AUDIT REPORT

Implementation of routine IGRA testing in a South London HIV cohort.

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Abstract (197; 200 words max)

HIV infection is a major risk factor for development of tuberculosis (TB). Although guidelines recommend that people with HIV from high TB incidence countries and those with risk factors are screened for latent TB infection (LTBI) using interferon-gamma release assays (IGRA), this has not been widely implemented in the UK. We introduced universal LTBI screening using IGRA at nurse-led induction clinics for patients newly presenting, transferring or re-presenting for HIV care and conducted a prospective audit from 01/01/2018 to 30/06/2019 to identify operational challenges as well as opportunities for TB prevention. Of the 223 patients, 17 had active or previously treated TB. Of the remaining 206 individuals who were eligible for IGRA testing, 78 (38%) were not tested due to logistical issues, failure to request the test, or no induction visit taking place. Of the 128 (62%) individuals who were tested for LTBI; three (2.3%) had a positive IGRA, four (3.1%) an indeterminate result, and 121 (94.5%) a negative result. All seven with positive/indeterminate tests were of African/Caribbean background, had CD4 cell counts >200 cells/mm^3 and HIV RNA <400 copies/ml. Our audit suggests that universal LTBI screening was logistically challenging and provided few opportunities for TB prevention.

Introduction

Tuberculosis (TB) may result from recent infection (progressive primary infection) or reactivation of latent TB infection (LTBI). In low incidence settings including the UK, preventive treatment of individuals with LTBI provides an important opportunity to reduce the burden of TB. The presence of LTBI may be detected through tuberculin skin testing (TST) or interferon-gamma release assays (IGRA). These tests serve as risk stratification tools, with a 5.4 to 8.8-fold greater incidence of TB among the UK general population in those with positive vs. negative IGRA [1].

British HIV Association (BHIVA) guidelines recommend testing people with HIV from countries with high and medium TB incidence for LTBI regardless of their CD4+ cell count and receipt of antiretroviral therapy (ART), with particular attention to those with newly-diagnosed HIV or recent exposure to TB, as well as those from low-incidence countries if they have TB risk factors [2]. These guidelines also suggest that IGRA, rather than TST, are used to detect LTBI. However, a survey of UK HIV clinics revealed that only 35.5% and 6.5% were fully compliant with the National Institute for Health and Care Excellence (NICE) LTBI screening guidelines respectively [3]. Moreover, 95% of patients who developed TB more than six months after HIV diagnosis in a Central London clinic had not been screened for LTBI [4]. These observations suggest that there may be substantial barriers to implementing risk-based LTBI testing and that universal testing at entry to care might be a better approach. Of note, IGRA are not recommended to confirm or exclude TB in symptomatic patients and should not be used in those with a history of TB [5].

In November 2017 we introduced universal LTBI screening for individuals at King's College Hospital, London, who were newly diagnosed with HIV infection, represented for care after at least one year without regular follow-up, or transferred HIV care, and conducted a prospective audit to identify operational challenges as well as opportunities for providing preventive therapy.

Methods

In 2018/2019, the Kings College Hospital HIV service provided care for about 2,800 adult patients (39% women, 53% heterosexual, 56% black ethnicity). An IGRA (T-spot®.*TB*: Oxford Immunotech, Oxford, UK) was added to the panel of tests routinely performed during nurse-led induction visits for people entering HIV care. For logistic reasons, IGRA was performed irrespective of reported symptoms, a person's risk profile or their history of past TB. In this audit, we included patients with a first HIV outpatient appointment between 01/01/2018 and 30/06/2019. Data were collected from electronic health records and reasons for not having an IGRA result were investigated.

Results

A total of 223 individuals presented for care. A diagnosis of previous TB was reported by 17, leaving 206 who were eligible for IGRA testing (Table). Seventy-eight (38%) individuals did not have an IGRA result. The test was not performed in 26 because of logistic issues (incorrect, aged or no sample received by the laboratory) and not requested at induction in 23 (initially – prior to June 2018 - tests were not offered to individuals who transferred care); 29 did not have an induction visit (care through outreach to prison or residential care homes, specialist clinics such as antenatal, liver, lymphoma, paediatrics, satellite HIV clinics, or medical admissions) (Figure 1).

A total of 128 (62%) individuals were tested for LTBI; three (2.3% overall; 4.7% of black patients) had a positive IGRA, four (3.1%) an indeterminate (or borderline positive) result, and 121 (94.5%) a negative test (Figure 1). All seven with positive or indeterminate tests were of African or Caribbean background, had CD4 cell counts >200 cells/mm^3 and HIV RNA <400 copies/ml. Of the four individuals with indeterminate IGRA, one had severe liver disease (LTBI treatment contraindicated) while the others await the results of repeat testing.

