Effect of Antiretroviral Therapy in Human Immunodeficiency Virus-infected Children

Pimpanada Chearskul MD*, Kulkanya Chokephaibulkit MD*,
Sanay Chearskul MD*, Wanatpreeya Phongsamart MD*,
Nottasorn Plipat MD, MS*, Keswadee Lapphra MD*,
NirunVanprapar MD, MS*

**Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *The appropriate timing of antiretroviral (ARV) therapy initiation in children with human immunodeficiency virus (HIV) infection has been uncertain. There was evidence of poorer outcome in adults who initiated treatment at lower baseline CD4 cell count. However, early initiation may not be possible in resource-limited setting and would increased risk of long term side effects and non-adherence.*
Objective: *To elucidate the outcome of HIV-infected children who ARV treatment was initiated at different disease stages.*
Material and method: *Data from medical records of HIV-infected children who had been followed at Infectious Disease Division, Department of Pediatric Siriraj Hospital were retrospectively reviewed. Clinical response and outcome data were analyzed.*
Results: *From September 1996 to March 2004, there were 200 patients with a median age at treatment initiation of 38 (2-175) months. The median duration of follow up period was 26 (1-91) months. The median baseline CD4 cell count was 545 (2-5016) cells/mm^3. The median baseline CD4 percentage was 14.25 (0.11-60). Monotherapy or dual nucleoside reverse transcriptase inhibitor (NRTI) regimens were initiated in 134 (67%), and HAART was initiated in 66 (33%) patients. The survival rate in patients who initiated with HAART tended to be better than those initiated with dual NRTI regimens but salvaged appropriately (p=0.2377). The survival rate in those initiated treatment at baseline CD4 ≥15% was better than those initiated at baseline CD4 < 15% (p=0.0471).*
Conclusion: *Initiation of ARV treatment at CD4 more than 15% resulted in a better survival rate than at CD4 below 15%. Initiation with HAART regimen tended to improve survival and resulted in higher CD4 gain especially in cases with baseline CD4< 15%.*

Keywords: *HIV-infected children, Antiretroviral therapy, Survival, HAART*

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Several studies have demonstrated that highly active antiretroviral therapy (HAART) could modify the natural courses of human immunodeficiency virus (HIV) disease in both adult[1] and children[2]. HAART prevented the progression to acquired immunodeficiency syndrome (AIDS) and improved survival of HIV infected individuals[3]. Because the baseline CD4 cell count is an important prognostic factor[7-8], it has been routinely used as primary criteria for initiation of treatment[9]. The United State (US) guidelines consider treatment initiation when CD4 below 25%[13]. The European guidelines consider treatment initiation when CD4 below 20%[14]. The WHO guidelines for resource-limited settings recommend treatment initiation when CD4 below 15%[15]. In Thailand, the guideline issued by the Ministry of Public Health (MOPH) recommend treatment initiation when CD4 below 20%[16]. As well as other developing countries,Thailand has a limited

Correspondence to: Pimpanada Chearskul MD, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, 2 Prannok Rd., Bangkok-noi, Bangkok 10700, Thailand Tel: 661-6110371 Fax: 662-4180544 E-mail: pimpanada@hotmail.com

antiretroviral drugs availability that precludes patients from early treatment initiation. Although most patients response to HAART satisfactorily regardless of the CD4 cell count at baseline[6], there was evidence in adults of poorer outcome when ARV is initiated at a lower baseline CD4 cell count[7]. The aim of this study was to elucidate the outcome of children in whom treatment was initiated at different immunological stages. The result of the study would be helpful to guide treatment consideration.

