ABSTRACTS


A selection of the best abstracts from the first Southern African HIV Clinicians Society Conference, held in November 2012, is provided here. Presentations from the conference may be viewed online (http://www.sahivsoc2012.co.za).

First place

SALIVARY MUCIN MUC5B INHIBITS HIV-1 SUBTYPES A AND C IN AN IN VITRO PSEUDOVIRAL ASSAY

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Category: Clinical laboratory science

Background. Sub-Saharan Africa is the world’s most HIV/AIDS-affected region. More interventions to manage this pandemic are urgently required. Transmission of the virus through saliva exchange is rarely known to occur. Using an in vitro pseudoviral assay, we sought to further describe findings that crude saliva and its purified mucins inhibit HIV-1. A robust assay is key to the identification of the mechanism involved in the inhibition of the virus by mucins. It could also help to identify a peptide sequence in mucins that could be used as a basis for the development of a microbicide.

Methods. Mucus was extracted in 4.0 M guanidinium hydrochloride and a cocktail of protease inhibitors (pH 6.5). Sepharose 4B gel filtration was used to separate MUC5B and MUC7 in saliva, and mucins were purified by density-gradient ultra-centrifugation in caesium chloride. Sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting were used to determine the size, purity and identity of the mucins. The inhibitory activity of crude saliva and purified MUC5B and MUC7, from HIV-negative (n=20) and HIV-positive (n=20) donors, was tested by their incubation with subtypes A and C HIV-1 pseudovirus and infection of susceptible epithelial tumour cells (genetically modified TZM-BL cells).

Results. Crude HIV-negative and HIV-positive saliva inhibited HIV-1 in an in vitro pseudoviral assay in a dose-response nature. Salivary MUC5B neutralised HIV-1 subtype C pseudoviruses CAP45 (KZN) and DU422 (Durban) and Q168a.2 (Kenya) of subtype A, when purified from HIV-negative and HIV-positive individuals. The neutralisation capability of MUC5B appeared greater than that of MUC7 for the HIV-negative group.

Conclusion. Crude saliva and its purified mucins from uninfected controls and HIV-positive individuals inhibited HIV-1 in an in vitro pseudoviral assay. The different inhibitory capabilities are postulated to be due to altered glycosylation of the mucins. Further work using liquid chromatography-mass spectrometry (LC-MS), to analyse glycosylation between mucin groups, is anticipated to reveal such differences.

Second Place

A RANDOMISED CONTROLLED TRIAL OF TWO SPUTUM SAMPLE ACQUISITION METHODS IN PERSONS WITH SMEAR-NEGATIVE OR SPUTUM-SCARCE TUBERCULOSIS IN PRIMARY CARE PRACTICE

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Category: HIV complications

Background. Sputum obtained either through dedicated healthcare-worker-provided instruction or sputum induction can improve tuberculosis (TB) case detection. However, the optimal initial sputum sampling strategy for adults with smear-negative or sputum-scarce TB in high-HIV-prevalent primary care practice is unknown.

Methods. Adults with suspected TB from 3 primary care facilities in Cape Town, South Africa, who were sputum-scarce or smear-negative, underwent open-labelled randomisation to receive induction (N=268; HIV-infected n=96) or healthcare-worker-provided instruction (N=213; HIV-infected n=75) to obtain sputum samples. An intention-to-treat analysis was undertaken and the primary outcome measure was time to treatment initiation. The study is registered with Clinicaltrials.gov (http://www.clinicaltrials.gov) (NCT01545661).

Results. Although a sputum sample >1 ml was acquired in a higher proportion of induced v. instructed participants (90% v. 76%; p<0.001) and culture-based TB case detection was higher in induced v. instructed participants (22% v. 14%; p=0.03), case detection was similar in both arms using either smear-microscopy or Xpert-MTB/RIF. However, given higher empirical treatment rates in instructed v. induced participants (62% v. 43%; p=0.04), a similar proportion in each group initiated TB treatment during the study (30% v. 29%), and at 10 days post-enrolment, a greater proportion of instructed v. induced participants had commenced treatment (75% v. 56%; p=0.03). Differences between groups were unchanged if the analysis was restricted to HIV-infected participants only, with the exception that culture-based case detection and empirical treatment rates were similar in instructed v. induced participants. The per-procedure sampling cost was lower for instructed than induced patients (US$2.14 v. US$7.88).

