Nevirapine Discontinuation within One Year of Anti Retroviral Treatment among HIV-infected Patients in Dr. Sardjito Referral Hospital, Yogyakarta, Indonesia

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INTRODUCTION

Nevirapine remains a common first line medication in HIV treatment regimens in Indonesia.

WHO and Indonesian HIV treatment guidelines recommend efavirenz over nevirapine as the preferred non-nucleoside reverse transcriptase inhibitor (NNRTI) in first line antiretroviral therapy (ART) for HIV.[1,2,3,4] Nonetheless, nevirapine is still commonly used in Indonesia.[5]

The proportion of patients discontinuing treatment due to any adverse event is reported to be higher among those using nevirapine compared to those using efavirenz.[6,7]

Predictors of nevirapine discontinuation differ between countries.[6,8,9,10] There have been few studies examining nevirapine discontinuation in Indonesia.

AIMS

To determine the risk factors associated with nevirapine discontinuation during the first year of ART among patients in Yogyakarta, Indonesia

METHODS

Study Design and Population

A retrospective longitudinal cohort study was conducted among HIV patients receiving nevirapine as a first line regimen at Dr. Sardjito Hospital between January 2008-December 2013. Patients were excluded if they were less than 18 years of age, or pregnant.

Dr. Sardjito Hospital is a referral hospital for HIV-AIDS patients in Jogjakarta Special Province and the southern part of Central Java Province.

Data Collection

The data were collected from the ART register at Dr. Sardjito Hospital and were cross-checked with patient medical and pharmacy records.

Statistical Analysis

The cumulative incidence of nevirapine discontinuation was calculated using Kaplan-Meier analysis. A multivariate Cox proportional hazards regression model was used to examine predictors of nevirapine discontinuation.

Proportional-hazards assumption test were conducted also by log-log plot of survival and predicted survival plot. All analyses were performed using STATA 12.

