P-075 HAART exacerbates anti-Koch-induced reproductive toxicity via suppression of androgen and down-regulation of cGMP signaling

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Study question: Will highly active antiretroviral drugs (HAART) and antikochs impair reproductive function when used singly and concurrently?
Summary answer: HAART exacerbates antikoch-induced reproductive toxicity by stimulating testicular and penile oxido-inflammatory response. This was associated with suppression of androgen and down-regulation of cGMP signaling.
What is known already: Although the advent of HAART and antikochs has significantly improved the clinical status, life expectancy and quality of life of patients with HIV/tuberculosis, these drugs are with shortcomings. Studies have reported that HAART induces testicular toxicity and impairs sperm quality. Similarly, antikochs has been shown to trigger oxidative testicular and sperm damage. Available data have implicated HAART and antikoch in the pathogenesis of male infertility via oxidative stress-mediated mechanism. However, no study has reported the impact of the concurrent administration of both HAART and antikochs as seen in patients with TB/HIV co-infection on testicular function, sexual behaviour and fertility outcome.
Study design, size, duration: This is a prospective experimental study using animal model. Forty sexually mature inbred male Wistar rats of comparable age were used for the study. The study lasted 8 weeks.
Participants/materials, setting, methods: Animals were acclimatized for two weeks after which they were randomly allotted into four groups (n=10). The control rats 0.5mL of distilled water as vehicle, anti-Koch-treated rats received a cocktail of anti-tuberculosis drugs (Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol), HAART-treated animals received a cock-tail of antiretroviral drugs (Efavirenz, Lamivudine, and Tenofovir), while the HAART+antikochs-treated rats received treatment as HAART-treated as well as antikoch-treated. The doses of drugs used were the Human Equivalent doses for rats.
Main results and the role of chance: HAART exaggerated antikoch-induced increase in testicular lactate dehydrogenase activity, concentrations of lactate and uric acid, and reduced testicular sorbitol dehydrogenase activity. Furthermore, HAART worsens antikoch-induced decline in the activities of testicular and penile superoxide dismutase, catalase, glutathione peroxidase, and glutathione-S-transferase, as well as glutathione concentration, but increased malondialdehyde levels in testicular and penile tissues, as well as penile and testicular DNA fragmentation. Similarly, HAART aggravates antikoch-driven reduction in penile cGMP, circulatory and testicular testosterone, serum prolactin, LH and FSH, impaired sperm quality, sexual behaviour, and fertility outcome.
Limitations, reasons for caution: This is a prospective study using animal model; hence findings should be extrapolated to human with care. Human studies are thus recommended.
Wider implications of the findings: This study demonstrates for the first time the impact of HAART and antikoch, when used singly or in combination, on sexual behaviour, sperm quality and penile and testicular integrity. The findings add to the available literature by providing the molecular mechanism through which HAART and/or antikoch possibly impair reproductive function.
Trial registration number: N/A