Identification by Tuberculin Sensitivity Testing and Treatment of Latent TB Infection Continues to be Effective for TB Control in a Setting of Universal Access to HAART and Intermediate Burden of TB

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Background

In resource-constrained settings with high burden of TB, treatment of latent TB infection in HIV infected patients is highly effective in preventing TB disease. However, highly active antiretroviral therapy (HAART) per se also reduces TB incidence. It is unclear if a policy of annual tuberculin sensitivity testing (TST) and treatment of latent TB will continue to be effective in a setting with access to HAART and an intermediate burden of TB.

Methods

All patients of the largest HIV Clinic in Hong Kong were offered annual TST. Those with latent TB were treated with 9 months of isoniazid. HAART was prescribed according to current guidelines of developed countries. All patients on HAART were followed for the development of new TB disease. Using logistic regression and multivariate Cox proportional hazards, we calculated the hazard ratio of disease associated with various risk factors.

Results

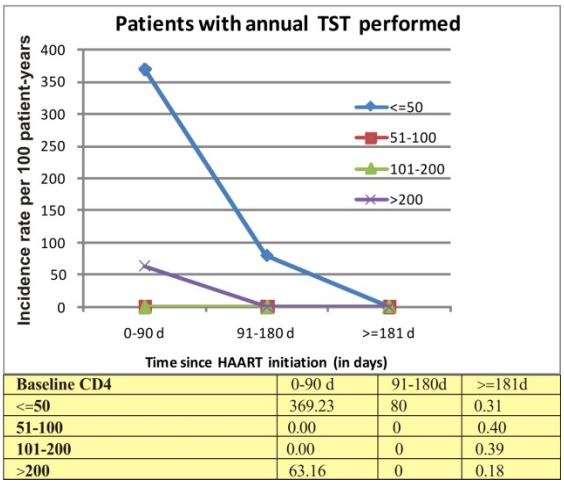
From 1989 to 2011, 1166 patients were on HAART, contributing to 5,582 patient-years of observation. 1043 patients (89%) received annual TST. Their baseline characteristics did not significantly differ from those who declined testing with respect to CD4 count (247/mm3 vs 238/mm3, respectively), age, gender, body mass index and the presence of diabetes. More intravenous drug users were among those who declined testing (13.8% vs 3.3%, p=0.004).

The overall incidence of TB disease was 0.59 cases per 100 patient-years. It was lower in those who received annual TST than those who did not (0.41/100 p-y vs 3.85/p-y, p<0.0001). Using multivariate analysis, only a low baseline CD4 count and a history of TST were shown to be significant factors of incident TB disease (Table). The hazard ratio was 0.36 (95% CI: 0.16-0.85, p=0.02) for those with a baseline CD4 count >=100/mm3; 0.26 (95% CI: 0.08-0.77, p=0.016) for those who received annual TST. The incidence of TB disease was highest within 90 days of HAART initiation, especially for those with a baseline CD4 count <50/mm3 and who did not receive annual TST (p=0.003) (Figure).

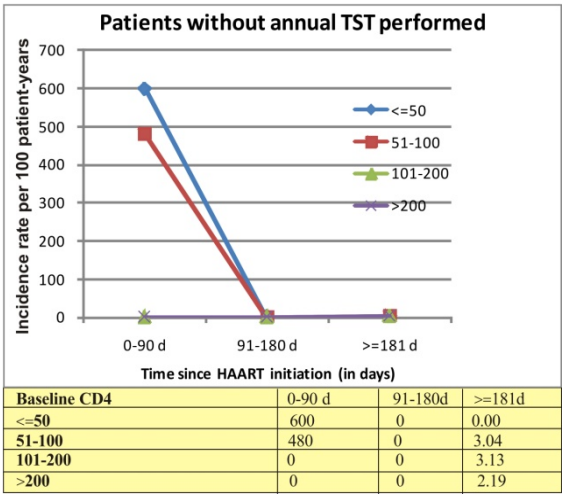
Conclusions

In a setting of ready availability of HAART and intermediate burden of TB, a policy of annual TST and treatment of latent TB infection continues to reduce the development of TB disease in the HIV infected population. The high risk of TB disease during early period of HAART supports the early use of TST in HIV care. Alternatively, the strategy of universal isoniazid preventive therapy at HAART initiation could be studied for those with very low baseline CD4 count.

Figure: Incidence Rates of TB by Time on HAART and Baseline CD4 Count Category



Baseline CD4	0-90 d	91-180d	>=181d
<=50	369.23	80	0.31
51-100	0.00	0	0.40
101-200	0.00	0	0.39
>200	63.16	0	0.18



Baseline CD4	0-90 d	91-180d	>=181d
<=50	600	0	0.00
51-100	480	0	3.04
101-200	0	0	3.13
>200	0	0	2.19

Table: Univariate and Multivariate Analysis of Factors Associated with Incident TB Disease on Patients Receiving HAART

	On HAART with incident TB (n=33)	On HAART without incident TB (n=1133)	P value (Univariate)	P value (Multivariate)	Hazard Ratio in 95% CI
Annual TST performed					
Yes	22	1021	<0.0001^(0.1-0.46)	0.016*	0.26 (0.08-0.77)
No	11	112			1
Age at HAART started			0.50^ (0.79-1.6)		
<=20	0	4			
>20 and <=30	6	211			
>30 and <=40	10	434			
>40 and <=50	11	298			
>50	6	186			
Gender			0.674^ (0.31-2.13)		
Male	28 (84.85%)	929 (82%)			
Body mass index			0.117^ (0.8-1.03)		
Mean	21.02	21.99			
Duration of HAART (months)			0.004^ (0.97-0.99)		
Mean	29.78	58.31			
Baseline CD4 count (cells/mm3)			0.044^ (0.99-1)		
Mean	172.55	247.86			
Baseline CD4 count (cells/mm3)					
<100	17 (50%)	352 (31%)	0.017^ (0.21-0.85)	0.02*	1
>=100	16 (50%)	774 (68.3%)			0.363 (0.16-0.85)
Baseline HIV viral load (copies/ml3)			0.507^ (0.51-1.39)		
<400	3 (9.09%)	102 (9%)			
401-10000	7 (21.21%)	155 (13.68%)			
>10000	23 (69.69%)	866 (76.43%)			
History of diabetes mellitus	4 (12%)	92 (8.1%)	0.413^ (0.22-1.86)		
Baseline hemoglobulin level (g/L)			0.021^ (0.66-0.96)		
mean	13.27	12.27			
Ethnicity			0.756^ (0.35-2.12)		
Chinese	27 (81.81%)	902 (79.61%)			
Non Chinese	6 (18.18%)	231 (20.39%)			
HIV transmission route			0.031^ (0.24-0.93)		
Heterosexual	23 (69.69%)	558 (49.24%)			
MSM	9 (27.27)	504 (44.48%)			
IDU	1 (3.03%)	50 (4.41%)			
Blood transfusion	0	15 (1.32%)			
Undetermined	0	6 (0.53%)			