Poster sessions

Abstract P190 Table 1

	Controls (n = 200)	Cases (n = 105)	P-value†
	n (%)	n (%)	
Characteristics of cases (DILI) and controls			
Sex			0.49
Age (years)			0.34
Ethnic origin			0.46
HIV +ve	4/185 (2.2%)	7/95 (7.4%)	0.03
Quinolone use	26 (13.0%)	48 (45.7%)	<0.001
	median (IQR)	median (IQR), n	
Baseline ALT (IU/L)	19 (14–29), n = 185	24 (17–35), n = 105	0.02
Baseline ALP (IU/L)	86 (71–102), n = 187	96 (75–121), n = 105	0.02
Baseline BILI (μM/L)	8 (5–10), n = 185	8 (6–13), n = 105	0.03
Weight (kg)	61.2 (54.5–69.6), n = 178	55.0 (49.0–65.0), n = 101	0.001
Rifampicin dose per kg (if given)	9.7 (8.6–10.7), n = 178	10.0 (9.0–11.2), n = 100	0.08
Isoniazid dose per kg (if given)	4.9 (4.3–5.5), n = 178	5.5 (4.6–6.1), n = 101	<0.001
Pyrazinamide dose per kg (if given)	25.0 (22.0–27.6), n = 166	26.1 (23.1–29.9), n = 98	0.06
Moxifloxacin dose per kg (if given)	6.2 (5.7–7.0), n = 21	7.2 (6.2–8.1), n = 46	0.04
Odds ratios for exposures among DILI cases compared with controls			
	Cases, controls	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)† ‡
Log baseline ALT (IU/L)	105, 185	1.44 (1.02, 2.03)	1.35 (0.93, 1.96)
Log baseline ALP (IU/L)	105, 185	2.12 (1.20, 3.76)	1.87 (0.99, 1.02)
Log baseline BILI (μM/L)	105, 185	1.80 (1.12, 2.87)	1.79 (1.09, 2.96)
Weight (kg)	101, 175	0.97 (0.95, 0.99)	0.96 (0.94, 0.98)
Rifampicin dose per kg	100, 175	1.14 (0.97, 1.33)	1.18 (1.00, 1.39)
Isoniazid dose per kg	101, 175	1.57 (1.22, 2.03)	1.77 (1.34, 2.34)
Pyrazinamide dose per kg	98, 163	1.04 (0.98, 1.10)	1.05 (1.00, 1.11)
Moxifloxacin dose per kg	46, 21	1.56 (1.03, 2.37)	1.85 (1.13, 3.04)
Quinolone use (yes/no)	105, 185	5.15 (2.93, 9.06)	5.41 (2.96, 9.91)
HIV	95, 183	3.56 (1.02, 12.5)	3.81 (1.03, 14.0)

† P-values from Chi-squared test (proportions) or Kruskal-Wallis test (medians)

‡ Adjusted for age, sex and baseline ALT, ALP and BILI

risks of drug-induced hepatitis, and reduced diagnostic sensitivity of LTBI in >35's. 3 months Rifampicin/Isoniazid (3RH) is commonly used however in a review of LTBI treatment, only one Hong-Kong based study found 1766/100,000 (n = 170) had symptomatic hepatitis or alanine aminotransferase (ALT) >250 IU (Grade 3 hepatitis).¹

Prompted by improved sensitivity of LTBI case finding with interferon gamma testing, and local case of active TB in a contact >35 yrs, we studied whether those >35 yrs with LTBI, treated with 3RH experienced greater hepatotoxicity than

Method We retrospectively analysed electronic patient records detailing LTBI patient treatments from June 2008–2013 from two hospitals, collecting baseline clinical data and ALT level >2 weeks into treatment.

Results Of 270 eligible patients, 151 had complete results and were included. 98/151 (65%) were 35 yrs (range 35–75), of whom 32 (60%) were male.

