PostScript

LETTERS

Simvastatin co-prescribed with protease inhibitors despite dangerous drug interactions

Drug interactions with anti-retrovirals are frequent and can be dangerous. Protease inhibitors (PIs) inhibit the metabolism of simvastatin, and co-administration is contra-indicated. Despite this, we have seen a recent cluster of patients prescribed simvastatin whilst on PIs.

A 58-year-old man was taking abacavir, lamivudine, atazanavir and ritonavir. His HIV physician noted raised cholesterol and wrote to the patient and his general practitioner (GP), stating that simvastatin is not recommended with his antiretroviral combination, but low dose atorvastatin or pravastatin is safe. Simvastatin was prescribed by the GP.

A 52-year-old woman was taking didanosine, efavirenz, atazanavir and ritonavir, as well as gliclazide, doxazosin and bendroflumazide. A letter from her HIV physician to her GP listed her medications and mentioned that her cholesterol was 8.5. Her GP started simvastatin. The patient took the first dose but stopped after reading the medication insert leaflet.

A 53-year-old man was taking stavudine, lamivudine and nelfinavir. Pravastatin was started by his HIV physician, and letters were written regularly to his GP about current medications. Pravastatin was changed to simvastatin by his GP 6 years later.

At least four other patients at our centre on protease inhibitors (PIs) have recently been switched to simvastatin by GPs. None have suffered adverse consequences, although similar cases have resulted in rhabdomyolysis and death.¹

PIs, including ritonavir, atazanavir, lopinavir, saquinavir and nelfinavir, inhibit cytochrome P450 (CYP) 3A4 activity, which metabolises simvastatin and atorvastatin. Simvastatin exposure is increased by up to 3000% by PIs,² and co-administration is contra-indicated. Atorvastatin concentrations are increased by a much smaller margin, and atorvastatin may be used cautiously. Pravastatin and rosuvastatin are not metabolised by CYP3A4 and are safe to use with PIs.

It should also be noted that efavirenz, a non-nucleoside reverse transcriptase inhibitor, is an inducer of CYP3A4 metabolism, and reduces the concentrations of active simvastatin, atorvastatin and pravastatin by 58%, 34% and 40%, respectively.³

GPs, and all physicians, are under pressure to prescribe cheaper medications where possible, and this is driving the switch to simvastatin. Simvastatin is also available without prescription in pharmacies. These cases highlight the importance of effective communication between HIV physicians, GPs and the patient, not only about current medications but also about potential drug interactions. Where PIs are being used, simvastatin must be avoided.

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Informed consent was obtained for publication of the patients' details in this report.

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The extent of self-initiated STI and HIV prophylaxis (auto-PEP) and treatment in MSM attending GUM and HIV clinic services

In response to a decline in sexually transmitted infection (STI) diagnoses¹ and rising gonococcal antibiotic resistance in men who have sex with men (MSM) attending our genitourinary medicine (GUM) service², we set out to describe patient's STI treatment histories (including the extent of patient self-initiated

treatment). Ethical approval was obtained to provide anonymous questionnaires to 150 consecutive patients in two clinics: a GUM and human immunodeficiency virus (HIV) outpatient clinic located in central London. Following consent, participants were given a questionnaire, which asked details regarding STI diagnosis and treatment over the preceding 5 years. Reasons for non-participation were not collected. No significant differences in the response rate were observed between the GUM clinic (70%) and the HIV outpatient clinic (64%; $p = 0.269$). The median age groups of respondents from the sexual health and HIV outpatient clinics were 26–30 and 36–40 years of age, respectively. Analysis of MSM responses are presented in table 1.

Approximately twice the percentage of MSM attending the HIV outpatient clinic reported previous infections with gonorrhoea and syphilis compared with those attending GUM clinic services. The majority of participants reported receiving STI treatment from GUM or HIV clinics. However, in both groups, approximately 5% reported self-initiating STI prophylaxis or treatment at some time in the past 5 years. All of these men reported at least one STI diagnosis over this recall period. One MSM respondent reported giving anti-retroviral treatment to a partner as HIV post-exposure prophylaxis ('auto-PEP') without medical supervision. Two non-MSM respondents reported providing 'auto-PEP' to a partner.

