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Colette Smith
Department of Primary Care and Population Sciences, Royal Free and UC Medical School,
Tel: +44 (0) 2078302239
E-mail: c.smith@pcps.ucl.ac.uk

Incidence of pancreatitis amongst HIV-positive individuals, and the association with triglycerides and antiretroviral use

CJ Smith[1], A Mocroft[1], CH Olsen[9], F Antunes[2], S Staszewski[3], P Domingo[4], J Weber[5], E Vinogradova[6], H Sambattakou[7], JP Viard[8], Jens Lundgren[9] and the EuroSIDA Study Group

[1]Royal Free and University College Medical School, London, UK; [2]Hospital Santa Maria Lisbon, Portugal; [3]JW Goethe University Hospital, Frrankfurt, Germany; [4]Hospital Sant Pau, Barcelona, Spain; [5]Imperial College School of Medicine at St. Mary's, London, UK; [6]St Petersburg AIDS Centre, St Petersburg, Russia; [7]Ippokration Genereal Hospital, Athens, Greece; [8]Hôpital Necker-Enfants Malades, Paris, France; [9]Copenhagen HIV Program, Copenhagen, Denmark

BACKGROUND

- There is evidence from previous studies that the occurrence of pancreatitis may be associated with antiretroviral use, especially with the NRTIs d4T and ddI
- Furthermore, it is not yet clear whether triglyceride (TG) levels are also associated with pancreatitis risk

AIM

We aimed to:

- investigate the incidence of pancreatitis amongst a cohort of HIV-positive individuals
- assess the association between pancreatitis and TG levels
- assess the association between pancreatitis and antiretroviral therapy use, focussing on the use of d4T and/or ddI

METHODS

- Data on the occurrence of pancreatitis has been prospectively collected in the EuroSIDA cohort since June 2001 and all patients under follow-up from this time onwards were included
- Patients were followed until the date of their last EuroSIDA study visit or the date of pancreatitis, whichever occurred first. Only the first pancreatitis event in the follow-up period per individual was considered
- TG measurements are both fasting and non-fasting
- Factors associated with the occurrence of pancreatitis were assessed using Poisson regression models. Most recent TG level (time-updated) and cumulative antiretroviral use (time-updated) were automatically included in the multivariable model as these were the factors of interest. Other variables were included if p<0.1 in univariable analysis (CD4 count, prior AIDS diagnosis, BMI, haemoglobin level, HBV and HCV status and viral load level at study entry, gender, age, calendar time [time-updated] and region)

RESULTS

- Of 9678 individuals under follow-up in the EuroSIDA cohort from June 2001 onwards, 9175 (94.8%) had at least one TG measurement (**Table 1**)
- There were 43 pancreatic events in 33742 person-years of follow up, corresponding to a rate (95% confidence interval) of 1.27 per 1000 person years (0.89, 1.66)
- There was no evidence that the rate of pancreatitis differed according to the most recent TG measurement (**Figure 1**)
- There was also no evidence that the rate of pancreatitis differed according to cumulative ddI/d4T use (**Figure 2**)
- In a multivariable Poisson model **(Table 2),** pancreatitis was associated with lower CD4 counts (incidence: 1.93 per 1000 person years for CD4 count ≤414 cells/mm3 and 0.64 per 1000 person years for CD4 count >414 cells/mm3) and earlier calendar years (incidence 1.51 per 1000 person years for 2001-2003 and 1.05 per 1000 person years for 2004-2006)
- There was no evidence of an association with most recent TG level, ddI without d4T use, d4T without ddI use, ddI with d4T use and other ART use
- Considering TG as a categorical variable led to similar results (adjusted RR=1.15 for >2.3 mmol/l compared to ≤2.3 mmol/l; 95% CI 0.59-2.25; p=0.68)
- Various sensitivity analyses, such as only including patients from centres in which >75% of patients had at least one TG measurement, led to similar results

CONCLUSIONS

- The rate of pancreatitis recorded in this cohort since 2001 is low
- There was no evidence of an association between triglyceride levels and pancreatitis
- There was no evidence of an association between antiretroviral use and pancreatitis
- However, caution must be taken when assessing the association of covariates with pancreatitis due to a small number of events