Only 3 patients (2 males) developed ALT >250 IU/L (rate of 1,987/100,000), all patients were symptomatic and required

treatment cessation. Ages were 31, 32 and 52 yrs and the single female patient was pregnant starting treatment. None required admission and all liver function returned to normal following cessation.

Discussion This study, although small, provides a similar rate of hepatitis (defined >250 IU/L or symptoms) to the only previous study using the 3RH regimen and shows no age specific differences in ALT results. In light of this, we raise the question; with increasing rates of TB in the UK, a large proportion of which is attributable to latent infection, should we be offering LTBI treatment to more patients >35 yrs? This study suggests the need, and provides important information for, planning a larger study to help answer this question.

REFERENCE

- 1 Ormerod *et al.* BTS recommendations for assessing risk and for managing Mycobacterium tuberculosis infection and disease in patients due to start anti-TNF- α Thorax 2005;60:800–805

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ASIDE FROM AGE, DO OTHER FACTORS INCREASE THE RISK OF HEPATOTOXICITY IN PATIENTS TREATED FOR LATENT TB INFECTION?CY Ma, JL Potter, H Kunst, VLC White. *Barts Health NHS Trust, London, UK*

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Background Reactivation of latent tuberculosis infection (LTBI) occurs in a number of at-risk groups including: tuberculosis (TB)

Abstract P191 Table 1 Absolute ALT rise and number of patients whose peak ALT rose x2 upper limit of normal (>70 IU/L)

	<35 (n = 98)	>35 (n = 53)	Total (n = 151)
Rise in ALT IU/L (+/-95% CI)	18.1 (10.4)	12.4 (17.8)	16.1 (9.0)
Number of patients with ALT >70 IU/L (%)	10 (10.2)	3 (5.7)	13 (8.6)
Number of patients with ALT >250 IU/L (%)	2 (2.0)	1 (1.8%)	3 (2.0%)

contacts, migrants from high prevalence countries and those who are immunosuppressed. The risk of hepatotoxicity in treating LTBI is thought to be low but much of this evidence is in patients treated with 6 months of isoniazid (6H) rather than 3 months of rifampicin and isoniazid (3RH). Equally, other than age, there is limited data on other factors which may contribute to the risk of developing hepatotoxicity.

Methods A retrospective study was performed at our centre. We analysed all patients treated with chemoprophylaxis, regardless of indication, between 2009 and 2013. Demographic data, treatment regimens and adverse drug reactions, including hepatotoxicity, were recorded. Severe hepatotoxicity was defined as either a rise in ALT five times greater than the upper limit of normal, or as any change in liver function that required an interruption or alteration in treatment. Liver function tests (LFTs) were routinely measured at baseline and then again at two weeks.

Results 290 cases were identified. 84.5% of patients were treated with 3RH, 12.1% were treated with 6H. 2.1% experienced severe hepatotoxicity 2 weeks into treatment. None had symptoms which prompted blood tests prior to our standard 2 week LFTs. Gender, age, documented co-existing liver disease, regimen choice, concomitant use of hepatotoxic drugs and reason for giving chemoprophylaxis were not significantly associated with an increased risk of hepatotoxicity. LTBI treatment was case managed by TB nurses with 91.7% of patients successfully completing treatment. There was no significant difference in treatment completion or adherence rates in those who developed hepatotoxicity compared with those who did not.

Conclusions Our review demonstrates a low incidence of hepatotoxicity associated with treatment of LTBI and highlights the difficulty in predicting those in whom it will occur. If management of LTBI moves from primary to secondary care it will remain important to perform LFTs at two weeks.

Cystic fibrosis

P193 LONGITUDINAL ASSOCIATIONS BETWEEN FEV1 AND HbA1c IN A UK COHORT OF YOUNG PEOPLE WITH CYSTIC FIBROSIS

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Objectives To interrogate the UK national data set and explore longitudinal relationships between FEV1, HbA1c and OGTT parameters in young people with CF up to the age of 23 years.

