

EFFECTIVE OFFICE PROTOCOL SYSTEM
FOR DELIVERY OF TESTOSTERONE INJECTIONS
TO FEMALE PATIENTS WHO FIT THE CRITERIA
OF HYPOACTIVE SEXUAL DESIRE DISORDER
AS STATED IN THE DSM-IV-TR

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ABSTRACT

OBJECTIVE: The purpose of this dissertation was to find a standard protocol for delivery of testosterone to women who came to a medical practice seeking relief from symptoms that are indicative of the DSM-IV-TR definition of Hyposexual Desire Disorder. **QUALITY OF EVIDENCE:** Literature documenting that replacement of physiological levels of testosterone is beneficial and safe are scant. The journal articles searched contained the most literature on menopausal women. The testing and research is being done on this group more than any other. An underserved group is the women who are age 35 to menopause. They were the women in this study. They present to medical practices with complaints of low sexual desire. Trying to find a way to separate those who truly have a deficiency versus others is difficult because there is no standard. A test that could be used in a clinical setting that identifies women with low sexual desire disorder is the Brief Index of Sexual Functioning for Women (BISF-W). It was used in this study. It confirms the self-report of women with the scoring dimensions used for desire and sexual function. Blood assay test were also used for free and bound testosterone levels. Protocols were explored from printed literature and contacts with researchers. **CONCLUSION:** There is no standard or criteria for the treatment of women with testosterone to relieve the symptoms of low desire levels. The FDA has not approved any testosterone therapies for women. There is a committee of international scientists who is looking at ways of framing this for treatment. Until then, the physician and other trained specialist will have to come to do what they think is best for their patients.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

VITA

ABSTRACT v

TABLE OF CONTENTS vi

LIST OF TABLES viii

Chapter

1. LITERATURE REVIEW 1

 Introduction 1

 Types of Women Studied 1

 Menopausal 2

 Perimenopausal 3

 Protocols 4

 Criteria 6

 BSFI-W 6

 Blood Assay Test 7

 Summary and Criticism 7

 Statement of Research Problem 8

2. METHODOLOGY 9

 Screening of Patients 9

 Group with Case Studies 10

 Patients #001-#015 12

3. DISCUSSION	25
Introduction	25
Laboratory Testing	25
Office Sexual Assessment and History	26
Written Assessment Tests	29
BSFI-W	29
ASEX	29
Protocol Suggestions	30
The Future	31
SELECTED BIBLIOGRAPHY	33
Appendices	
1. SEXUAL FUNCTIONING ASSESSMENT AND HISTORY	36
2. BRIEF INDEX OF SEXUAL FUNCTIONING FOR WOMEN	37
3. SCORING RANGES AND DIMENSIONS FOR BISF-W	41
4. INSTRUCTIONS FOR TESTOSTERONE ADMINISTRATION	45
5. ADULT CONSENT FOR OWN PARTICIPATION	46
6. QUESTIONS ASKED BY DE-BRIEFER AT END OF STUDY	47
7. CURRENT PHARMACEUTICAL APPROACHES FOR TREATMENT OF WOMEN WITH FADS AND ANDROGEN-RELATED FEMALE SEXUAL DYSFUNCTION	48

CHAPTER 1

LITERATURE REVIEW

Introduction

Articles were surveyed from several professional journals in the fields of obstetric, gynecology, women's health, geriatrics, endocrinology, metabolism, sex education, marital therapy, reproductive medicine, fertility and psychosomatic medicine. Textbooks from pharmacology, obstetrics and gynecology, endocrinology and fertility were used. The DSM-IV-TR was used as a reference.

Types of Women Studied

The articles fell into three categories of women studied. The first group is the menopausal group, both natural by age and surgical. The second group is perimenopausal, those women who are in the age range of 35 until cessation of the menses for at least one year. A third group, with several different medical interventions, was being studied with testosterone as a component of the research. The articles reviewed women who had breast cancer and the effects of the powerful drugs taken for chemotherapy. There was a study on the Aids Wasting Syndrome (AWS) in women and the treatment modalities involved using testosterone. The study on vascular reactivity was using estrogen and androgens to see what type of positive effect the combination would have on arteriole health. The acne study discussed the amounts of androgens in women with different levels of problematic acne. Since the focus of the last group of studies was not to treat low sexual desire dysfunction, they were not used to find a protocol

Menopausal

The postmenopausal state is characterized by an absence of ovulation and a reduction of ovarian estrogen secretion. It is associated with several disturbances, including vasomotor flushes, atrophic vaginitis and osteoporosis. This can be as a result of age-related menopause or surgical menopause. If it is by age, there is a cessation of menses for one year. Removal of the ovaries places a woman no matter what her age into menopause. The Helgason et al. study looked at the effect estrogens had when given to post-menopausal women. It was looking to see if it lowered the androgen production. Suppression was detected. They concluded that estrogens inhibit the adrenal cortex. One of the areas where testosterone is made is in the adrenal glands. When the ovaries stop making estrogen at menopause, there is more testosterone available for the woman.

