, Saag M, van Der HC, Powderly W, Cloud G, et al. Diagnosis and management of increased intracranial pressure in patients with AIDS and cryptococcal meningitis. The NIAID Mycoses Study Group and AIDS Cooperative Treatment Groups. Clin Infect Dis 2000; 30: 47-54.
25. Inverarity D, Bradshaw Q, Wright P, Grant A. The spectrum of HIV-related disease in rural Central Thailand. Southeast Asian J Trop Med Public Health 2002; 33: 822-31.
26. Chetchotisakd P, Sungkanuparph S, Thinkhamrop B, Mootsikapun P, Boonyaprawit P. A multicentre, randomized, double-blind, placebo-controlled trial of primary cryptococcal meningitis prophylaxis in HIV-infected patients with severe immune deficiency. HIV Med 2004; 5: 140-3.
27. Lortholary O, Poizat G, Zeller V, Neuville S, Boibieux A, Alvarez M, et al. Long-term outcome of AIDS-associated cryptococcosis in the era of combination antiretroviral therapy. AIDS 2006; 20: 2183-91.

อัตราการรอดชีวิตของผู้ป่วยโรคเอดส์ที่มีสภาวะแทรกซ้อนจากเยื่อหุ้มสมองอักเสบจากเชื้อ *Cryptococcus neoforman*

สุทัศน์ โชตนะพันธ์, ประตาป สิงหศิวานนท์, จรณิต แก้วกังวาล, กนิษฐา จำรูญสวัสดิ์, วีรวัฒน์ มโนสุทธิ์

วัตถุประสงค์: *เพื่อศึกษาปัจจัยเสี่ยง และระยะเวลาการรอดชีวิตในผู้ป่วยติดเชื้อเอดส์ที่มีสภาวะแทรกซ้อนจากเยื่อหุ้มสมองอักเสบจากเชื้อ Cryptococcus neoforman ระหว่างกลุ่มที่ได้รับยาต้านไวรัสเอดส์ และกลุ่มที่ไม่ได้รับยาต้านไวรัสเอดส์*

ระเบียบวิจัย: *เป็นการศึกษาแบบย้อนหลัง*

วัสดุและวิธีการ: *การศึกษาจากเวชระเบียนผู้ป่วยติดเชื้อเอดส์ที่มีสภาวะแทรกซ้อนจากเยื่อหุ้มสมองอักเสบจากเชื้อ Cryptococcus neoforman เปรียบเทียบระยะเวลาการรอดชีวิตระหว่างผู้ป่วยที่ได้รับยาต้านไวรัสจำนวน 281 ราย (51.2%) กับกลุ่มที่ไม่ได้รับยาต้านไวรัส 268 (48.8%) ที่มารับการรักษาในสถาบันบำราศนราดูร ระหว่างเดือนมกราคม พ.ศ. 2545 ถึง เดือนธันวาคม พ.ศ. 2547*

ผลการศึกษา: *ผู้ป่วยที่ได้รับยาต้านไวรัสมีอายุเฉลี่ย 33.4 $\pm$ 6.9 ปี ผู้ป่วยที่ไม่ได้รับยาต้านไวรัสมีอายุเฉลี่ย 33.6 $\pm$ 7.0 ปี พบว่าผู้ป่วยส่วนใหญ่ของทั้งสองกลุ่มเป็นเพศชาย ผู้ป่วยที่ได้รับยาต้านไวรัสเป็นเพศชาย 207 ราย และหญิง 74 ราย ผู้ป่วยที่ไม่ได้รับยาต้านไวรัสเป็นเพศชาย 195 ราย และหญิง 73 ราย ค่าเฉลี่ยของเม็ดเลือดขาวชนิดซีดี 4 ในกลุ่มผู้ป่วยที่ได้รับยาต้านไวรัสคือ 20 (6-74) เซลล์/มิลลิลิตร ในกลุ่มผู้ป่วยที่ไม่ได้รับยาต้านไวรัสคือ 24 (9-72) เซลล์/มิลลิลิตร ผู้ป่วยประมาณ 30% เคยได้รับการรักษาโรคติดเชื้อแทรกซ้อนอื่น ๆ มาก่อน ผู้ป่วยทุกรายได้รับการรักษาโดยการให้ยา amphotericin B เป็นเวลาสองสัปดาห์แล้วตามด้วยการให้ยา fluconazole แปดสัปดาห์ พบว่าการไม่ได้รับยาต้านไวรัสจะมีความเสี่ยงต่อการเสียชีวิตจากเยื่อหุ้มสมองอักเสบจากเชื้อ Cryptococcus neoforman มากกว่ากลุ่มที่ได้รับยาต้านไวรัส 4.87 เท่า (95%CI = 2.48-9.44, $p < 0.01$) อัตราการรอดชีวิตในกลุ่มที่ได้รับยาต้านไวรัสที่ 12, 24 และ 36 เดือน อยู่ที่ 92.8%, 87.4% และ 85.4% ซึ่งแตกต่างอย่างมีนัยสำคัญกับกลุ่มที่ไม่ได้รับยาต้านไวรัส ที่มีอัตราการรอดชีวิต 55.3%, 42.2% และ 36.8% ตามลำดับ ($p < 0.01$) ระยะเวลารอดชีวิตเฉลี่ยในกลุ่มที่ไม่ได้รับยาต้านไวรัสคือ 15 เดือน*

สรุป: *การให้ยาต้านไวรัสสามารถลดอัตราการเสียชีวิตจากเยื่อหุ้มสมองอักเสบจากเชื้อ Cryptococcus neoforman ในผู้ป่วยเอดส์ได้ ซึ่งยาต้านไวรัสนั้นรวมถึงยา GPO-VIR ขององค์การเภสัชกรรมด้วย*