Material and Method

Data from medical records of HIV-infected children who had been followed at Infectious Division, Department of Pediatric Siriraj Hospital, Bangkok, from September 1996 to March 2004, were collected. The patients were vertically HIV infected who had been receiving antiretroviral therapy. Antiretroviral agents were mostly supported by the Ministry of Public Health. The clinical stages were stratified by the 1994 revised human immunodeficiency virus pediatric classification system[17]. Weight and height were measured and calculated into times of standard deviations (Z-scores) by a nutritional anthropometry program (NutStat). Laboratory testing including complete blood count (CBC), CD4 cell count, and CD4 percentage were performed at baseline and every 6 months after treatment initiation. The patients who received HAART were also tested for alanine aminotransferase (ALT) and lipid profiles (cholesterol, triglyceride, low density lipoprotein-cholesterol and high density lipoprotein) every 6 months. Those who received indinavir (IDV) had urinalysis performed every 6 months and whenever indicated. Adverse drug reactions from ARV regimens were monitored. Changing of the ARV regimen was decided base of on clinical and immunological consideration according to the us guidelines[13].

Data analysis

Descriptive analysis was performed on the demographic data, the Z-scores of weight and height gain and the CD4 cell count and percentage gain by each antiretroviral regimen. The survival rate after each treatment regimen was analyzed by intention-to-treat manner using Kaplan-meier (K-M) analysis with Log Rank test for comparison. The Z-scores of weight, height, weight and height gain, CD4 cell count and CD4 percentage, CD4 cell count gain and CD4 percentage gain between different treatment regimens and different initial CD4 percentage were compared by Mann-Whitney U test, and among different class based HAART and different initial clinical stages by Kruskal-Wallis H test and Dunn s multiple comparison test.

Results

From September 1996 to March 2004, there were 200 patients in the cohort; 105 (52.5%) male and 95 (47.5%) female, with the median age at treatment initiation of 38 (2-175) months. Baseline characteristic of the patients were tabulated in Table 1. The median time of follow up was 26 (1-91) months. Monotherapy or dual nucleoside reverse transcriptase inhibitor (NRTI) regimens were initiated in 134 (67%) and HAART in 66 (33%) of the patients. The HAART regimens used initially were protease inhibitor (PI) based in 5 (7.6%), efavirenz (EFV) based in 30 (45.5%), and nevirapine (NVP) based in 31 (47%). The choices of initial ARV regimen were based on drugs availability, patient's socioeconomic status, and caretaker's decision. Some patients who initiated treatment before 1998 received monotherapy. Most patients who initiated treatment before 2002 received dual NRTI regimens, because of limited availability of HAART. After the year 2002, all the initial regimens initiated were HAART.

The patients who initiated with HAART were older (median age of 64.50 vs. 20.54 months, $p<0.001$), had lower initial CD4 cell count (median CD4 of 91 vs. 859 cells/mm^3, $p<0.001$), lower initial CD4 percentage (median CD4 of 3.83 vs. 17%, $p<0.001$, Table 1) than those of patients who initiated with mono or dual NRTI regimens. Among children who initiated with HAART, those who received NVP- based HAART had baseline CD4 cell count and percentage higher than those who received EFV-based HAART (median CD4 cell count of 307.5 vs. 27.5 cells/mm^3, $p<0.05$; median CD4 percentage of 11.65 vs. 1.49%, $p<0.05$, Table 2)

Of the 134 patients who were initiated with monotherapy or dual NRTI regimens, 59 (44%) had changed regimen to HAART at the median duration of 32 (4-80) months (Figure 1). The reasons for treatment regimen changed were immunological failure in 53 (90%) and immunological failure with clinical failure in 6 (10%). The new HAART regimens changed to were PI based in 6 (10.2%), EFV- based in 34 (57.6%) and NVP-based in 19 (32.2%). Of these 59 patients who were switched to HAART, 10 had clinical and/or immunological failure while on HAART for the median duration of 14 (6-24) months and need to change to the second salvage regimens guided by the genotypic resistant patterns. Of the 66 patients who were initiated with HAART, 62 (93.9%) are still on treatment with the median duration of followed-up of 11 (1-66) months.