A recent article by Simon et al. looked at the bioavailability of protein bound and free androgens during three months of therapy with estrogen and androgens or matched estrogen only therapy in postmenopausal women. Another research group stated that “routine estrogen replacement substantially decreases free testosterone (49%)”. (Slater et al. 2001)

The Shifren et al. study did use a group of women ages 31 to 56 to test a transdermal testosterone patch in women who had impaired sexual function. The group had undergone oophorectomies and hysterectomies as well as receiving conjugated estrogens. The use of both laboratory and psychological tests provide a more complete understanding of a woman's impaired sexual functioning level.

The Watts study discussed the effects estrogens and androgens had on bone mineral density, menopausal symptoms, and lipid-lipoprotein profiles. It was most concerned with what estrogens do to the hepatic system. There were other studies with menopausal women as subjects and the effects of sex steroids on their sexual functioning. One from Sweden actually

discussed the psychological reactions and sexual life of women who had had hysterectomies with and without oophorectomies. (Boos & Schoultz 1992)

The ground breaking Sherwin et al study is cited in many of the journal articles read. It was done in 1985 but still has implications for today. It comprehensively defined the use of androgens for sexual motivation of menopausal females. The use of intramuscular injections was used. Researchers also drew blood plasma levels to determine a baseline for testosterone levels of each woman. The results demonstrated the positive effects of androgen with this group of women.

Perimenopausal

Less research is being done on this group of women. Around age 35 women start to have fluctuations in their testosterone levels until they reach menopause. There is also evidence that the ovaries fluctuate in their production of estrogen. Dr. Barbara Levy, a contributing editor for OBG Management, reported the number of women in this group who had low levels of desire was 40%. The article discussed various ways of incorporating sexual assessments into a practice to serve this group. She cites areas of assessment that are worth consideration. The model of inquiry with a patient in an OB-GYN practice was detailed. The four areas needing to be considered were physical, psychological, relational, and situational. Her sexual assessment patient information form was extremely useful in covering these areas. It is used in this protocol study. (Appendix 1) It was modified for use in this study.

An article by DeCherney summarizes many of the current findings and studies about androgen replacement with this group. He gives a comprehensive literature review having to do with androgen replacement for women. He states:

Although positive results have been shown in these well-designed studies, it should be noted that there are no standardized methods to measure libido in women. Libido is a complicated end point that may be affected by both hormonal and nonhormonal factors,

making it difficult to establish standardized controls. Because the outcomes and end points are subjective, it is difficult to formulate concrete objective conclusions. However, we do know that there are androgen receptors in the brain, and there is inferential evidence suggesting that testosterone administration may increase libido in women with this problem. Much of this is confirmed by data derived from studies in animals and inferential material generated in studies on women. (DeCherney 2000)

It is important to remember that before the Waxenberg study in 1959 there was very little being tested for women in this area, either in research or clinical practice. It is an under served group.

The Saks article was noteworthy because of the development of the sex receptor theory. “Sexual desire is a psychosomatic process that relies on brain activity for its generation and cognitive scripting for aspiration and motivation” (Saks 1999). The article explains the different effects medications have on testosterone production. It lists many of the currently prescribed medications for depression and anxiety. Davis makes many good points about the fact that testosterone levels fall during the reproductive years. And in fact that unless the woman has had an oophorectomy there is little change at menopause. She also reports:

The biological availability of testosterone is determined by levels of SHBG; therefore the administration of exogenous estrogens, which increase SHBG, may precipitate relative androgen insufficiency. Specifically, synthetic estrogens in the form of oral contraceptive pills or estrogen given for hormone replacement therapy have been found to suppress circulating free testosterone levels. (Davis, 1998)

The perimenopausal group in this protocol study fits this profile.