The percentage of individuals reporting self-initiated prophylaxis or treatment in this study is low. However, the issues for this group of patients are important and include the need to screen for co-existent STIs, inappropriate drug use, antimicrobial resistance and partner notification. The use of HIV treatments as 'auto-PEP' in HIV-negative individuals, if poorly monitored, may be dangerous (e.g. abacavir or nevirapine). It is important that easy access for such patients is maintained and that they are properly educated regarding the relevant issues.

Table 1 MSM questionnaire responses

	GUM clinic	HIV outpatient clinic
Number of respondents describing themselves as MSM	21/105 (20.0%)	78/96 (81.3%)
Recall of STI history		
No previous STI	5/21 (23.8%)	9/78 (11.5%)
Gonorrhoea diagnosed or suspected	6/21 (28.6%)	43/78 (55.1%)
Syphilis	2/21 (9.5%)	18/78 (23.1%)
More than one STI	8/21 (38.1%)	42/78 (53.8%)
HIV positive	2/21 (9.5%)	78/78 (100%)
Not tested for HIV	5/21 (23.8%)	–
Recall of sources of previous STI antibiotic treatment		
GUM clinic	16/21 (76.2%)	72/78 (92.3%)
HIV outpatient clinic	0/21 (0%)	22/78 (28.2%)
GP/NHS walk-in clinic	1/21 (4.8%)	7/78 (9.0%)
Pharmacy abroad	1/21 (4.8%)	1/78 (1.3%)
Internet	1/21 (4.8%)	1/78 (1.3%)
Other	–	4/78 (5.1%)
Recall of STI or HIV prophylaxis		
HIV post-exposure prophylaxis (via GUM clinic or A&E)	2/21 (9.5%)	2/78 (2.6%)
Self-initiated STI prophylaxis	1/21 (4.8%)	4/78 (5.1%)
Provided anti-retroviral treatment to a partner as HIV prophylaxis ('auto-PEP')	–	1/78 (1.3%)

GUM, genitourinary medicine; HIV, human immunodeficiency virus; MSM, men who have sex with men; STI, sexually transmitted infection

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Gender transformation requires population approaches to addressing gender-based violence and HIV

In the June 2007 issue of *Sexually Transmitted Infections*, Dunkle and Jewkes make a much needed case for increased attention to the role of gender-based violence (GBV) in fuelling the HIV pandemic. Referring to an article published in the same issue regarding GBV and STI risk in Bangladesh,¹ they find mounting evidence for national generalizability across a range of cultural settings “supporting the link between perpetration of GBV and STI/HIV risk”. While agreeing with the spirit of their editorial, I question the logic they use to derive their recommendations and propose an alternative method for analysing the relationship among social ideals of masculinity, GBV and HIV/STI transmission using an ecological and comparative framework to explain population-level variations in GBV and HIV prevalence.

Dunkle and Jewkes accurately point to the growing body of evidence that demonstrates unequivocally that women who experience GBV are at greater risk of HIV at the *individual level*. However, at the *ecological level*, it does not necessarily hold that countries with high rates of GBV/gender inequality experience heightened rates of HIV/STIs. For instance, although the WHO multi-country study on GBV has found that Bangladesh has among the highest rates of GBV of the countries studied^{2,3} (findings reinforced in the Silverman *et al* study), Bangladesh has a negligible national HIV prevalence rate of <0.1%. Evidence suggests that Muslim societies, though often endorsing highly repressive gender norms, have extremely low rates of HIV/

STIs.⁴ Likewise, the WHO multi-country study found Ethiopia's and Peru's prevalence of intimate partner violence to be the highest of the 10 countries under study respectively; yet, adult HIV prevalence was estimated at 4.4% in Ethiopia and 0.6% in Peru. Countries with higher national HIV prevalence rates, including Namibia (19.6%) and Tanzania (6.5%), exhibited relatively lower rates of GBV.

