

DYSLIPIDEMIA IN AN ASIAN POPULATION FOLLOWING TREATMENT FOR 2 YEARS WITH FIVE DIFFERENT PROTEASE INHIBITOR-CONTAINING REGIMENS: THE HIV-NAT COHORT

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Background

Protease inhibitor (PI)-containing antiretroviral therapy (ART) is frequently associated with elevated triglyceride (TRIG) or total cholesterol (CHOL) levels, or decreased high-density lipoprotein (HDL) levels.

Data in an Asian population are limited. We describe lipid changes in a Thai population treated with five different PI-containing regimens.

Methods

We retrospectively compared fasting lipid levels in patients for 2 years after starting one of five different PI-containing HAART regimens between 1998 and 2002. All patients were PI naïve, but had previously received nucleoside ART.

Regimens were:

1. stavudine, didanosine and saquinavir (Fortovase®) (d4T/ddI/SQV) n=46
d4T 30/40mg BID, ddI 400/250mg OD, SQV 1200mg TID
2. zidovudine, lamivudine and saquinavir (Fortovase®) (AZT/3TC/SQV) n=44
AZT 300mg BID, 3TC 150mg BID, SQV 1200mg TID
3. zidovudine, lamivudine and indinavir (AZT/3TC/IDV) n=43
AZT 300mg BID, 3TC 150mg BID, IDV 800mg TID
4. zidovudine, lamivudine and ritonavir-boosted indinavir (AZT/3TC/IDV/r) n=38
AZT 300mg BID, 3TC 150mg BID, IDV 800mg BID, RTV 100mg BID
5. Efavirenz and ritonavir-boosted indinavir (EFV/IDV/r) n=57
EFV 600mg OD, IDV 800mg BID, RTV 100mg BID

Fasting samples were collected at weeks 8, 24, 48, 72 and 110. TRIG concentrations were measured for all patients, but CHOL and HDL levels were only measured in patients on the latter three regimens. Patients who started therapy with a hypolipidemic agent were censored from the time the hypolipidemic agent was prescribed.

Patients were classified as having dyslipidemia if their TRIG or CHOL levels were above, or HDL level was below, the threshold cut off level for high cardiovascular risk in the general population. These threshold levels for TRIG (>200mg/dL), CHOL (>240mg/dL) and HDL (<40mg/dL) were those recommended in the US National Cholesterol Education Program guidelines [1] and have been used in other studies of dyslipidemia in patients receiving ART [2].

The Kruskal-Wallis test was used for comparisons between groups at each time point. The Wilcoxon signed rank test was used to compare changes from baseline values within individual regimens. Multivariate analysis of risk factors used logistic regression to obtain odds ratios and 95% confidence intervals for patients who were not dyslipidemic at trial entry but had developed dyslipidemia at week 110.

Results

Patient characteristics at baseline are shown in **table 1**. Baseline TRIG and CHOL levels and proportion of patients with baseline TRIG and CHOL levels above 200mg/dL and 240mg/dL respectively were equivalent in each treatment group.

Changes in TRIG, CHOL and HDL levels from baseline values were significantly different between treatment groups at all time points ($p < 0.0001$) and are shown in **figures 1a-c**. Ritonavir-boosted regimens resulted in significant changes from baseline in all lipid measurements.

Percentage of patients with dyslipidemia at each time point is shown in **figures 2a-c**.

In logistic regression analyses, gender and baseline values for CDC clinical stage, transmission group, viral load, age and weight were not independent risk factors for the development of hypertriglyceridemia or hypercholesterolemia, and were also not associated with reductions in HDL to levels below 40mg/dL. In univariate analyses, lower baseline CD4 count was associated with development of hypertriglyceridemia ($p=0.027$) (not other dyslipidemias) but was no longer significant in multivariate analyses after controlling for the effect of ART. Odds ratios for development of dyslipidemia are shown in **table 2**.

Twenty-nine patients (4 treated with d4T/ddI/SQV, 1 treated with AZT/3TC/SQV, 3 treated with AZT/3TC/IDV, 5 treated with AZT/3TC/IDV/r and 16 treated with EFV/IDV/r) began treatment with fenofibrate or gemfibrozil as a hypolipidemic agent. The median (IQR) time to initiating treatment was 48 (25–68) weeks.

Table 1. Patient characteristics at baseline.

| Variable | d4T/ddI/SQV (n=46) | AZT/3TC/SQV (n=44) | AZT/3TC/IDV (n=43) | AZT/3TC/IDV/r (n=38) | EFV/IDV/r (n=57) | p |
|---|--------------------|--------------------|--------------------|----------------------|------------------|---------|
| Gender | | | | | | |
| Male, n (%) | 26 (57) | 20 (45) | 14 (33) | 14 (37) | 22 (39) | NS |
| Transmission group | | | | | | |
| Heterosexual, n (%) | 41 (89) | 42 (95) | 37 (86) | 33 (87) | 53 (93) | NS |
| CDC C, n (%) | 1 (2) | 0 | 14 (33) | 9 (24) | 11 (19) | <0.0001 |
| Median age, years (IQR) | 29 (26–34) | 30 (26–32) | 36 (31–38) | 35 (31–41) | 35 (32–41) | <0.0001 |
| Median weight, kg (IQR) | 55 (47–62) | 56 (49–64) | 59 (48–66) | 59 (52–67) | 55 (50–65) | NS |
| CD4 count, cells/mm³ (IQR) | 358 (306–428) | 314 (240–419) | 74 (27–322) | 151 (32–269) | 162 (60–270) | <0.0001 |
| Log₁₀ viral load, copies/mL (IQR) | 4.88 (4.43–5.55) | 4.42 (4.11–5.08) | 3.99 (3.07–4.75) | 3.95 (3.24–4.49) | 4.16 (3.75–4.57) | <0.0001 |
| Median TRIG level, mg/dL (IQR) | 86 (66–146) | 120 (71–161) | 116 (79–166) | 128 (73–215) | 123 (91–182) | NS |
| Median CHOL level, mg/dL (IQR) | NC* | NC* | 163 (146–180) | 173 (159–191) | 168 (149–205) | NS |
| Median HDL level, mg/dL (IQR) | NC* | NC* | 43 (34–57) | 43 (36–57) | 35 (29–41) | <0.0001 |