Methods The UK CF data set (2007 to 2012) recording annual measurements of height, weight, BMI, % predicted FEV1 and FVC, HbA1c and 2 h glucose (2 hrGlu) (>10 years only) was interrogated. HbA1c values >6.5% and 5.7–6.5% were used to define ‘undiagnosed’ diabetes and a pre-diabetic state respectively in patients not labelled as having CFRD. Data from cases with known CFRD were censored. Longitudinal models analysed %FEV1 and %FVC as dependent variables and HbA1c or 2 hrGlu, BMI SDS and age as covariates in patients with HbA1c in the pre-diabetic range.

Results 2105 patients (1097 males), 87.9% with DF508 mutations, median (range) age 13.7 (5.6–22) years, mean (SD) BMI Z score -0.11/+1.1, %FEV1 82.1/+20.3 at first visit were

Abstract P193 Table 1 Longitudinal relationships between lung function and glycaemia

Dependent Variable	Slope (per% higher HbA1c)	P value	95% CI
%FEV1	-2.9	0.016	-5.1 to -0.5
%FVC	-2.1	0.08	-4.4 to +0.3

included. Median range follow up was 3 (1–5) years. 2 hrGlu was available in a subgroup (n = 636). Median HbA1c (Table 1) but not 2 hrGlu (slope -0.1, p = 0.3), within the pre-diabetic range (5.7–6.5%) were inversely associated with %FEV1.

Conclusion In this large UK data set, longitudinal increases in HbA1c within the pre-diabetic range were associated with declining lung function. Our findings support the rationale for trials to intervene early to manage hyperglycaemia in young CF patients with pre-diabetes.

P194 PREVALENCE OF UNDIAGNOSED PRE-DIABETES AND DIABETES IN A UK COHORT OF YOUNG PEOPLE WITH CYSTIC FIBROSIS

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Background In children with cystic fibrosis (CF), cystic fibrosis related diabetes (CFRD) typically develops from adolescence onwards and coincides with deteriorating lung function. Currently, diagnosis of CFRD is based on WHO oral glucose tolerance test criteria rather than HbA1c (used as part of the diagnostic criteria for diabetes mellitus).

Objective To interrogate a national data set and determine prevalence of pre-diabetes and diabetes in patients not diagnosed with CFRD as based on HbA1c.

Methods A national CF data set (2007 to 2012) recording annual measurements of height, weight, BMI, %predicted FEV1 and FVC and HbA1c was interrogated. Young people up to the age of 23 years were included. HbA1c values between 5.7–6.5% and >6.5% were used to diagnose pre-diabetes and diabetes respectively in patients not labelled as having CFRD. Prevalence of pre-diabetes, diabetes and %FEV1 were determined by age group using the first visit values for each individual.

Results 3759 patients (1627 males, 87.5% with DF508 mutations), median (range) age 14.5 years (4.5–23 years), BMI Z score -0.17 (-5.7 +/- 3.6) were included. Prevalences of known CFRD, pre-diabetes and undiagnosed diabetes are shown in Table 1. In cross sectional analyses adjusted for gender, age,

Abstract P194 Table 1 Prevalence of known CFRD, and undiagnosed pre-diabetes and diabetes by age group

N = 3759 all patients	5–10 years	10–16 years	16–23 years
first encounter	n = 801	n = 1121	n = 1837
FEV1 mean +/- SD	89.8 +/- 17.0	80.9 +/- 18.9	70.5 +/- 24.1
BMI SDS mean +/- SD	+0.05 +/- 1.0	-0.11 +/- 1.1	-0.45 +/- 1.2
Undiagnosed CFRD n (%)	16 (2)	122 (10.9)	485 (26.4)
Undiagnosed pre-diabetes			
(HbA1c 5.7–6.5%) n (%)	300 (38.2)	445 (44.5)	617 (45.6)
Undiagnosed diabetes (HbA1c >6.5%) n (%)	14 (1.8)	58 (5.8)	89 (6.6)