Table 1. Baseline characteristics of the patients who were initiated with ARV agents

	All patients (N =200)	**Initiated with Mono or Dual NRTI (N = 134)**	**Initiated with HAART (N = 66)**	***p* value**
Median age (month)	38 [2 - 175]	20.54 [2 - 121]	64.5 [4 - 175]	< 0.001
Clinical staging before initiation of treatment	N = 22 (11 %) A = 59 (29.5 %) B = 77 (38.5 %) C = 42 (21.0 %)	N = 18 (13.4 %) A = 52 (38.8 %) B = 48 (35.8 %) C = 16 (11.9 %)	N = 4 (6.1 %) A = 7 (10.6 %) B = 29 (43.9 %) C = 26 (39.4 %)	
Median CD4 cell count at the time of treatment initiation (cells/mm^3)	545 [2 - 5016]	859 [2 - 5026]	91 [2 - 2016]	< 0.001
Median CD4 percentage at the time of treatment initiation (%)	14.24 [0.11- 60.0]	17 [0.23 - 60.0]	3.83 [0.11 - 35.0]	< 0.001
Median Follow-up time (month)	26 [1 - 91]	38.5 [1 - 91]	10.5 [1 - 66]	< 0.001

Table 2. Baseline characteristics of patients who were initiated treatment with different regimens of HAART (N = 66)

	PI based HAART Median [range] N = 5	**EFV based HAART Median [range] N = 30**	**NVP based HAART Median [range] N = 31**	***p* value**
Age (month)	51 [4 - 84]	72 [10 - 160]	53 [4 - 175]	0.198
Clinical staging	N = 0 A = 0 B = 2 C = 3	N = 0 A = 5 B = 13 C = 12	N = 4 A = 2 B = 14 C = 11	
CD4 cell count (cells / mm^3)	7 [6 - 1984]	27.5 [2 - 1084]	307.5 [2 - 2016]	0.023*
CD4 percentage (%)	1.34 [0.54 - 26.82]	1.49 [0.11 — 31.0]	11.65 [0.14 — 35]	0.038*
Median time of F/U (month)	19 [4 - 29]	11 [1 - 66]	7 [1 - 22]	0.118

* P < 0.05 between EFV based HAART and NVP based HAART
(P values were analyzed by multiple comparison)

During this period of follow-up, there was only one patient who was initiated with HAART and had immunological and clinical failure lead to the subsequent salvage regimen at 11 months of treatment.

The median change in Z-scores of weight and height at 6 and 12 months after treatment initiation with HAART tend to be higher than with monotherapy or dual NRTI regimens, but no statistical significant difference (Table 3). There was a significantly higher CD4 cell count and percentage gain among those

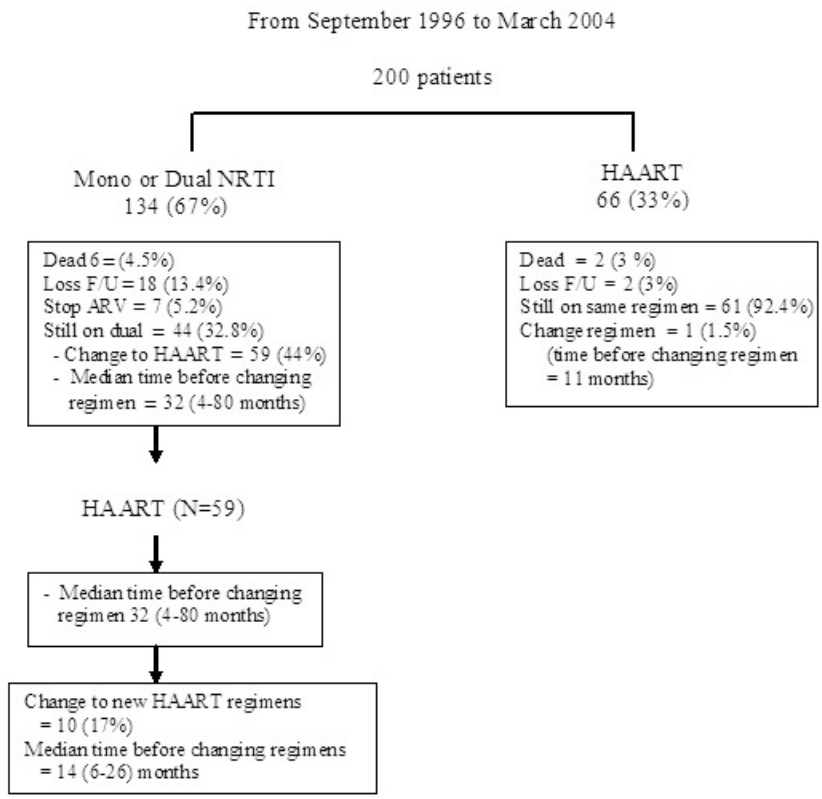


Fig. 1 Diagram of patients initiated with antiretroviral therapy and their outcome