*Not collected

Figure 1. Median lipid changes from baseline. Error bars represent interquartile range. P values represent comparison of baseline and week 110 values using Wilcoxon signed rank test.

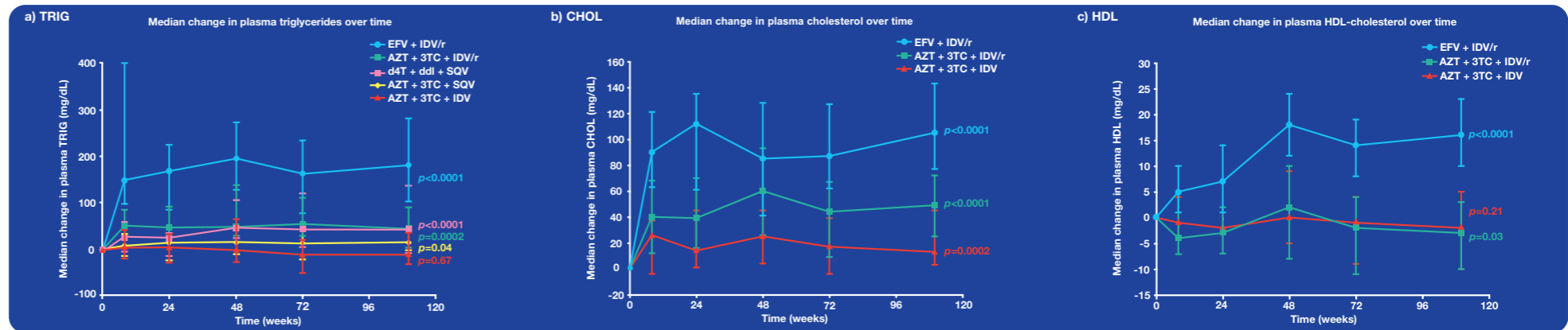
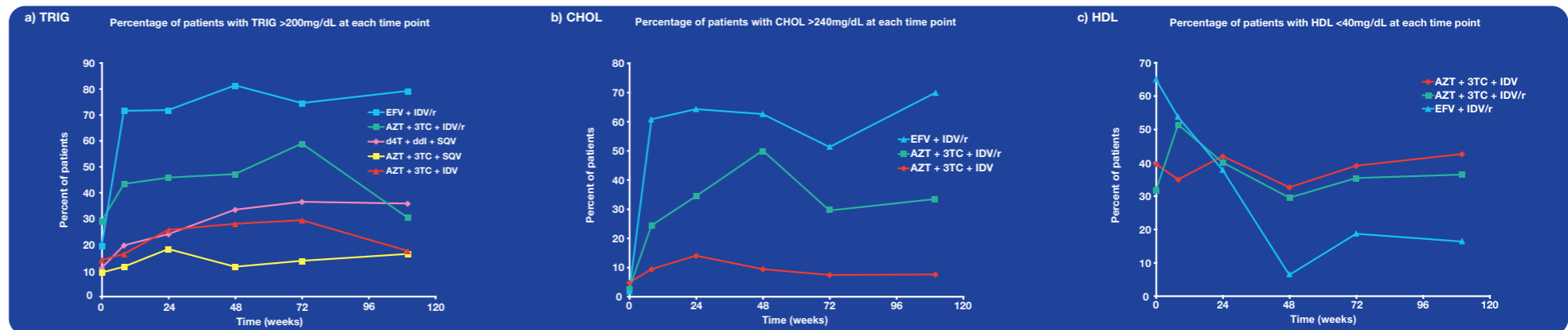


Figure 2. Prevalence of dyslipidemia at each time point in patients treated with different ART regimens.



Conclusions

At week 110, ritonavir-boosted indinavir regimens resulted in significant changes in TRIG, CHOL and HDL from baseline values, and a greater proportion of patients with dyslipidemia over time compared to unboosted indinavir regimens. The addition of efavirenz to a ritonavir-boosted regimen exacerbated the TRIG and CHOL dyslipidemia, but improved the HDL profile (relative to that seen with nucleoside backbones).

Although HDL and CHOL measurements were not available, at week 110 the stavudine-containing regimen resulted in significant changes in TRIG levels from baseline values, and a greater proportion of patients with hypertriglyceridemia at all time points compared to non-boosted, non-stavudine-containing regimens.

Non-boosted, non-stavudine-containing regimens did not significantly impact on the development of dyslipidemia.

References

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**12th Conference on
Retroviruses and
Opportunistic Infections
Boston, MA, USA
February 22–25, 2005**

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