A NEW NONOXYNOL-9 FORMULATION (ACIDFORM) SIGNIFICANTLY IMPACTS EXPERIMENTAL GENITAL CHLAMYDIA INFECTION IN A MOUSE MODEL.

Objective: To evaluate in a mouse model of genital Chlamydia infection the protective efficacy afforded by prophylactic treatment with a new nonoxynol-9 (N-9) preparation (ACIDFORM) designed to acidify semen during intercourse and form a bioadhesive layer over the vaginal surface.

Methods: Groups of female Swiss Webster mice received 15μl of ACIDFORM placebo gel, ACIDFORM+N-9 (5%) gel or PBS by intravaginal instillation. Twenty seconds later animals were challenged intravaginally with 5.0 log₁₀ IFU C. trachomatis mouse pneumonia biovar. Vaginal swabs were collected from all animals on days 3 and 6 post challenge to determine the effect of treatment on the incidence and magnitude of infection in the lower genital tract. Animals were sacrificed at different times post challenge and upper genital tract tissue collected and assayed by culture.

Results: Treatment with ACIDFORM+N-9 significantly reduced the number of animals from which C. trachomatis was isolated in the upper tract compared to both control groups (p<0.05). Further, C. trachomatis was isolated on days 6 and 7 post challenge from the upper genital tracts of all ACIDFORM placebo (23/23) and PBS (24/24) control animals, but from only 17/23 of the ACIDFORM+N-9 group (p<0.05). In ACIDFORM+N-9 animals from which organism was isolated in the upper tract, titers were also significantly lower than in the PBS control animals (0.26±0.23 log₁₀ IFU/mg vs 0.79±0.11 log₁₀ IFU/mg; p<0.05).

Conclusion: Treatment with the ACIDFORM+N-9 formulation significantly impacted both lower and upper genital tract disease in our mouse model of genital chlamydia infection. Further studies to more fully evaluate this formulation are warranted.

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PHASE I STUDIES OF POTENTIAL VAGINAL MICROBICIDES: COMPARATIVE RESULTS FROM STUDIES OF FOUR AGENTS

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Objectives: To assess the safety and tolerability of four potential vaginal microbicidal gels: (nonoxynol-9, sodium docusate, dextrin-2 sulphate and PRO-2000) in sexually inactive healthy female volunteers.

Methods: These agents were studied in separate double-blind, placebo-controlled trials conducted at our centre. The impact on genital epithelium was assessed macroscopically by colposcopy, and microscopically by histological examination of vaginal biopsy specimens obtained pre and post-gel exposure. The impact of the study gels on vaginal lactobacilli was quantified, and laboratory safety data were obtained in all trials of novel agents, to assess systemic toxicity.

Results: Dextrin-2-sulphate and PRO-2000 were found to be safe and well tolerated at the doses tested. The use of nonoxynol-9 at a dose of 100 mg was associated with genital inflammation, although histological evidence of this correlated poorly with colposcopic appearance. Exposure to sodium docusate resulted in a degree of epithelial stripping in over 90% of the subjects who received the active agent, possibly due to phase separation of the gel.

Conclusions: These studies have, in our view, confirmed the value of vaginal biopsy in the assessment of the local safety of these agents. Using the phase 1 methodology described, we have identified two potential vaginal microbicidal agents (dextrin-2-sulphate and PRO-2000) for further investigation in phase II trials.