

A VAGINAL PLETHYSMOGRAPHY PILOT STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF PLACEBO AND THREE DIFFERENT DOSES OF TOPICAL ALPROSTADIL USP (PROSTAGLANDIN E1) CREAM IN FEMALE PATIENTS WITH SEXUAL DYSFUNCTION

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INTRODUCTION

STUDY OBJECTIVES
The objectives of this pilot study were to evaluate the efficacy and safety of 3 doses of topical alprostadil USP (prostaglandin E) cream in comparison with placebo in 8 female patients with sexual dysfunction.

METHODS

STUDY DESIGN
Single-blind, single-center, within-subject, escalating single dose study in premenopausal women diagnosed with female sexual arousal disorder (FSAD).
* DSM-IV criteria used for clinical diagnosis.

PRIMARY EFFICACY
1. Subjective evaluation of arousal and vaginal sensations during visual sexual stimulation (VSS), as measured by quantitative ratings on Video Assessment Questionnaire (VAQ).
2. Vaginal photoplethysmography (VPP) estimate of vaginal blood flow during VSS.

SECONDARY EFFICACY
Physician visual assessment of vaginal erythema, exudate volume, and swelling

STATISTICAL ANALYSIS
Paired t-test, two-sided, $\alpha=0.05$

STUDY MEDICATION
A proprietary cream formulation containing 0.05%, 0.1% or 0.2% alprostadil USP. A placebo cream was used as the control.

DOSING and DATA COLLECTION
1. Investigator visually inspects the external genitalia, vagina, and cervix.
2. Investigator inserts Geer gauge into the patient's vagina. VPP is continually recorded until 60 minutes post dosing.
3. Fifteen minutes after insertion of Geer gauge, patient receives a single-blinded dose of medication to vagina administered by the investigator.
4. Thirty minutes post dosing VSS* is initiated. VSS duration is 30 minutes.
5. Geer gauge removed and investigator inspects vagina.
6. Patient completes a Video Assessment Questionnaire (VAQ).

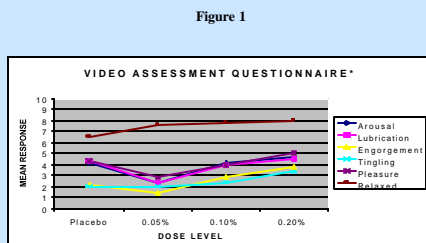
*VSS is a sexually explicit video. Patient had a choice of 4 videos.

RESULTS

Eight patients completed the study (Table 1). The effects of Alprostadil cream on primary and secondary clinical endpoints are summarized in Table 1-5 and Figure 1, and Table 6 and 7, respectively. The Alprostadil cream was well tolerated and produced only mild acceptable local irritation (Table 8 and 9).

Table 1
PATIENT DEMOGRAPHICS

	Mean±SD	Frequency
Age	40.4 ± 7.7	
Weight	150.3 ± 42.3	
Height	63.9 ± 2.5	
Race: Caucasian		6
Black		1
Asian		1



* Scale: 0 (Not at All) to 10 (Very Much)

Table 2
VIDEO ASSESSMENT QUESTIONNAIRE
Within-Subject Differences Between PGE₁ 0.05% and Treatment (Means ± SD)

	Placebo vs. PGE ₁ 0.05% (N = 8)	Placebo vs. PGE ₁ 0.1% (N = 8)	Placebo vs. PGE ₁ 0.2% (N = 7)
Arousal	-1.88 ± 1.1 (p = 0.13)	0 ± 0.8 (p = 1.0)	0.29 ± 0.4 (p = 0.46)
Lubrication	-2.00 ± 1.2 (p = 0.13)	-0.38 ± 1.0 (p = 0.73)	0 ± 0.5 (p = 1.0)
Engorgement	-0.75 ± 1.1 (p = 0.52)	0.75 ± 0.5 (p = 0.20)	1.57 ± 1.0 (p = 0.17)
Tingling	0 ± 1.2 (p = 1.0)	0.38 ± 0.8 (p = 0.64)	1.14 ± 0.5 (p = 0.07)
Pleasure	-1.50 ± 1.3 (p = 0.27)	-0.38 ± 1.0 (p = 0.73)	0.57 ± 0.5 (p = 0.32)
Relaxed	1.00 ± 0.6 (p = 0.15)	1.25 ± 1.0 (p = 0.27)	1.00 ± 1.0 (p = 0.38)

Table 3
VIDEO ASSESSMENT QUESTIONNAIRE
Within-Subject Differences Between PGE₁ 0.05% Dose and the Other Doses (Means ± SD)