Conclusions. Healthcare-worker-provided instruction is the preferred initial sputum sampling strategy in primary care practice for adult participants with sputum-scarce or smear-negative TB, irrespective of HIV status.
Runners up
(alphabetical according to first author)

VIRAL RE-SUPPRESSION IN THE PRESENCE OF HIV-1 DRUG RESISTANCE MUTATIONS
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Category: Antiretroviral therapy

Background. HIV-1 drug resistance mutations present the most common reason for loss of antiretroviral activity and frequently herald a regimen change. However, small studies have demonstrated re-suppression without a switch in regimen, even in the presence of specific drug-resistance mutations. We aimed to identify the HIV genotypic background of patients who re-suppressed while remaining on the same regimen after initial failure.

Methods. Patients were enrolled in a prospective workplace HIV cohort (Aurum Cohort) with routine HIV RNA and CD4 monitoring. Suppression (HIV RNA <400 copies/µl), failure (viral load (VL) >1000 copies/µl), and subsequent re-suppression were identified from serial HIV RNA values. First-line regimens were lamivudine (3TC) plus efavirenz (EFV)/nevirapine (NVP) with either stavudine (d4T) (75%) or zidovudine (AZT) (21%). Population-based sequencing was performed using plasma RNA and resistance mutations were identified with the Stanford HIV database.

Results. A total of 71 failing patients who re-suppressed on the same regimen were included. The average VL at failure was log10 4.6 and the average time to re-suppression was 31.8 weeks. At failure, 31/71 (44%) patients had resistance-associated mutations, including M184V (58%), K103N (52%) and V106M (29%). Both the M184V and K103N mutations occurred in 9/31 (29%) of the re-suppressors. The prevalence of TAMs and other resistance mutations was <3%. The median VL at the time of genotyping was log10 3.9 among those with resistance mutations and log10 4.3 among those without mutations (p=0.02).

Conclusion. While the majority of patients who re-suppressed after virological failure were infected with wildtype virus, 44% had one or more drug-resistance mutations. Further work is needed to explore the long-term virological outcomes of patients who re-suppress despite resistance mutations.

HIGH RATE OF VIROLOGICAL RE-SUPPRESSION AMONG PATIENTS FAILING SECOND-LINE ART: A MODEL OF CARE TO ADDRESS ADHERENCE IN A RESOURCE-LIMITED SETTING IN KHAYELITSHA
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Category: Operational research

Background. The rapid scale-up of antiretroviral therapy (ART) coverage in the last decade has improved access to treatment; however, it has coincided with an increasing number of patients failing treatment. In the public sector, patients failing their second-line regimens cannot access costly third-line drugs. Treatment failure may be due to poor adherence, rather than drug resistance. An intervention to improve adherence in patients failing second-line ART was introduced at a primary care clinic in Khayelitsha.

Methods. The intervention included counsellor-led support groups and adherence-focused clinical consultations. It aimed to identify and overcome practical and psycho-social barriers to adherence. Support groups allowed patients with similar difficulties to share experiences and solutions. The consultations were individual, addressing each patient’s particular barriers. A descriptive analysis of patients’ viral load history during July 2010 and December 2011 was undertaken using routinely collected data.

Results. A total of 69 patients were enrolled in the programme, 25 patients were excluded due to insufficient follow-up time. Four patients enrolled with known PI resistance and were switched to a third-line regimen. Of the remaining 40 patients: 27 (68%) went on to achieve virological suppression during 9 months of follow-up time and 5 patients left the programme (2 to death, 2 were lost to follow-up and 1 transferred). Seven patients (18%) continued to experience viraemia, either with known adherence problems or known to be treatment-sensitive following genotyping. One patient was resistant on genotype and switched to third-line treatment.

