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Heidi Wise

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Effectiveness of Topical Alprostadil for the Treatment of Female Sexual Arousal Disorder

Abstract

Background: Female sexual dysfunction (FSD) is a vast problem in the medical community and in the world. It affects more than just sexual experiences of women and their partners, but also vitality and many other aspects of health. Female Sexual Arousal Disorder (FSAD) is one subcategory of FSD disorders. Since arousal has been found to be a key component in the female sexual response cycle, possible treatments would ideally target local arousal. Topical alprostadil has been proposed to be a vasodilator and could possibly affect chemoreceptors locally in the genitalia. Thus, it is a probable treatment for the many women who live with FSAD.

Methods: An exhaustive search of available medical literature was conducted utilizing MEDLINE-Ovid, CINAHL, and Web of Science. Keywords used to search were *alprostadil*, *sexual dysfunction* and *female*. GRADE was utilized to evaluate the evidence

Results: Two journal articles were found that met all the inclusion and exclusion criteria. A dose related response was found for improvement of FSFI scores, sexual arousal rates, and sexual satisfaction vs. placebo in both studies. The rates of sexual arousal and sexual satisfaction were significantly higher in the 400 mcg group in the Heiman et al, 2006 study and the 900 mcg group of the Liao et al, 2008 study. Adverse events were low in all treatment groups, and lowest in the placebo, 100 mcg, 500 mcg and 700 mcg groups respectively.

Conclusion: Topical alprostadil is an effective and safe treatment option for patients with FSAD. This treatment significantly improved sexual arousal rates and sexual satisfaction for most all treatment groups.

Keywords: *Alprostadil, female sexual dysfunction, female sexual arousal disorder*

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Effectiveness of Topical Alprostadil for the Treatment of Female Sexual
Arousal Disorder

Heidi L. Wise



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Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS

Biography

[Redacted for privacy]

Abstract

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List of Abbreviation

FSD	Female Sexual Dysfunction
FSAD	Female Sexual Arousal Disorder
FSFI	Female Sexual Function Index
FSDS	Female Sexual Distress Scale

Effectiveness of Topical Alprostadil in the Treatment of Female Sexual Arousal Disorder

BACKGROUND

Female sexual dysfunction (FSD) which is a multidisciplinary, distressing group of disorders which encompasses many symptoms such as low sexual desire, decreased sexual arousal, and discomfort during sexual activity¹ plagues many women. For example, in 1999 Laumann et al² polled almost 3000 men and women, which was the first survey to be conducted like this since the Kinsey era, to determine rates of sexual dysfunction in the United States. Their research found 43% of the women who were surveyed had been experiencing some kind of sexual dysfunction, as compared to 31% of the male subjects.² More recent reports³ have yielded similar results, showing women with sexual concerns at 40%.

Sexual dysfunction is not only an issue with satisfaction and arousal rates, but also with the overall health of the human being. There have been statistically significant correlations between sexual dysfunction and decreases in mental health, social function, relationship problems, undiagnosed medical conditions and overall vitality.¹ Cardiovascular risk factors have also been correlated in several studies⁴ with women who have clitoral and vaginal dysfunction as well. Therefore there is a large need for treatments to be

researched and studied for efficacy and safety, not only for sexual function but for overall health. A number of treatments are on the market for male patients with sexual dysfunction, but very few are available for women. Frankly, this is unacceptable due to these serious risks and ramifications that dysfunction of sexual health can affect both men and women.

Female sexual arousal disorder (FSAD) is one of the many subtypes of FSD that involves "...the persistent or recurrent inability to attain, or to maintain sufficient sexual excitement and satisfaction, causing personal distress."⁵ Since FSAD typically involves the excitement phase of the sexual experience, topical alprostadil has been suggested as a potential treatment for this disorder due to its proposed mechanism of action and its safety.

Topical alprostadil is a prostaglandin E₁ (PGE₁) which is naturally occurring in humans and is a vasodilator.¹ Clinicians have tried other vasodilators for the treatment of sexual dysfunction in women, such as sildenafil--a PDE5 inhibitor, but these studies⁶ have resulted in no decisive conclusions due to varying populations and measurements as well as genital engorgement without any subjective arousal. Thus, the mechanism of alprostadil, as of yet is not fully understood. Sun et al⁷ studied the mechanism by applying alprostadil to female rats, concluding that there must be some other chemoreceptor mechanism

and/or hormone response in the brain that is different from other vasodilator treatments. Another potential benefit of topical alprostadil may be its potential to decrease systemic side effects, unlike other current treatment suggestions for FSAD.