Table 1

Characteristics of patients at the time of study entry

		All patients	With ≥1 triglycerides measurement
Number		9678	9175
Gender	Male	7211 (74.5)	6916 (75.4)
CD4 count	Cells/mm³	415 (266, 593) n=9606	414 (266, 592) n=9125
Viral load	Copies/ml	141 (49, 3800) n=9181	106 (49, 3100) n=8844
HCV antibody	Positive	2261 (23.4)	2029 (22.1)
HBV surface antigen	Positive	711 (7.4)	678 (7.4)
Age (years)	Median (IQR)	40 (34, 47)	40 (35, 47)
Prior AIDS diagnosis	Yes	2814 (29.1)	2726 (29.7)
Cumulative ddI exposure (years)*	Median (IQR)	1.1 (0.5, 2.2) n=3300	1.1 (0.5, 2.2) n=3250
Cumulative d4T exposure (years)*	Median (IQR)	2.3 (1.2, 3.4) n=4548	2.3 (1.2, 3.4) n=4463
Cumulative ddI+d4T exposure (years)*	Median (IQR)	1.2 (0.5, 2.2) n=2165	1.2 (0.5, 2.2) n=2118

Figure 1

Rate of pancreatitis according to most recent triglycerides measurement

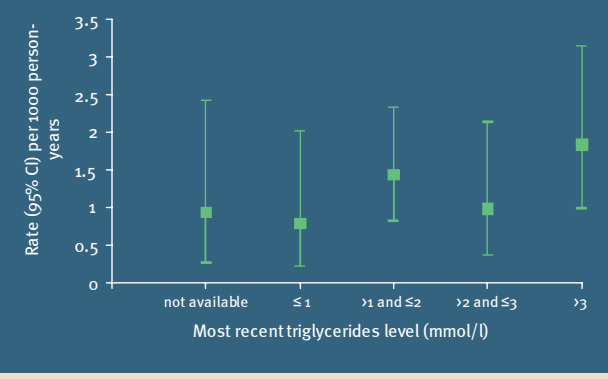

Figure 2

Rate of pancreatitis according to cumulative ddI/d4T use

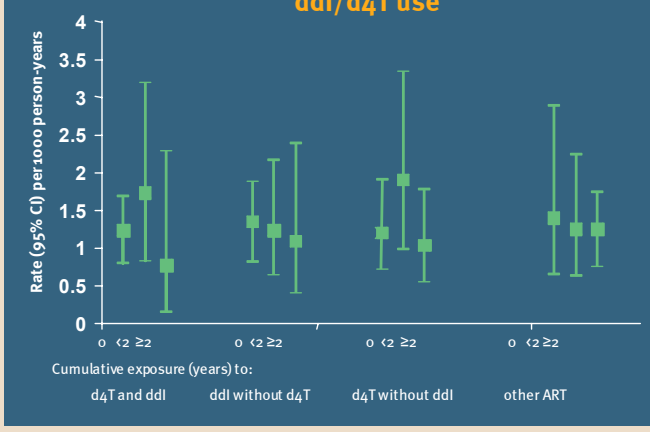

Table 2

Factors associated with occurrence of pancreatitis

		Unadjusted analysis			Adjusted analysis*		
		RR	95% CI	P	RR	95% CI	P
Most recent TG	/1 mmol/l higher	1.03	0.92, 1.15	0.57	1.04	0.93, 1.16	0.54
ART exposure							
ddI without d4T	/year longer exposure	0.91	0.71, 1.16	0.45	0.91	0.69, 1.19	0.49
d4T without ddI	/year longer exposure	0.93	0.79, 1.10	0.39	0.98	0.82, 1.18	0.85
ddI+d4T	/year longer exposure	0.89	0.66, 1.22	0.48	0.90	0.64, 1.28	0.57
Other	/year longer exposure	0.98	0.88, 1.10	0.75	1.03	0.92, 1.16	0.59
CD4 count	/100 cells/mm³ higher	0.72	0.60, 0.86	0.0003	0.80	0.66, 0.96	0.02
Calendar time	/year later	0.77	0.60, 0.97	0.03	0.74	0.58, 0.96	0.02

RR=relative risk; *also adjusted for VL, and prior AIDS diagnosis; Cumulative ART exposure times include a 6-month time lag to account for delayed presentation

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