Protocols

Even though there is not evidence of a global or generalized protocol for delivery of testosterone to women for lack of libido, several articles talked about what physicians did in their clinical setting. Dr. John Lamont who has a sexual medical clinic in Winnipeg, Canada, screens his patients by both laboratory test and interview. He uses the test levels of free testosterone in

the lower normal range especially if the patient has decreased fantasy and desire levels for sexual interaction. His dosage is 25-100 mg. intramuscularly every three to four weeks. There is also available an oral dose as well as a testosterone ointment for use on the labia. Testing of testosterone levels every three months is advised so that there are no virilizing effects.

Davis (1998) explores the different types of androgen treatments available for women in Australia and Great Britain. There is also information about testosterone given intramuscularly at a dose of 50-100 mg. at four to six week intervals in a study she reviewed.

Kaplan and Owett's article was excellent. It dealt with Female Androgen Deficiency Syndrome (FADS). They studied 11 women who had hysterectomies with bilateral salpingo-oophorectomies or chemotherapy with cytotoxic drugs. Their testosterone levels were 10ng/ml or less, this was considered low. They also had another group of women comparable in age, medical, marital, sexual and menopausal histories. Their testosterone levels were 30ng/ml or higher, this was considered normal.

Comparing the two groups there was a discovery that FADS also mimics the same symptoms of low libido or Hypoactive Sexual Desire Disorder (DSM-IV-TR). The only difference is that the women who had had cancer therapy and hysterectomies with oophorectomies had some type of medical procedure that preceded the drop in testosterone levels. When given androgen replacement in the form of testosterone there was restoration of their sexual functioning level. Kaplan also tells us "androgen replacement for women is a neglected area of medicine. None of the standard textbooks of medicine, endocrinology, clinical pathology or pharmacology which we reviewed made any mention of androgen deficiency in women, although the signs and symptoms of the virilizing effects of excessive androgens in females were cited in all." (Kaplan, Owett, 1993).

The same was found to be true in a search of textbooks in the same areas as indicated in the opening sentence by this author's literature search. Kaplan and Owett suggest that in order to receive a benefit but not the virilizing effects of androgens it should be 1/10 of the dose given to hypogonadal men. The standard treatment for treatment of hypogonadal adult men is 5mg. per day. (Mazer, 2000) The research by Mazer and other articles read say 1/20 of the androgen given to hypogonadal adult men. Another article by Mazer (2002) reviews all the pioneering studies that have addressed androgen therapy with women and its current status. Female Androgen Deficiency Syndrome (FADS) first discussed by Kaplan and Owett, has now become the focus of a conference of international experts who are attempting to define the clinical and laboratory criteria for its diagnosis. A standard protocol for giving androgen to women with impaired sexual desire is needed. The article gives a list of preparations now used and their doses. (Appendix 7) It also looks at the pharmaceuticals now being developed. A dermal patch looks to be the next new therapy.

Criteria

BISF-W

Reading text and articles for this paper the Brief Index Sexual Functioning for Women (BISF-W) test seemed to be used by several researchers for the testing of their subjects having to do with low sexual desire. It was originally for clinical trials of large numbers of patients. It went through several revisions before the current test was made. Other tests were very lengthy and focused on several areas not being explored in this research for protocol.

BISF-W (Mazer, Leiblum, Rosen) was originally developed to test women who were healthy and in the age group of this protocol study. It had also been developed for use in clinical trials. It had 22 questions with each of these representing different dimensions having to do with sexual functioning. (Appendix 2) It could be used in an office setting that would have the ease of

knowing the score quickly and have another example of what the patient was experiencing. It was used to show that what the self report of the women in the protocol study said was reinforced by their test scores. If they scored below 21 they were in the low range. The scoring computation tables are shown at the end of this paper. (Appendix 3)

Blood Assay Test

Each patient in the study had to take a blood assay test for testosterone levels. There were four laboratories that were used, only because the patient's insurance company chose the one they would pay for. The patients were being tested for:

total testosterone levels

free testosterone levels

free and weakly bound testosterone levels

albumin

SHGB (this was not always a part of the test)

These hormones are indicative of what level a women has in her system to support the sexual drive. They are not the same for each women because some can have a normal range and report low sexual desire. There is usually a reference range with each test. If a patient is in the normal or low normal range she was allowed to be in this study. Several researchers such as Davis rely on this same criteria. Others like Mazer use a formula that takes all these hormones and weights them for bioavailability.