Alprostadil as a treatment also conceptually makes sense when looking at female sexual response in general. Levine et al⁸ theorizes that desire is a complex part of the sexual experience that encompasses both sexual drive and sexual motivation. This builds on the idea that was proposed by Basson⁹ in the late 1990's, that the precursor to desire for females is often sexual arousal, since most females tend to start a sexual encounter from a position of sexual neutrality. Thus treating sexual arousal may be the key to helping many sexual function disorders and an integral piece to the FSD puzzle.

METHODS

An exhaustive literature search was performed using the following search engines: MEDLINE-Ovid, CINAHL, and Web of Science. The key terms which were searched included *alprostadil*, *sexual dysfunction* and *female*. The following eligibility criteria was applied to each of these studies: studies published in the English language, studies which were conducted on human women 22-70 years of age who were all diagnosed with female sexual dysfunction, and studies that were

published after May 2006 or were not included in Kielbasa, L et al literature review titled *Topical Alprostadil Treatment of Female Sexual Arousal Disorder*¹⁰ and studies which compared topical Alprostadil with placebo treatments. Articles were assessed for quality using the Grade of Recommendations, Assessment, Development and Evaluation.¹¹

RESULTS

The search of the 3 databases yielded a total of 55 articles. These studies and articles were run through the inclusion criteria and 2 studies resulted.^{5,12} See Table 1.

Heiman et al, 2006

The Heiman et al¹² study measured outcomes in 79 postmenopausal or hysterectomized women ages 40-70 and their response to either 100 mcg of topical alprostadil or 400 mcg of topical alprostadil in a prospective, randomized, multicenter, double-blind, crossover design study. Each subject was also given a placebo dose which was compared to their response to the allotted alprostadil dose. These doses were administered in the clinic and were immediately followed by 60 minutes of video stimulation which was selected according to sexual orientation and from most commonly requested videos from a female audience.¹²

Subjects were periodically asked to rate their overall genital wetness, pelvic fullness, warmth/tingling, any pain, sexual arousal,

satisfaction with the level of arousal and sexual satisfaction itself, as well as overall physical comfort. Vital signs were also assessed on each subject and investigators assessed the erythema and edema of the genitalia immediately before dosing, and at 60 minutes and 120 minutes afterwards.¹²

This Heiman et al¹² study included subjects who were mostly white EuroAmericans, married, satisfied with their current relationship and all of who were diagnosed with FSAD. Baseline scores of the Female Sexual Function Index (FSFI; this index measures different aspects of sexual function on a scale of 0 to 6 for a total of 19 questions) and the Female Sexual Distress Scale (FSDS) were conducted prior to the study in all the participating women. There was no significant difference between the dosage groups for these demographic parameters.¹²

When the observers rated genital vasocongestion at 60 minutes and 120 minutes for each of the doses of alprostadil, 100 mcg and 400 mcg, there was a significant local vasodilatory response for both groups at each time increment. In terms of pelvic fullness, the 100mcg dose did not show significant difference between placebo scores, however, the 400 mcg dose group showed a significant change, peaking at 30 minutes, when compared the placebo.¹²

Genital warmth and tingling were both significantly greater in the 100 mcg and the 400 mcg doses compared to placebo, with the 400 mcg group showing a greater significant difference over the entire 120 minutes (6.95 vs. 2.74; $p=0.002$).¹² Genital wetness and lubrication did not significantly change between 100 mcg, 400 mcg and placebo, but the changes from baseline over a 2 hour observational period significantly increased for all study groups, including placebo.¹²

Sexual arousal levels were significantly different from baseline in both the 100 mcg and the placebo groups. However, there was no significant difference between these 2 groups. On the other hand, the 400 mcg dose group vs. placebo did show a significant difference, and especially when summed up as a change over baseline over the entire 120 minutes (5.42 vs. 2.61; $p=0.017$).¹²

Satisfaction with the level of sexual arousal was significant for both alprostadil and the placebo, but this was not the case between each treatment group. Sexual satisfaction was very similar to the results of sexual arousal levels. Both the 100 mcg and placebo resulted in significantly different results than baseline, but not when compared to each other. On the contrary, the 400 mcg group showed a significantly greater sexual satisfaction rate than the placebo group over the entire 120 minutes of observation (4.74 vs. 2.42; $p=0.015$).¹²