Discussion

Our audit found that, despite committing considerable resources, over one-third of new patients did not have an IGRA test and that scale up to become fully BHIVA/NICE compliant is challenging. Although we included IGRA in standard order sets (rendering requests operator-independent), there were logistic challenges in terms of availability of specimen tubes, accompanying forms and timing of blood sampling. It also became apparent that individuals entered the service through non-standardised pathways, thereby missing induction visits/blood tests. Importantly, this included pregnant women, prisoners and nursing home residents who may at greater risk of LTBI and TB and who should thus be targeted in screening and prevention programmes.

Consistent with data from East London [6], the yield of LTBI screening of white populations was low and future efforts should probably target African/Caribbean and other populations from medium/high TB incidence settings and only white individuals with risk factors. However, case selection will inevitably increase the complexity of screening. While immune restoration and control of HIV viraemia reduce the risk of developing TB [7], CD4 cell count and HIV viral load should not be used to determine eligibility for LTBI screening [2].

Some of the identified barriers to the scale up of LTBI screening are likely to be relevant to other HIV clinics in the UK. Mandatory induction visits at central (non-satellite) clinics, scheduled in the morning or early afternoon so that samples can reach the laboratories in time for processing and dispatch, allows more patients to be tested but restricts patient choice, may be difficult to achieve for those receiving their care in a nursing home or prison, and may increase the rate of missed appointments. Robust standard operating procedures and staff training programmes will need to be put in place to avoid delays or inappropriate samples reaching the laboratory. Electronic prompts and use of standardized consultation proformas may facilitate the identification of those requiring LTBI screening but require information technology support that may not be available in every clinic.

In conclusion, universal LTBI screening was logistically challenging and provided few opportunities for TB prevention. Future efforts should evaluate barriers to successful implementation of risk-based LTBI screening.

References

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Table **Patient c**haracteristics of 206 individuals who were offered screening for LTBI using IGRA testing

		IGRA performed (n=128)	IGRA not done (n=78)	P value
Age, years	(mean, SEM)	42.1 (1.1)	42.2 (1.6)	0.919
Gender (female)	N (%)	47 (36.7)	25 (32.1)	0.496
Ethnicity				0.641
Black African or Caribbean	N (%)	63 (49.2)	41 (52.6)	
White/other	N (%)	65 (50.8)	37 (47.4)	
HIV risk factor				0.963
MSM	N (%)	48 (37.5)	29 (37.2)	
HTS/other	N (%)	80 (62.5)	49 (62.8)	
Recreational drug use				0.325
Ever	N (%)	13 (11.3)	11 (16.4)	
Never	N (%)	102 (88.7)	56 (83.6)	
HIV presentation				<0.001
New diagnosis	N (%)	76 (59.4)	23 (29.5)	
Re-presentation	N (%)	8 (6.3)	6 (7.7)	
Transfer of care *	N (%)	44 (34.3)	49 (62.8)	
Time since HIV diagnosis, years	(median, IQR)	0.2 (0, 7.0)	4.0 (0.1, 10.4)	0.006
Time since starting ART, years	(median, IQR)	0 (0, 2.9)	2.5 (0, 8.5)	<0.001
CD4 current, cells/mm^3	(median, IQR)	352 (187, 586)	411 (242, 633)	0.159
HIV RNA, log copies/ml	(mean, SEM)	2.3 (0.1)	2.0 (0.1)	0.123
HBsAg, positive	N (%)	3 (2.5)	1 (1.6)	0.694
HCV Ab, positive	N (%)	6 (4.9)	9 (15)	0.019

Legend: Data were compared by T, Chi squared or Mann-Whitney U test, as appropriate. Individuals without IGRA results were more likely to have transferred HIV care, had been diagnosed with HIV and in receipt of ART for longer, and were more often hepatitis C co-infected.

* IGRA tests were added to the panel of investigations regarded as being mandatory for all patients transferring their care to the HIV service at Kings College Hospital, after 01 June 2018.

Abbreviations: IGRA = interferon-gamma release assay; MSM = men who have sex with men; HTS = heterosexual; ART = antiretroviral therapy; HBsAg = hepatitis B surface antigen; HCV Ab = hepatitis C antibody; SEM = standard error of the mean; IQR = inter-quartile range

Missing data: recreational drug use (n=24), ART start date (n=11), current CD4 (n=3), HIV RNA (n=2), HBsAg (n=21), HCV Ab (n=23)