Summary and Criticism

All the articles read were very helpful in expanding the knowledge of the medical aspects of women's impaired sexual functioning. Much research going on with regards to menopausal women and is usually funded by the pharmaceutical companies who produce estrogen. Androgen use in menopausal women was also researched, some in correlation with estrogens. Again these

were funded by the pharmaceutical companies who were developing some type of treatment with both androgen and estrogens. There were articles in journals like Journal of Sex and Marital Therapy that addressed aspects in the psychosexual area, but very little literature in other publications. There seems to be more articles from outside the United States. Finding protocols was more difficult. There is no prescribed treatment for women using androgens to alleviate impaired sexual functioning. The Federal Drug Administration (FDA) has not approved any administration of testosterone treatment for women.

The small amount of literature about this subject must have to do with the lack of demand by women or their lack of focus on their need for treatment. Tailoring a program for each woman who has this problem can be done, but it is only through the efforts of a staff of trained professionals. The cost would be prohibitive. Most of these studies were done in huge university settings with unlimited patients and personnel available. A better diagnosis criteria that is a standard would help. Managed health care will not allow this unless women demand it. Or as one of the respondents said, "I thought I just had to put up with this."

Statement of Research Program

Can delivery of testosterone in a controlled medical setting assure relief of symptoms that meet the criteria for lack of sexual desire as stated in the DSM-IV-TR for female patients seeking improved sexual functioning?

302.71 DSM-IV-TR: Hypoactive Sexual Desire Disorder: Persistently or recurrently deficient (or absent) sexual fantasies and desire for sexual activity. The judgment of the deficiency or absence is made by the clinician, taking into account factors that affect sexual functioning, such as age and context of the person's life. There is evidence from the history, physical examination, or laboratory findings that sexual dysfunction is fully explained by the direct physiological effects of the general medical condition.

CHAPTER 2

METHODOLOGY

Screening of Patients

As part of each new and returning patient's annual examination in this private obstetrics and gynecological practice, a set of questions having to do with the patients sexual functioning is asked. If there are problems further inquiry is done as to the nature of the problem. If the patient complains of lack of desire, a sexual history assessment is done. (Appendix 1). There were always therapy interventions introduced to the patient by the medical staff at that time. For this protocol study if the patient fell within the criteria for the DSM-IV-TR definition of Hypoactive Sexual Desire they are offered serum screening for normal, free and bound testosterone levels. If they fall below the lower normal range or lower they are offered testosterone therapy.

For this protocol study, only those patients who wanted the intramuscular (IM) were used. At the time they are told of the side-effects are of this type of testosterone therapy. (Appendix 4) They were also asked to sign a release form if they wanted to be part of this study. (Appendix 5) The patient is given a prescription, from the physician, for testosterone to take to her pharmacy. She is told to bring it back and she will be given a written BISF-W test and receive her injection. A telephone call from the on staff sex therapist furthers the screening process. Patients excluded from the study were: Any patient having major depression, problems, involved with physical or sexual abuse, drug abuse, or divorce.

When the patient returns to the office she is given the BISF-W test. After taking the test, she is given her first injection of testosterone. She is again told if she has any problems to call immediately. Her vial of testosterone is kept in a safe area with her patient number and name on it. She is the only patient using that substance. First injection is 200 mg. IM and it is noted on her chart as to time and date. Topical creams and the oral testosterone tablets were rejected for this protocol study because of the 'forget factor'. "Forget when the pill was taken and forget when the cream was used." The absorption level of the cream was not known for each patient and is hard to control the dosing. They are offered at this practice but these patients were the ones who wanted the testosterone injections. The patients are set up on a three-month return schedule. At that time they are evaluated and either the dose is the same or is reduced. A nurse gives the patient the BISF-W test in an empty office. The patient is told to not put her name on the test. It has her patient number on the top of the test. When she is finished she places the test in a large manila envelope and leaves it on the desk. She is asked to sign a patient consent form (Appendix 5). She is given a copy. At that time she would then be given her injection of testosterone. She is told that all this information will be kept confidential and if she has any problems to please call the office and someone will answer her questions.