Table 3. Median change in z-scores of weight and height, CD4 cell count and CD4 percentage gain at 6 and 12 months after treatment initiation in patients initiated treatment with dual NRTI regimens and HAART

	Mono or Dual NRTI regimens **Median [range]** **N = 134**	**HAART** **Median [range]** **N = 66**	***p* value**
Change in z-scores of weight			
At 6 month	0.2 [- 2.28, 3.49]	0.42 [-1.27, 2.52]	0.160
At 12 month	0.23 [-2.47, 4.49]	0.71 [-0.34, 3.16]	0.077
Change in z-scores of height			
At 6 month	0.08 [-1.70, 3.62]	0.075 [-1.25, 1.58]	0.820
At 12 month	0.29 [-2.42, 4.49]	0.34 [-1.08, 2.25]	0.932
CD4 cell count gain (cells/mm^3)			
At 6 month	108.5 [-2066, 2676]	315 [-596, 3660]	0.002
At 12 month	18.5 [-2234, 1317]	613 [9, 1852]	< 0.001
CD4 percentage gain (%)			
At 6 month	3.6 [-30, 20.22]	7.14 [-4.52, 18.36]	0.001
At 12 month	3.54 [-42, 192.9]	15.2 [1.78, 28.99]	< 0.001

Table 4. Baseline z-scores of weight and height, CD4 cell count, CD4 percentage and median change in z-scores of weight and height, CD4 cell count gain and CD4 percentage gain between patients initiated treatment at baseline CD4 percentage of less than 15 or more than 15