Conclusion. Poor adherence was the primary reason for virological failure among patients failing second-line ART. Identification of virological escape followed by simple, targeted adherence support can reduce treatment failure, improve treatment outcomes and decrease the need for costly and inaccessible third-line ART.

CHARACTERISTICS, SEXUAL BEHAVIOUR AND RISK FACTORS OF FEMALE, MALE AND TRANSGENDER SEX WORKERS IN SOUTH AFRICA
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Category: Women’s health

Background. Information on the characteristics, sexual behaviour and health needs of sex workers in South Africa is limited. Current social, legal and institutional factors impede a safe working environment for sex workers and their clients.

Objectives. To describe the characteristics and sexual behaviour of female, male and transgender sex workers, and assess risk factors for unprotected penetrative sexual intercourse.

Methods. Repeat cross-sectional surveys among sex workers were conducted in Hillbrow, Sandton, Rustenburg and Cape Town. Sex workers were interviewed once and those reporting a re-interview were excluded from the analysis. Unprotected sex was defined as any unprotected penetrative vaginal and/or anal sexual intercourse with the last two clients.

Results. A total of 1 799 sex workers were interviewed between May 2010 and September 2010. Sex work was a full-time profession for most participants. Participants who reported daily or weekly binge-drinking
were 2.1-fold more likely to have unprotected sex than those who reported never binge drinking (adjusted odds ratio (AOR), 95% CI 1.2 - 3.7; \( p=0.011 \)). Compared with females, male sex workers were 2.9-times more likely (AOR, 95% CI 1.6 - 5.3; \( p<0.001 \)) and transgender people were 2.4-times more likely (AOR, 95% CI 1.1 - 4.9; \( p=0.021 \)) to have unprotected sex. Sex workers in Hillbrow, where the only sex-work-specific clinic was operational, were less likely to have unprotected sex than those in other sites.

**Conclusion.** Tailored sex-work interventions should: explicitly include male and transgender sex workers and sex-work-specific clinics; focus on the risks of unprotected anal sex; and include interventions to reduce alcohol harms.

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**HIGH RATE OF ABACAVIR RESISTANCE IN CHILDREN LIMITS THE CHOICE OF NRTI USED IN SECOND-LINE ART**

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**Category:** Children and adolescents

**Background.** Since 2010, initial antiretroviral therapy (ART) for HIV-infected children in South Africa has consisted of abacavir (ABC), lamivudine (3TC), and efavirenz (EFV), while second-line ART has comprised zidovudine (AZT), didanosine (ddI) and ritonavir-boosted lopinavir (LOP/r). We sought to determine the rate of virological failure (VF) and describe prevalent drug-resistance mutations among Clade C-infected children.

**Methods.** At the Sinikithemba Clinic at Mc Cord Hospital in Durban, a retrospective chart review was performed to identify children who initiated ABC/3TC/EFV or were switched to this treatment without interruption between April 2010 and January 2012. Children receiving ABC/3TC/EFV for at least 24 months and with no prior history of VF (viral load > 1000 copies/µl following at least 6 months of ART) were included. Characteristics at ART initiation, virological outcomes and genotypic resistance patterns (using Trugene assay and the Stanford database) were recorded with a standardised instrument.

**Results.** A total of 221 children receiving ABC/3TC/EFV were identified; 154 (69.7%) were initiated on this treatment and 67 (30.3%) underwent an uninterrupted switch. Fourteen (6%) children experienced VF following a median treatment duration of 11 months (interquartile range (IQR) 8 - 13). Ten patients underwent genotyping: 4 (40%) had the K65R mutation, 4 (40%) had the L74V mutation, 4 (40%) had the L74I mutation, 3 (30%) had the K65R mutation, 4 (40%) had the L74V mutation and 1 (10%) had the L74I mutation. Nine (90%) patients had major non-nucleoside reverse transcriptase inhibitor (NNRTI)-resistance mutations.