Group with Case Studies

There were 15 patients initially. Three dropped out and two did not start the therapy. The age of this group was 27-45 when we started in 2001. All were married. All had children. Two were taking medications for thyroid disease. None of them smoked or had had cancer. All of them had a normative functioning sex life until the onset of the loss of sexual functioning. Five had taken oral contraceptives. Three had partial hysterectomies with ovaries intact. Each was de-briefed in person by the staff sex therapist. Two had to be debriefed over the telephone. The following are their case studies and findings with anecdotal comments. The test results of the

pre-test before the injection of testosterone is shown. The laboratory analysis is shown with the reference range that is used for that test. There is also a list of the debriefing questions asked verbally by the staff sex therapist about the protocol and the patient reactions. (Appendix 6)

PATIENT: 001

AGE: 34

ANNUAL EXAM: 07/18/02

CHIEF COMPLAINT: Low sexual desire

LMP: 06/20/02 - Not pregnant

LAST PAP SMEAR: 07/02

CONTRACEPTION: None

MEDICATIONS: None

ALLERGIES: Dogs and dust

PREGNANCIES - 2 LIVE BIRTHS - 1 C-SECTIONS - 1

Recent desire change

Pain during intercourse - not noticed

Arousal - difficult

Orgasmic - yes

Sexual desire last month - low

Frequency of intercourse - two times per month.

Reported orgasm was 50% of the time.

Does not smoke or drink.

Changes in: Had a change in sleep habits and weight gain.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: C-section - 3/2001

Total testosterone: 31 Reference range: 20-76

Free testosterone: 4 Reference range: 1-21

(Free testosterone in the low level)

BISF-W score: 3.44 - also considered low. (Taken 7/18/02)

First shot of testosterone was given 08/13/02. Signed consent form for study and then moved out of state because of husband's job, 10/02. Patient discontinued in study.

PATIENT: 002

AGE: 40

ANNUAL EXAM: 09/27/02

CHIEF COMPLAINT: Low sexual desire

LMP: 09/15/02 - Not pregnant

LAST PAP SMEAR: 06/02

CONTRACEPTION: Tubal ligation

MEDICATIONS: Vitamins

ALLERGIES: None

PREGNANCIES - 4 LIVE BIRTHS - 4 C-SECTIONS - 0

Recent desire change

Pain during intercourse - not noticed

Arousal - normal

Orgasmic - yes

Genitals - some dryness in genital area

Sexual desire last month - very low

Frequency of intercourse - seven times per month.

Reported orgasm was 50% of the time.

Does not smoke or drink.

Changes in: Had a change in fatigue level, very fatigued.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: Tubal ligation - 6/90, vaginal hysterectomy and AP repair - 10/22/02.

Patient's total testosterone levels were not sent over with records from last physician. She started testosterone treatment with that physician on 06/01/02.

First injection: 06/01/02 - 200 mg IM

Second injection: 10/01/02 - 200 mg IM

Third injection: 02/13/03 - 200 mg IM

BISF-W score: 14.1 - considered low. (Taken 9/27/02)

She reported that she felt a heightened sense of sexual desire and frequency of intercourse increased, but it took three weeks before she felt the effects. It lasted more than one week. She feels a sense of well-being and has high energy levels. No side-effects from this treatment. The stressors in her life would be that she has a mentally ill son, who is sixteen-years old and violent. He is currently living outside the home. She is receiving counseling for this family problem. Patient's husband is not the father of this son, but is supportive of her and their relationship is good at this time.

PATIENT: 003

AGE: 46

ANNUAL EXAM: 07/03/02

CHIEF COMPLAINT: Low sexual desire

LMP: 12/01 - Not pregnant

LAST PAP SMEAR:

CONTRACEPTION: None

MEDICATIONS: Celexa, Prevacid, Mycelex, Premarin

ALLERGIES: Lactose and Codeine

PREGNANCIES - 3 LIVE BIRTHS - 3 C-SECTIONS - 0

Recent desire change - 02/02

Pain during intercourse - not noticed, but uses lubricants

Arousal difficulties - normal

Orgasmic - yes

Sexual desire last month - absent

Frequency of intercourse - two times per month.

Reported that she is always orgasmic.

Does not smoke or drink.

Changes in: Had a change in sleep habits, mood, and weight gain.

Weight has always been a problem for her.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: vaginal hysterectomy - 12/01 (ovaries intact).

First injection: 08/01/02 - 200 mg IM, Depo-Testosterone

Second injection: 11/21/02 - 200 mg IM, Depo-Testosterone

Third injection: 02/13/03 - 200 mg IM, Depo-Testosterone

Free testosterone: None could be tested.

BISF-W score: 33.975

Patient has three teenagers in family. Stressor level is high. Patient reports that after her first injection it took three to four weeks for effects. Patient had two or three days of high sexual desire. Side effects of some facial hair. After second injection of testosterone the effects wore off quickly. Patient just had third injection. This patient had testosterone treatment in 2001 and had much better success with the injections at that time. Same level of injection. No perceptible reason for this noted at this time.