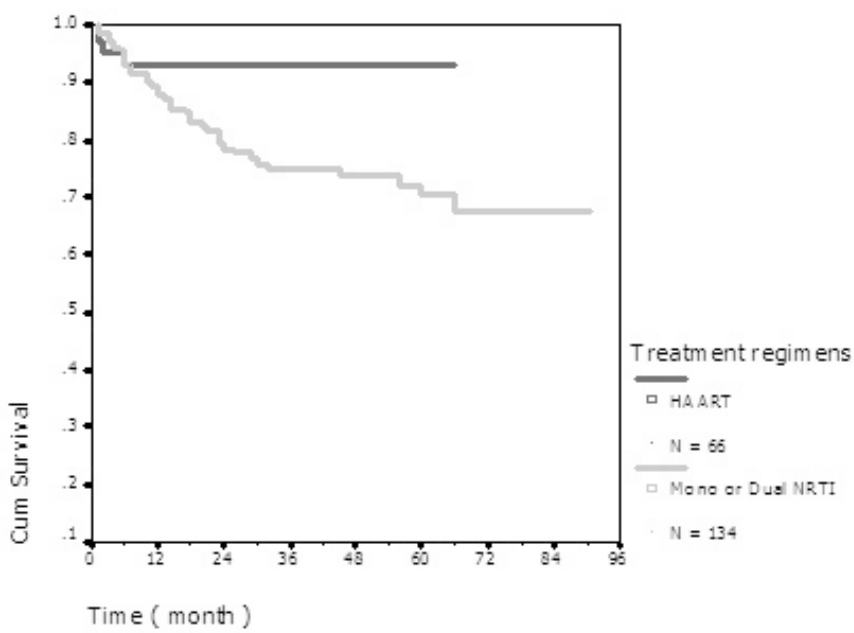
	Initiated with Mono or Dual NRTI regimen N=115			Initiated with HAART N=65		p value between Mono or Dual & HAART		
	Baseline CD4 <15% N=49	Baseline CD4 ≥15% N=66	P value	Baseline CD4 <15% N=47	Baseline l CD4 ≥15% N=18	p value	Baseline < 15%	Baseline ≥ 15%
Baseline								
z-scores of weight	-2.01 [-5.10, 4.36]	-1.39 [-5.80, 2.42]	0.039	-2.58 [-5.11, -0.60]	-1.25 [-3.22,2.29]	<0.001	0.014	0.429
z-scores of height	-2.21 [-5.56, 0.96]	-1.40 [-4.83, 1.19]	0.003	-2.47 [-6.15, -0.22]	-1.03 [-4.87, 0.79]	0.001	0.625	0.220
CD4 cell count (cells/mm^3)	271 [2, 2515]	1270 [293, 5016]	<0.001	27 [2, 637]	642.5 [221, 20161]	<0.001	<0.001	0.001
CD4 percentage (%)	8.94 [0.23, 14.76]	23.12 [15.19, 60]	<0.001	1.49 [0.11, 14.62]	21.18 [15.32, 35]	<0.001	<0.001	0.160
Median change in z-scores of weight								
At 6 months	0.13 [-2.28, 2.79]	0.20 [-1.32, 3.49]	0.724	0.63 [-1.27, 2.52]	0.12 [-1.15, 0.91]	0.064	0.060	0.720
At 12 months	0.31 [-2.47, 3.41]	0.16 [-2.46, 4.68]	0.776	0.76 [-0.28, 3.16]	-0.10 [-0.43, 1.73]	0.176	0.049	0.800
Median change in z-scores of height								
At 6 months	0.08 [-0.65, 0.98]	0.09 [-1.70, 3.62]	0.225	0.04 [-1.06, 1.58]	0.20 [-1.25, 0.50]	0.570	0.874	0.853
At 12 months	0.25 [-0.81, 3.04]	0.43 [-2.42, 4.49]	0.891	0.06 [-1.08, 2.25]	0.60 [0.38, 1.23]	0.069	0.448	0.308
Median CD4 cell Count gain (cells/mm^3)								
At 6 months	70 [-156, 819]	152 [-2066, 2676]	0.835	302.5 [-1510, 3660]	446 [-596, 1839]	0.902	0.001	0.116
At 12 months	31 [-734, 1317]	-20 [-2234, 1080]	0.527	613 [9, 1839]	626.5 [178, 1852]	1.00	<0.001	0.006
Median CD4 Percentage gain (%)								
At 6 months	3.49 [3.3, 15.92]	3.63 [-30, 20.22]	0.193	7.97 [1.52, 18.36]	2.86 [-4.52, 17.56]	0.015	0.002	0.661
At 12 months	2.33 [-9.04, 16.93]	4.6 [-42, 192.9]	0.845	17.77 [1.78, 28.99]	8.31 [6.64, 11.88]	0.003	<0.001	0.069

initiated with HAART than those initiated with monotherapy or dual NRTI regimens at 6 months (median CD4 cell count gain of 315 vs 108.5 cells/mm^3, p=0.002; median CD4 percentage gain of 7.14 vs. 3.6, p=0.001) and at 12 months (median CD4 cell count gain 613 vs. 18.5 cell/mm^3, p=0.001; median CD4 percentage gain 15.2 vs. 3.54, p<0.001, Table 3). There was no significant difference in the median change of Z-scores of weight and height or CD4 cell count and CD4 percentage gain at 6 and 12 months after treatment among those initiated at different clinical stages, or at baseline CD4 percentage more or less than 15% (Table 4). Among the patient initiated with HAART, those with baseline CD4 more than 15% had a CD4 percentage gain at 6 and 12 month less than those with baseline CD4 below 15% (median CD4 percentage gain at 6 months of 2.86 vs. 7.97, p=0.015, and at 12 months of 8.31 vs. 17.77, p=0.003, Table 4).

There was no statistical significant difference in the median change of Z-scores of weight and height, CD4 cell count gain and CD4 percentage gain and survival, among children initiation with different HAART regimens. However, there was a trend of better survival in EFV-based than in NVP-based regimens (data not shown).