Pain ratings and physical discomfort showed no significant difference between baseline or one another. In terms of adverse events for the 100 mcg group, 28% of subjects treated with 100 mcg dose of alprostadil and 18% of subjects treated with the placebo reported adverse events. These included genital erythema, which was the most common reported event, genital edema, and genital burning. All of these cases were considered mild to moderate in severity. Within the 400 mcg group, 50% of subjects reported adverse events and 32% of the placebo reported adverse events as well. These events were the same for the 100 mcg group above in terms of events and the severity.¹²

Liao et al, 2008

This study⁵ took the Heiman et al, 2006 study to another level with the number of participants and a slightly different study design. Liao et al was a multicenter, randomized, double-blind parallel and placebo-controlled study that took 374 female participants of which were non-menopausal (268 participants) and post-menopausal (106). Their mean age was 45 years, ranging from 22-62. All of the female participants showed no significant differences when it came to medical history or FSDS and FSFI scores, and all were screened via strict eligibility criteria including having a diagnosis of FSAD and currently being in a stable monogamous relationship.⁵

Participants in the Liao et al study were randomly assigned to 1 of 4 groups, 1 group was placebo and the others were differing levels of topical alprostadil 500 mcg, 700 mcg, and 900 mcg. All of the patients received 10 identical, placebo matched, individually packaged plastic dispensers with white cream. These were applied by the patient to the clitoris and anterior vaginal G-spot 5-30 minutes prior to anticipated sexual intercourse. Patients were required to attempt sexual intercourse 5 times during three 4-week windows and record their responses in a patient diary which included the Female Sexual Encounter Profile (FSEP), the FSFI, the Female Sexual Distress Scale (FSDS), and the global assessment questionnaires (GAQ).⁵

The outcomes for sexual arousal rates showed a significantly higher rate as compared to baseline across all placebo and treatment groups. Also, when comparing all the treatment groups to placebo, these scores for sexual arousal were all significantly higher in the treatment groups than the placebo (Table 2). When looking specifically at change between each of the individual treatment group and placebo, the 500mcg treatment group and placebo was not significant, but the differences between the 700 mcg, the 900 mcg vs. placebo did show significant differences (Table 2) in terms of sexual arousal rate. These two groups also showed significantly higher scores in the areas of sexual satisfaction with overall sex life as well.⁵

There were significant differences in all measured areas of the FSFI when comparing the 900 mcg group to placebo. These included desire, arousal, lubrication, orgasm, satisfaction, and pain. This trend also held true for the FSDS score as well. Sexual satisfaction was measured with the GAQ which resulted in a significant increase in all 3 dose groups when compared to placebo.⁵

Adverse events were reported as well throughout the study groups. The most frequent adverse events included genital burning, itching, swelling, irritation, or soreness which were mostly all rated mild or moderate in intensity. These adverse events were highest in the 900 mcg group, similar in the 500mcg and 700 mcg group and lowest in the placebo group. Five of the patients withdrew due to adverse events.⁵

DISCUSSION

The data and results of both studies^{5,12} analyzed showed that topical alprostadil is indeed a possible treatment in treating women with FSAD. Both of the studies demonstrated a positive response in the measured outcomes of sexual arousal rates and sexual satisfaction by the participants. This was confirmed by the use of FSDS and FSFI which are both reliable and valid measures of female sexual dysfunction, which demonstrated increased rates of sexual satisfaction and arousal, rated by participants. Both of these rates were linked

most significantly to the administration of the higher dose of alprostadil, 400 mcg in the Heiman et al¹² and 900 mcg in the Liao et al.⁵ Thus, indicating a dose related response gradient.

Both studies^{5,12} alluded to the physiological response of the female body to alprostadil, but in different ways. It has been postulated that alprostadil increases intracellular cyclic adenosine monophosphate (cAMP) and activation of protein kinase A resulting in vasodilation. ¹ Heiman et al¹² found this to be indeed true as observed by the raters of increased erythema and edema with the use of the alprostadil vs. placebo and in subject reports of sexual arousal and satisfaction. Liao et al⁵ echoed this information; however, he postulated that due to an increase in subjective reports of sexual satisfaction, which differed from reports of women who have tried to use sildenafil, which has been physiologically proven to be a vasodilator in men, then there must be another action of alprostadil that needs further study. They reported that other studies have suggested the influence on neurotransmitters or reflexes via chemoreceptors. Sun et al⁷ took this theory to the next level when they applied alprostadil to the vagina of rats. Their study showed significantly increased expression of oxytocin-immunoreactive (OT-IR) cells and c-fos-immunoreactive (c-fos-IR) cells in the paraventricular nucleus of the hypothalamus (PVN) which supports the

theory discussed in the Liao et al study,⁵ suggesting alprostadil's potential action on the genital nerve terminals signaling the brain.⁷