RESULTS

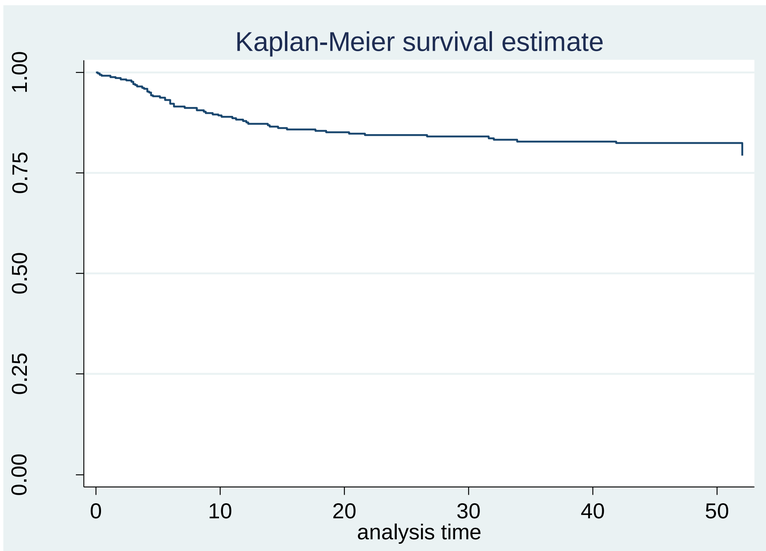
Table 1. Baseline Charateristic

Variable	Frequency (N=362)	Outcome: Discontinuation n=61	Outcome: Not-Discontinuation n=301
age (years) median IQR	31 (27-40)	31 (27-42)	31 (27-39)
marital n (%)			
yes	179 (49.45)	31 (50.82)	148 (49.17)
no	148 (40.88)	25 (40.98)	123 (40.86)
no data	35 (9.67)	5 (8.20)	30 (9.97)
occupation n (%)			
yes	117 (32.32)	25 (40.98)	92 (30.56)
no	167 (46.13)	24 (39.34)	143 (47.51)
no data	78 (21.55)	12 (19.67)	66 (21.93)
sex n (%)			
male	223 (61.60)	43 (70.49)	180 (59.80)
female	139 (38.40)	18 (29.51)	121 (40.20)
suffer from anemia n (%)			
yes	160 (44.20)	27 (44.26)	133 (44.19)
no	137 (37.85)	19 (31.15)	118 (39.20)
no data	65 (17.96)	15 (24.59)	50 (16.61)
weight (kg) median (IQR)	51 (45-60)	51 (48-60)	51 (45-60)
CD4 (cells/mm3) median (IQR)	79 (18-191)	40 (10-163)	89 (21-195)
NRTI n (%)			
AZT+3TC	310 (85.64)	50 (81.97)	260 (86.38)
Others	52 (14.36)	11 (18.03)	41 (13.62)
cotrimoxazole n (%)			
yes	153 (42.27)	24 (39.34)	129 (42.86)
no	209 (52.73)	37 (60.66)	172 (57.14)
tuberculosis n (%)			
no	319 (88.12)	51 (83.61)	268 (89.04)
yes	43 (11.88)	10 (16.39)	33 (10.96)
clinical stage n (%)			
1st & 2nd	179 (49.45)	31 (50.82)	148 (49.17)
3rd & 4th	172 (47.51)	29 (47.54)	143 (47.51)
no data	11 (3.04)	1 (1.64)	10 (3.32)

A total of 362 patients met eligibility criteria; characteristics are the time of starting ART are detailed in Table 1.

Of these patients 61 (17%) discontinued nevirapine in the first 12 months of treatment.

RESULTS



The rate of discontinuation was 26-per-100-person-years. Among those who stopped nevirapine with the first year of treatment the median time to discontinuation was8 (IQR, 4-17) weeks. (Figure 1)

Figure 1. Survival Analysis for Nevirapine Discontinuation

Table 2. Hazard Ratio for Predictors of Nevirapine Discontinuation

Variable	Unadjusted HR: HR (95% CI)	Unadjusted HR: p-value	Adjusted HR: HR (95% CI)	Adjusted HR: p-value
age				
< 40	1	0.885		
≥ 40	0.96 (0.58-1.59)			
marital				
married	1	0.915		
not-married	0.95 (0.56-1.60)			
no data	1.16 (0.45-2.98)			
occupation				
yes	1	0.299		
no	0.64 (0.37-1.12)			
no data	0.79 (0.39-1.57)			
sex				
male	1	0.104*	1	0.185
female	0.63 (0.37-1.09)		0.69 (0.39-1.19)	
weight				
≥50	1	0.867		
<50	1.04 (0.61-1.76)			
CD4+				
≥50	1	0.005*	1	0.012**
<50	2.40 (1.31-4.43)		1.94 (1.16-3.23)	
haemoglobin				
not anemia	1	0.228		
anemia	1.19 (0.67-2.15)			
clinical stage				
1st & 2nd	1	0.987		
3rd & 4th	1.01 (0.61-1.67)			
NRTI				
AZT+3TC	1	0.237		
others	1.48 (0.77-2.85)			
tuberculosis				
no	1	0.182*	1	0.363
yes	1.59 (0.81-3.13)		1.38 (0.69-2.73)	
cotrimoxazole				
yes	1	0.693		
no	1.11 (0.66-1.85)			

*trace hold p-value for multivariate analysis p<0.25 **significant at p-value<0.05

Baseline variables with p-values less than 0.25 in the univariate analysis were included in the multivariate model, these included sex, CD4+ and presence of tubercolosis. CD4+count at baseline was found to be independently associated with nevirapine discontinuation. Patients with CD4+ counts less than 50 cells/mm^3 were nearly twice more likely to discontinue nevirapine than those with counts greater than 50 cells/mm^3.

CONCLUSION

Our findings are consistent with other studies showing that low CD4+ levels when starting ART are a risk factor for discontinuing nevirapine. Clinicians are advised to closely monitor or avoid nevirapine in patients with low CD4+ counts to avoid treatment failure.

ACKNOWLEDGEMENTS This research has been funded under the Australian Aid, Regional HIV Capacity Building Program. The views expressed in this publication do not necessarily represent the position of the Australian Government.

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