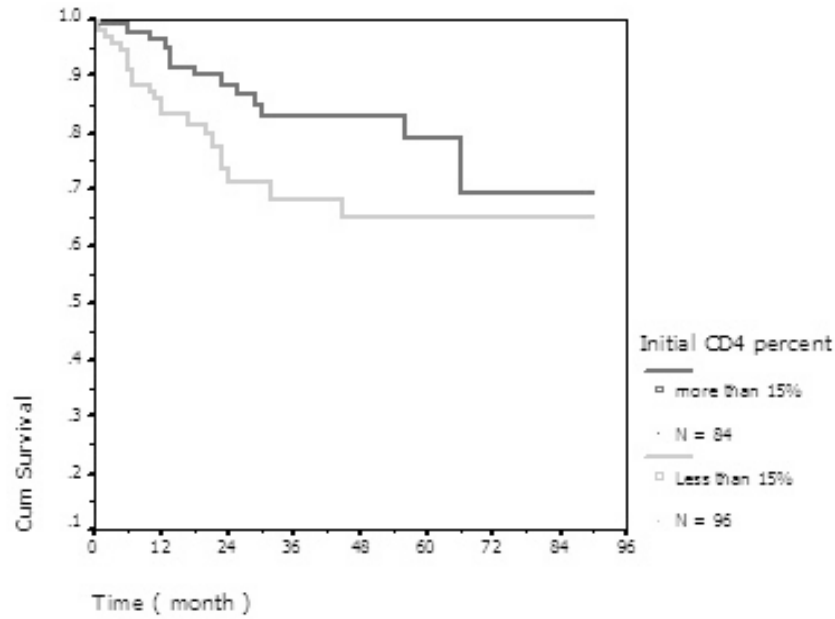
The survival rate in patients who were initiated with HAART tended to be better than those initiated with monotherapy or dual NRTI regimens regardless of baseline CD4 level (p= 0.2377, Figure 2). There was no statistical difference of the survival rate among patients initiated treatment at different clinical stages (p=0.2105), or at different immunological stages (p=0.2149). There was a significant better survival in those initiated treatment at baseline CD4 more than 15% than those initiated treatment when CD4 below 15% (p = 0.0471, Figure 3). Among patients who were currently on HAART, those naíve patients tended to had better survival than those NRTI experienced (p=0.3176).

There were 20 (10%) patients that lost to follow-up, 2 were on HAART and 18 were on monotherapy or dual NRTI regimens. The median age at treatment initiation of patients that lost to follow was 15.5 (3-96) months. The median duration of treatment before the patients lost to follow was 11.5 (1-60) months. Younger children tended to loss to follow more



Dual : N=	134	113	98	67	54	42	13	9	0
HAART: N=	66	22	5	2	1	1	0	0	0

Fig. 2 Kaplan-meier survival analysis between patients initiated treatment with mono or dual NRTI regimens and HAART (p = 0.2377)



CD4 < 15% : N =	96	55	34	21	18	13	3	2	0
CD4 ≥ 15% : N =	84	64	54	35	25	20	3	1	0

Fig. 3 Kaplan-meier survival analysis between patients initiated treatment at initial CD less than 15% or above 15% (P = 0.0471)

than those older ones.

The ARV agents were generally well tolerated. Of 156 patients who were ever experienced AZT, 6 (3.8%) had severe anemia that lead to drug changed. Two (2.9%) of the 67 patients developed skin rash from EFV; one was severe enough to withdrawn EFV. Four (17.4%) of the 54 patients who exposed to NVP developed skin rash, 3 of them also had hepatitis and NVP was discontinued. Of the 125 patients who had been on HAART, 74 (59.2%) experienced dyslipidemia. The most common type of dyslipidemia observed was hypo-high density lipoprotein (hypo-HDL); found in 24 of 74 (16.1%) patients. The second most common dyslipidemia was hypercholesterolemia with hyper-low density lipoprotein (hyper-LDL); found in 11 of 74 (7.4%) patients.