Whenever a new medication such as alprostadil is proposed, benefit vs. harm is always an important decision in its practical use. First of all, topical alprostadil is a local application, and thus, will most likely avoid many side effects which are associated with a systemic delivery method for the medication. ¹ Both studies^{5,12} looked at adverse events and the safety of topical alprostadil and both found it to have minimal adverse side effects. Most frequently reported adverse event in the Liao et al⁵ was irritation and signs and symptoms at the application site such as burning, itching, swelling, irritation and soreness. These reported signs and symptoms were very similar to the most commonly reported by the Heiman et al study¹² participants as well which included genital erythema (18% of subjects), genital edema and genital burning. Additionally, there seems to be a dose related response in terms of adverse events, which was seen in both studies^{5,12} with the larger amounts of alprostadil (400 mcg and 900 mcg) reporting the highest number of adverse events. However, as stated in the results, no patients in the Heiman et al¹² stopped due to adverse events, but 5 patients withdrew from the Liao et al study⁵ due to adverse events and those patients were either in the 700 mcg or 900 mcg group. However, 5 patients dropping out in a large study is

not significant if the benefits are indeed present for most people. Also, interestingly in the Heiman et al study,¹² overall ratings of comfort of the application did not differ significantly between the treatment and placebo groups; thus it was tolerated well by both groups.

When analyzing the subject demographics in both studies,^{5,12} there are a lot of similarities between the subject groups in terms of FSFI scores and mean ages, especially for the Heiman et al study¹² who only looked at postmenopausal or hysterectomized women. Also, Liao et al⁵ and Heiman et al¹² both included patients whom had FSAD. Neither study distinguished between patients who may be diagnosed with a subcategory of FSAD. Thus, one must take into consideration the similarity of each of the groups who were studied. Also, in the Heiman et al study,¹² most of the women were white (79%) and in the Liao et al study,⁵ most women were Han (up to 89% of the group). This makes sense due to the location in which both the studies were conducted and their mean ethnic population. However, it must be considered that some cultures have differing views on sex, and especially when it comes to satisfaction and arousal that women experience during sex. Sexual expectations and norms also differ across cultures and different parts of the world as well. Thus, this should be taken into consideration when analyzing the data from each of the studies.

Measurement of outcomes and design of the studies also varied and made for interesting influences on outcomes as well. Such as, Heiman et al¹² applied the topical medication to the women in the clinic and visually studied the erythema, vasocongestion, lubrication, etc. They did state that they chose to use this subjective method rather than using vaginal photoplethysmography, which utilizes a vaginal probe, because they were more interested in studying the subjective assessments such as sexual arousal and sexual satisfaction. However, this method of utilizing subjective questionnaires and clinical judgment may have affected the outcomes to some extent.

Conversely, the Liao et al study⁵ took a differing approach of having patients apply the medication to themselves, which potentiates risk and differences between groups. Even though allowing patients to apply the medication themselves, at home, and engaging in sexual activity with their monogamous partners, may have provided the best practical data for subjects since most patients whom may want to use this treatment are more likely to be engaging in sexual intercourse in their natural environments as opposed to the medical clinic.

Lastly, psychological factors play a role in every study. Due to the nature of FSAD, which may be partially psychological, the expectation to be treated may explain why there was a significant improvement from baseline for the majority of measured outcomes for

the placebo groups in addition to the treatment groups. This especially holds true for the Heiman et al study¹² which was a crossover study, thus subjects knew they would be treated at some point. In terms of efficacy of the medication itself, this may skew results. On the other hand, in terms of practical application of topical alprostadil, one must take into consideration if this really matters when it comes to treating patients. If they are getting positive results with few negative side effects, it may be a viable option for many individuals.