	PGE ₁ 0.05% vs. PGE ₁ 0.1% (N = 8)	PGE ₁ 0.05% vs. PGE ₁ 0.2% (N = 7)
Arousal	1.88 ± 0.8	2.57 ± 1.1
Lubrication	1.63 ± 0.7 *	2.57 ± 1.0 *
Engorgement	1.50 ± 1.0	3.00 ± 1.2 *
Tingling	0.38 ± 0.7	1.71 ± 1.0
Pleasure	1.13 ± 0.8	2.57 ± 1.2
Relaxed	0.25 ± 0.6	0.29 ± 0.6

* Significant at $\alpha=0.05$

Table 4
VIDEO ASSESSMENT QUESTIONNAIRE
Within-Subject Differences Between Placebo and Visit at Which Maximum Response was Report (Means ± SD)

	Placebo (N = 8)	Maximum Response (N = 8)	Difference
Arousal	4.13 ± 1.5 ²	5.50 ± 1.07	1.38 *
Lubrication	4.25 ± 2.2 ²	5.50 ± 1.60	1.25
Engorgement	2.13 ± 2.03	4.75 ± 2.49	2.63 *
Tingling	2.00 ± 2.20	4.00 ± 1.85	2.00 *
Pleasure	4.25 ± 1.91	5.88 ± 1.36	1.63 *
Relaxed	6.50 ± 2.7 ²	8.38 ± 1.41	1.88

* Significant at $\alpha=0.05$

Table 5
VAGINAL PHOTOPLETHYSMOGRAPHY
MAXIMUM AMPLITUDE CHANGE *
(Means ± SD)

Placebo (Visit 2)	PGE ₁ 0.05% (Visit 3)	PGE ₁ 0.1% (Visit 4)	PGE ₁ 0.2% (Visit 5)
N=6	N=8	N=8	N=7
10.00 ± 4.6	8.50 ± 4.1	10.88 ± 4.6	5.57 ± 3.5

* Maximum amplitude change is the variable derived from taking the difference between the baseline amplitude (averaged over the 15 minutes prior to drug administration) and the patient's maximum amplitude response (during the approximately 30 to 60 minute period of VSS following drug administration).

Table 6
SUBJECTIVE VISUAL INSPECTIONS*
Means of the Within-Subject Differences Between PGE₁ 0.05% Dose and the Other Doses (Means ± SD)

	PGE ₁ 0.05% vs. PGE ₁ 0.1% (N = 8)	PGE ₁ 0.05% vs. PGE ₁ 0.2% (N = 7)
Erythema	0.38 ± 0.32	0.71 ± 0.29**
Swelling	-0.25 ± 0.25	-0.14 ± 0.14
Exudates	0.63 ± 0.18**	0.71 ± 0.29**

* Ratings are as follows: 1=none, 2=minimal, 3=moderate, 4=pronounced.
** Significant at $\alpha=0.05$

Table 7
SUBJECTIVE VISUAL INSPECTIONS
Mean Change from Baseline at Placebo Versus Change from Baseline at Visit Associated With Maximum Response (Means ± SD)

	Placebo (N = 8)	Maximum Response (N = 8)	Difference
Erythema	0.25 ± 0.46*	1.38 ± 0.74	1.13 *
Swelling	0.13 ± 0.35	0.63 ± 0.52	0.50
Exudates	0.63 ± 0.74	1.38 ± 0.92	0.75

* Significant at $\alpha=0.05$

Table 8
ADVERSE EVENTS
Incidence per 23 total active doses

	Mild	Moderate	Severe
Vaginal Itching	3	1	None
Vaginal Burning	4	None	None
Vaginal Soreness	1	None	None

Table 9
SAFETY PARAMETERS

	Study Results
Vital Signs	No significant findings attributed to drug.
ECG	No significant findings attributed to drug.
Laboratory Results	No significant findings attributed to drug.

CONCLUSIONS

PRIMARY EFFICACY

A proprietary topical formulation of alprostadil produced dose dependent increases in arousal, engorgement, tingling and pleasure as assessed by patients' subjective responses to post dosing questionnaire.

Statistical significance was achieved when comparing the mean placebo response to the mean response of the dose producing the maximum result for each individual, for arousal, engorgement, tingling and pleasure.

This safety study design dictated dosing in sequential increasing doses however, the first dose, the placebo dose, produced relatively high values that precluded statistical significance when compared to the other doses. High first dose placebo values suggest that a stable baseline was not achieved with only one placebo dose.

Vaginal photoplethysmography readings did not differentiate the effects alprostadil treatments from placebo.

SECONDARY EFFICACY

A proprietary topical formulation of alprostadil produced dose dependent increases in erythema and exudates as assessed by subjective visual inspection by the investigator. Dose dependent increases in swelling were not seen.

SAFETY

Of the 23 active topical applications of a proprietary formulation of alprostadil only 8 mild and 1 moderate local side effects was observed. 1 clear dose dependent effect relationship could be established probably that this was a very small study.

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