Discussion

Antiretroviral therapy provides substantial benefit to symptomatic and immuno-suppressed HIV-infected children. Data from our cohort show that treatment initiation in those with severely immune suppressed status (initial CD4 less than 15%) resulted in substantial higher CD4 gain than in those with higher baseline CD4 percentage, but the survival in those initiated treatment at CD4 ≥15% was better. Many trials have clearly shown that dual combination therapies had a superior clinical, immunological and virological benefit than monotherapy[23-24]; and triple combination regimens, HAART, were better than dual regimens[25-27]. Especially in those with a low initial CD4 percentage, initiation with HAART resulted in a much higher survival rate than those initiated with dual NRTI regimens[28]. Our study showed a trend of better survival in those initiated with HAART than those initiated with dual NRTI regimens although the patients initiated with HAART were in more advanced stage. Dual NRTI therapies are generally no longer recommended except in special circumstances when HAART is not plausible[13]. Of note, there are many children who have been receiving long term treatment with dual NRTI regimens, initiated prior to the era of HAART, remained in good clinical status and immunologic function[29]. In our cohort, there were many patients who remained on treatment with dual NRTI regimens started before 2002 and were still in a stable condition . Among those patients who failed but were promptly change to HAART when indicated, most were remained in good condition. In our

study the survival in those initiated with HAART and those initiated with dual NRTI but were appropriately changed to HAART when indicated was not found to be different. However, longer follow-up period may reveal a different result. The impact of suboptimal viral suppression on viral resistance may cause unfavorable outcome in longer term among these initiated with dual NRTI regimens.

In our setting, non-nucleoside severs transcriptase inhibiter (NNRTI) - based HAART regimens were more available. The difference in outcome in those initiated with PI-based regimens and NNRTI-based HAART was not demonstrated in our study. This may due to small number of patients who initiated with PI-based regimen.

Efavirenz-based HAART tended to be more efficacious than nevirapine based HAART in several observational studies in adult patients[40-42], however, the difference had not been clearly shown in children. Considering a higher incidence of NVP toxicities[40], EFV is more preferable except for those younger than 3 years of age, in whom EFV has not been approved for use[13]. In Thailand, with the generic production of NVP by the Government Pharmaceutical Organization (GPO) in a fix dosed combination tablet with stavudine and lamivudine that come in low cost, had made NVP-based HAART regimen the more practical regimen in real life. In our cohort, survival rate in the group receiving EFV-based HAART tended to be better than those receiving NVP-based HAART although the baseline CD4 levels were lower. Another important issue was that NVP-based regimens are probably not appropriate in children who had perinatal exposure to NVP because of 46% rate of NVP resistance among these infected children[43].

The long term metabolic side effects from HAART are of concern in children, particularly that it may interfere with normal growth[18]. In our cohort, abnormal lipid metabolisms were the most common finding. Currently, there is no consensus guidelines for managing these complications in children[22]. With the increasing number of patients who received longer treatment, these emerging problems need more intensive studies.

The drawback of this retrospective study was that the management was under routine service without stringent protocol or incentive. Moreover, we evaluate the adherence by self report in this study, and may not be able to detect some suboptimal adherence. However, the strong point of this study was that it was an operational and reflects the real life practice.

Conclusion

Initiation with HAART tended to improve survival and resulted in more CD4 gain especially in those with baseline CD4 <15%. Initiation of treatment at CD4 ≥15% resulted in a better survival rate than at CD4 <15% Initiation treatment with EFV or NVP-based HAART resulted in a comparable response even in those with low initial CD4 percentage. Younger patients had higher tendency to loss follow up.

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การตอบสนองต่อการรักษาด้วยยาต้านไวรัสในผู้ป่วยเด็กที่ติดเชื้อไวรัสเอชไอวี

พิมพ์พัณณดา เจียสกุล, กุลกัญญา โชคไพบูลย์กิจ, เสน่ห์ เจียสกุล, วนัทปรียา พงษ์สามารถ, นทสร ผลิพัฒน์, เกษวดี ลาภพระ, นิรันดร์ วรรณประภา.