Further study is needed to give a more definitive answer to the question whether topical alprostadil is a beneficial treatment for women experiencing FSAD. Research potential is vast for studying and treating female sexual dysfunction in general. More research should be conducted on all the female sexual dysfunction subcategories, different groups of sexuality such as homosexual, bisexual, and other members of the LGBTQ community. Also, there should be further research on women on hormone replacement or utilizing differing birth control methods and the effect of the treatment and the differing androgens with and without the use of alprostadil. An ideal study would include all of these populations and perhaps result in getting to the root of the female sexual cycle and where the dysfunction is first resulting, making it easier to direct treatment and perhaps provide further understanding about female sexual dysfunction as a whole.

CONCLUSION

Topical alprostadil shows great potential and is a viable option for the treatment of FSAD. Due to its studied efficacy and low to moderate adverse events reported, it is a very plausible, easy to use option for women who continually experience such a disabling disorder. There needs to be much more research on this medication as well as other alternatives for women who cannot tolerate the minimal side effects or who do not want to apply a topical cream prior to sexual intercourse. Either way, there needs to be much better screening in the medical world and awareness that these disorders do indeed exist and that there are a number of women who may be aware that they do not have to feel distressed or place their overall health, personal relationships, and personal well-being at risk. Overall, treating with alprostadil is a very suitable option for most suffers of FSAD and a potential treatment for other aspects of FSD as a whole.

References

1. Goldstein SW, Gonzalez JR, Gagnon C, Goldstein I. Peripheral Female Genital Arousal as Assessed by Thermography Following Topical Genital Application of Alprostadil vs Placebo Arousal Gel: A Proof-of-Principle Study Without Visual Sexual Stimulation. *Sex Med.* 2016.
2. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA.* 1999;281:537-544.
3. Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol.* 2008;112:970-978.
4. Imbimbo C, Gentile V, Palmieri A, et al. Female sexual dysfunction: an update on physiopahtology *The Journal of Endocrinological Investigation.* 2003;26:102.
5. Liao Q, Zhang M, Geng L, et al. Efficacy and safety of alprostadil cream for the treatment of female sexual arousal disorder: a double-blind, placebo-controlled study in chinese population. *J Sex Med.* 2008;5:1923-1931.
6. Berman JR, Berman LA, Toler SM, Gill J. Safety and Efficacy of Sildenafil Citrate for the Treatment of Female Sexual Arousal

- Disorder: A Double-Blind, Placebo Controlled Study. *The Journal of Urology*. 2003;170:2333.
7. Sun X, Xu L, Zhang J, Guo F, Tang M. The Effects of Alprostadil on Hypothalamic and Amygdalar Function and the Central Expression of Oxytocin: A Potential Central Role of Alprostadil Cream. *J Sex Med*. 2009;6:81-90.
 8. Levine SB. *Sexual Life: A Clinician's Guide (Critical Issues in Psychiatry)*. New York, NY: Springer, 1992.
 9. Basson R. Human Sex-Response Cycles. *J Sex Marital Ther*. 2001;27:33-43.
 10. Kielbasa LA, Daniel KL. Topical alprostadil treatment of female sexual arousal disorder. *Ann Pharmacother*. 2006;40:1369-1376.
 11. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924-926.
 12. Heiman JR, Gittelman M, Costabile R, et al. Topical alprostadil (PGE1) for the treatment of female sexual arousal disorder: in-clinic evaluation of safety and efficacy. *J Psychosom Obstet Gynaecol*. 2006;27:31-41.

Table 1: Quality Assessment of Reviewed Articles									
Outcome	Number of studies	Study Designs	Downgrade Criteria					Upgrade Criteria	Quality
			Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		
Sexual Arousal Rate	2	RCT	Not Serious	Not Serious	Not Serious	Serious ^a	Not Serious	Dose-Response Gradient	High
Sexual Satisfaction	2	RCT	Not Serious	Not Serious	Not Serious	Serious ^a	Not Serious	Dose-Response Gradient	High

^aSmall sample size

Table 2. Summary of Findings Liao et al, 2008⁵					
Efficacy Endpoint		Placebo	500 mcg	700 mcg	900 mcg
Patient sexual arousal satisfaction rate, Entire treatment period-screening period, mean (SD)	Score	22.63 (32.70)	36.67 (38.44)	34.01 (39.21)	44.29 (39.66)
	<i>P</i> value		0.0224	0.0358	0.0002
FSFI, Total, Mean (SD)	Score	14.68 (20.36)	20.71 (17.91)	21.69 (17.95)	22.89 (19.77)
	<i>P</i> value		0.067	0.035	0.002

Abbreviations: Female Sexual Function Index Score Changes (FSFI), Standard Deviation (SD)