**Conclusion.** Among children failing ABC/3TC/EFV treatment, a high level of resistance to ABC and NNRTIs was observed. Importantly, resistance mutations (L74V, K65R and L74I) are likely to reduce the activity of didanosine (ddI) in the second-line regimen. Based on these initial data, in the absence of resistance testing and following failure of ABC/3TC/EFV, we recommend that second-line ART comprises AZT/3TC/LPV/r in South Africa. The recycling of 3TC in the second-line regimen will help to minimise side-effects and preserve AZT hyper-susceptibility, and is likely to result in a reduction of viral fitness.
Methods. We retrospectively reviewed clinical and laboratory data of children aged <2 years who initiated ART at Tygerberg Children's Hospital Infectious Disease Clinic, Cape Town, South Africa, from January 2003 to June 2010. TB immune reconstitution (TB-IRIS) and incident TB were defined as TB treatment episodes within or following 3 months, respectively, of ART initiation. The observation period ended when children exited the hospital system for any reason. Time spent in trials of novel ART agents and prolonged isoniazid prevention therapy were reasons for exclusion from the observation period.

Results. ART was initiated in 531 children including 254 (48%) males. The median age was 7.9 months (interquartile range (IQR) 3.6 - 31.5) and median CD4 cell count (percentage) was 17.5% (IQR 11.5 - 26.2). The median follow-up time was 11.4 months (IQR 3.6 - 31.5). Fifty-one (9.6%) of the children died. ART was initiated during TB treatment in 125 (23%) children. Seventy-one new TB episodes (29 TB-IRIS) were recorded after ART initiation: 58 pulmonary, 5 miliary, 4 TB meningitis, 3 lymphadenitis, and 1 osteo-articular TB. Nine (13%) episodes were bacteriologically confirmed. The incident TB rate was 4.6 episodes/100 person years of follow-up. Among children who developed TB, the median age and CD4 percentage at ART initiation was 6.3 months (IQR 4.5 - 12.2) and 18.0% (12.9 - 25.3), respectively. Baseline demographic and immunological characteristics were similar between children with TB-IRIS v. incident TB.

Conclusion. Young HIV-infected children remain at high risk of TB disease, including disseminated forms, despite a reduction in TB incidence with early ART initiation. Effective preventive strategies and improved diagnostic methods for TB in this vulnerable group could improve clinical outcomes.

SAFETY OF SUTHERLANDIA FRUCTESCENS IN HIV-SEROPOSITIVE SOUTH AFRICAN ADULTS: AN ADAPTIVE, DOUBLE-BLINDED, RANDOMISED, PLACEBO-CONTROLLED TRIAL

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Category: HIV complications

Background. Sutherlandia frutescens is widely used as a traditional medication by HIV-seropositive adults living in South Africa; however, the safety of the use of the plant has not been studied objectively. An adaptive 2-stage randomised double-blind placebo-controlled study was used to evaluate the use of S. frutescens in healthy HIV-seropositive adults with a CD4 T-lymphocyte count >350 cells/µl.

Methods. Fifty-six participants were randomised in stage 1 of the study to receive 400, 800 or 1 200 mg of S. frutescens twice daily or matching placebo for 24 weeks. No adverse events related to the consumption of S. frutescens were detected; subsequently an additional 77 participants were randomised to 1 200 mg S. frutescens or placebo. Data from stages 1 and 2 were combined so that a total of 106 participants were analysed with 53 in each arm, comparing 1 200 mg S. frutescens against placebo.

Results. S. frutescens was well tolerated; biochemical, haematological and electrocardiographic parameters remained within normal limits for the duration of the study. The changes in HIV viral load and CD4 T-lymphocyte count were similar in the two arms at 24 weeks (p>0.3). The questionnaire scores for physical vitality and energy were similar over the study period between the two arms (p>0.1). The burden of infection (BOI) (defined as the number of days of infection-related events experienced by each participant) was greater in the S. frutescens arm: mean 5.0 (5.5) v. 9.0 (12.7) days (p=0.045), and median 9.0 (12.7) v. 18.2 (25.4) days (p=0.065).

Conclusion. The implications of greater BOI observed in the S. frutescens arm need further evaluation. No other safety issues were identified in this cohort relating to the consumption of high-dose S. frutescens.