บทนำ: *ปัจจุบันเกณฑ์การเริ่มยาต้านไวรัสในเด็กที่ติดเชื้อไวรัสเอชไอวียังไม่มีแนวทางการปฏิบัติที่ชัดเจนตรงกัน การ เริ่มยาในผู้ป่วยเด็กมักถูกจำกัดด้วยปัจจัยหลายประการ การศึกษาในผู้ป่วยผู้ใหญ่พบว่าผลตอบสนองต่อการรักษาไม่ดีเท่าที่ควรเมื่อเริ่มยาเมื่อระดับภูมิคุ้มกันอยู่ในเกณฑ์ต่ำมาก แต่การเริ่มใช้ยาต้านไวรัสเร็วอาจทำไม่ได้ ในที่ที่มีทรัพยากรจำกัด และอาจเกิดผลข้างเคียงระยะยาวตามมา*

วัตถุประสงค์: *เพื่อศึกษาการตอบสนองต่อการรักษาด้วยยาต้านไวรัสในผู้ป่วยเด็กที่ติดเชื้อไวรัสเอชไอวีเมื่อเริ่มการรักษาในขณะที่ระยะโรคแตกต่างกัน*

วิธีการ: *โดยการเก็บรวบรวมและวิเคราะห์ข้อมูลที่ถูกบันทึกไว้ในบันทึกทางการแพทย์ของผู้ป่วยเด็กที่ติดเชื้อเอชไอวีที่ได้รับการรักษาด้วยยาต้านไวรัส ณ ภาควิชากุมารเวชศาสตร์ โรงพยาบาลศิริราช ผลของการรักษาจะถูกนำมาวิเคราะห์*

ผลการศึกษา: *จากการเก็บรวบรวมข้อมูลตั้งแต่เดือนกันยายน พ.ศ. 2539 ถึงเดือนมีนาคม พ.ศ. 2547 พบมีผู้ป่วยในการศึกษาทั้งหมด 200 คน, มีอายุเฉลี่ยขณะเริ่มรักษาด้วยยาต้านไวรัส 38 (2-175) เดือน, ค่ากลางของระดับเม็ดเลือดขาว CD4 ขณะเริ่มยาต้านไวรัสเท่ากับ 545 (2-5016) เซลล์/มม^3, ค่ากลางของเปอร์เซ็นต์ของเม็ดเลือดขาว CD4 ขณะเริ่มต้นการรักษาเท่ากับ 14.25 (0.11-60)%, เริ่มการรักษาด้วยสูตรยาที่ใช้ยากลุ่ม NNRTI หนึ่งหรือสองชนิดทั้งหมด 134 คน (67%), เริ่มการรักษาด้วยยาต้านไวรัสอย่างน้อยสามชนิด (HAART) 66 คน (33%), อัตราการมีชีวิตรอดในกลุ่มผู้ป่วยที่เริ่มการรักษาด้วย HAART มีแนวโน้มสูงกว่ากลุ่มที่เริ่มด้วยยาหนึ่งหรือสองชนิด และเปลี่ยนสูตรการรักษาทันทีอย่างเหมาะสมเมื่อจำเป็น (p=0.2377) อัตราการมีชีวิตรอดในกลุ่มผู้ป่วยที่เริ่มการรักษาด้วยยาต้านไวรัสในขณะที่ระดับเม็ดเลือดขาว CD4 มากกว่า 15% สูงกว่าในกลุ่มที่เริ่มการรักษาเมื่อระดับ เม็ดเลือดขาว CD4 ต่ำกว่า 15% (p=0.0471)*

สรุป: *ผู้ป่วยที่เริ่มการรักษาด้วยยาต้านไวรัสขณะที่ระดับเม็ดเลือดขาว CD4 มากกว่า 15% มีอัตราการรอด ชีวิตสูงกว่าผู้ป่วยที่เริ่มยาเมื่อระดับเม็ดเลือดขาวต่ำกว่า 15%, การเริ่มรักษาด้วย HAART มีแนวโน้มจะช่วยเพิ่มอัตราการรอดชีวิตโดยเฉพาะในกลุ่มผู้ป่วยที่ CD4 น้อยกว่า 15%*