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Unacceptable side effects of a hyperosmolar vaginal microbicide in a phase 1 trial Cai C(1), Sawant S(2), Qi Z(3), mccormack S(4), Weber JN(2), Jiang S(3), Lacey CJ(1) 1. University of York, York, UK; 2. Imperial College, St Mary's Campus, London, UK; 3. New York Blood Center, New York, USA, 4. Medical Research Council Clinical Trials Unit, London, UK; Background: Cellulose acetate phthalate (CAP) is a potential microbicide with a broad spectrum of action against HIV and STDs. However, suspension in water causes hydrolysis of CAP and nonwater based formulations have to be utilised. Methodology: We conducted a phase 1 trial using a glycerol-based formulation of CAP 13% used once a day for 14 days in healthy HIV negative women. After the trial we conducted laboratory experiments to assess the osmolarity and viscosity of the CAP vaginal microbicide and a range of other commonly used topical products. Results: The trial was stopped by the investigators after 5 women had completed dosing. All women had suffered heavy watery discharge, either requiring continuous use of panty liners (n=4) or sanitary towels (n=1). One woman developed a Candida vulvovaginitis after 7 days therapy. Laboratory investigations showed the CAP gel to have a high osmolarity (8511 mOsm; cf PBS 287), a high viscosity (96140 cps) and to show a dramatic drop in viscosity with dilution. Conclusion: A hyperosmolar vaginal microbicide formulation was associated with unacceptable side effects in a phase 1 trial. The hyperosmolarity was predominantly associated with the glycerin content of the microbicide. We presume that the hyperosmolar gel caused abnormal transudation of physiologic fluid across the cervico-vaginal mucosae. These findings mirror those recently reported for colonic application of hyperosmolar lubricants. We suggest that osmolarity needs to be considered in the design of vaginal microbicide formulations and interpretation of studies.