In essence, Dunkle and Jewkes' comment commits the atomistic fallacy, or incorrectly generalising an individual-level association to the group level.⁵ In order to assess the contribution of GBV to HIV at the ecological level, studies must move from thinking about the replication of findings in different settings to a comparative, population-level framework. In his classic piece “Sick Individuals and Sick Populations”, epidemiologist Geoffrey Rose⁶ reminds us that the question, “Why do individuals have hypertension?” is a quite different question from ‘why do some populations have much hypertension, whilst in others it is rare?’. In order to address this second question, Rose argues that “what distinguishes the two groups is nothing to do with the characteristics of individuals, it is rather a shift of the whole distribution”.

In the case of HIV, it remains somewhat of a mystery how individual HIV risk factors link up to population risk. Ultimately, due to the limited number of transmission routes, some variation in behaviour between populations, coupled with a tipping point and possible biomedical transmissible cofactors must be responsible for the heightened rate of HIV in certain populations. More evidence is needed to explain under what conditions gender inequitable beliefs link up with population-level GBV and HIV risk.

This comment is in solidarity with Dunkle and Jewkes' contention that “socially transformative programs that promote gender equality and discourage perpetration of gender-based violence are needed to combat the global HIV pandemic”. However, the modes by which to generate social transformation must stem from an understanding of the macro-level causes of social phenomena across populations. Dunkle and Jewkes point to microbicides as a gender-sensitive technology but one that fails to address the “underlying social constructions of gender”. To this, I would add male circumcision, an anti-HIV intervention increasingly gaining in prominence that has the potential to reinforce entrenched

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Abbreviation: GBV, gender-based violence

gender norms and male power. Public health interventions that reinforce gendered power relations should be eschewed in favour of gender transformative interventions that proceed at the population level.

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BOOK REVIEW

Fast facts: sexually transmitted infections

Edited by Anne Edwards, Jackie Sherrard, Jonathan Zenilman. Published by Health Press, Abingdon, pp 132, discount price for STI readers and BASHH members of £10 (usual price £15): order online from <http://www.healthpress.co.uk> quoting SN10 to obtain the discount price. ISBN 978-1-903734-95-7.

This short text provides a very readable summary of the management of sexually transmitted infections, including a short section on HIV. It is attractively laid out with good clinical pictures to illustrate points made in the text, and the use of summary tables and key point lists in each chapter greatly enhance its readability. By its nature it cannot cover issues in great depth but in general it provides clear guidance to the non-specialist with a suitably practical approach.

Although the role of the family physician in managing patients with sexually transmitted infections is mentioned in the introduction, the book is probably most appropriate for those with a special interest in STIs and would be a suitable primer for those entering the specialty or possibly developing an interest in this area whilst working in primary care. The combined UK/US authorship has led to some conflicts where recommendations in the two countries differ. In general the authors have handled this well, although occasionally their recommendations

Table 1 GBV estimates and national HIV prevalence rates

	Lifetime GBV (%)*	National HIV prevalence (%)†
Ethiopia Province	71	4.4 (2003)
Peru Province (City)	69 (51)	0.6 (2005)
Bangladesh Province (City)	62 (53)	<0.1 (2005)
Tanzania Province (City)	56 (41)	6.5 (2005)
Thailand Province (City)	47 (41)	1.4 (2005)
Samoa	46	No data available
Brazil Province (City)	37 (29)	0.5 (2005)
Namibia City	36	19.6 (2005)
Serbia-Montenegro City	24	0.2 (2005)
Japan City	15	<0.1 (2005)

Provincial estimates were utilised where available; otherwise, city estimates were used. As city estimates were lower than provincial estimates, where available, caution should be taken in comparing national estimates based on city estimates alone.

*Percentage reporting ever having experienced physical or sexual violence or both from the WHO multi-country study report.

†UNAIDS seroprevalence estimates. 2005 and 2003 Reports.