PATIENT: 004

AGE: 45

ANNUAL EXAM: 06/24/02

CHIEF COMPLAINT: Low sexual desire

LMP: 06/15/02 - Not pregnant

LAST PAP SMEAR: 03/07/02

CONTRACEPTION: Husband had vasectomy.

MEDICATIONS: None

ALLERGIES: Sulfa drugs

PREGNANCIES - 6 LIVE BIRTHS - 2 C-SECTIONS - 2

Recent desire change - one year ago

Pain during intercourse - none

Arousal - normal

Orgasmic - most of the time

Genitals - dry and experienced during intercourse

Sexual desire last month - low

Frequency of intercourse - three times per month.

Reported orgasm was 75-80% of the time.

Moderate drinker. Does not smoke.

Changes in: Had a change in moods.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: C-section - 1984 and 1997, BTL - 1990, tubal reversal - 1995.

Total testosterone: 38 Reference range: 28-76

Free testosterone: 8 Reference range: 1-27

(Free testosterone in the low level)

BISF-W score: Not taken and did not take testosterone.

Reported past sexual violence and so referred for counseling.

PATIENT: 005

AGE: 33

ANNUAL EXAM: 08/16/02

CHIEF COMPLAINT: Low sexual desire

LMP: 08/05/01 - Not pregnant

LAST PAP SMEAR: 06/27/02

CONTRACEPTION: Patch

MEDICATIONS:

ALLERGIES:

PREGNANCIES - LIVE BIRTHS - C-SECTIONS -

Recent desire change - no desire change

Pain during intercourse - yes

Arousal -

Orgasmic - non-orgasmic

Genitals - burning after intercourse because she is not sufficiently lubricated.

Sexual desire last month - very low

Frequency of intercourse - 3 times for the entire month and not willingly.

Does not smoke or drink.

Changes in: No change in sleep habits, although she only gets six hours of sleep by choice.

Weight gain due to the recent birth of baby.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: None

Total testosterone: 39 Reference range: 20-76

Free testosterone: 7 (low) Reference range: 1-21

BISF-W score: 12.14

First injection - 09/12/02

Second injection - 03/10/03

Patient presented with low desire levels very early on in her marriage. I did premarital counseling with this couple. She continues to have painful intercourse. She and her husband only have intercourse three times a month, unwillingly. They are currently in counseling with me for that problem. This patient is not responding to the testosterone treatment. My recommendation would be that she and her husband continue with counseling to resolve some of the issues that they are dealing with pertaining to their marriage and the stressors that this lack of sexual desire has on the couple.

PATIENT: 006

AGE: 30

ANNUAL EXAM: 08/09/02

CHIEF COMPLAINT: Low sexual desire

LMP: 08/04/02 - Not pregnant

LAST PAP SMEAR: 07/11/02

CONTRACEPTION: Nordette

MEDICATIONS: Levoxy for hypothyroidism, Serafin, 20 mg

ALLERGIES: NKDA

PREGNANCIES - 2 LIVE BIRTHS - 2 (youngest child, 21 months) C-SECTIONS - 0

Recent desire change - reported that she really hasn't had any desire over her lifetime

Pain during intercourse - no

Arousal - normal

Orgasmic - can be

Genitals- no problems as far as lack of lubrication

Sexual desire last month - absent

Frequency of intercourse - 3 times a month

Orgasmic 100% of the time.

Does not smoke or drink.

Changes in: no change in sleep, appetite, or weight.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: none

Total testosterone: so low they were not able to perceptively garner any of it for the test. The reference range is 20-76 and hers was less than 20.

No free testosterone could be detected.

Reference range is 1-21.

BISF-W score: 13 (low)

First injection - 08/12/02 200 mg

Second injection - 01/12/02 200 mg

Third injection - 02/13/03 200 mg

She reports the testosterone is having no effect on her at all. She feels no drive or sexual interest after the testosterone injections. This person may be a candidate for the female androgen deficiency syndrome study and should be referred out for testing. My recommendation would be that she seeks medical advice from an endocrinologist to see if there is something else going on with the lack testosterone that she has in her system.

PATIENT: 007

AGE: 37

ANNUAL EXAM: 09/04/02

CHIEF COMPLAINT: Low sexual desire

LMP: Unavailable - Not pregnant

LAST PAP SMEAR: 11/26/01

CONTRACEPTION: Yasmin

MEDICATIONS: Synthroid and Zoloft

ALLERGIES: Sulfa drugs

PREGNANCIES - 1 LIVE BIRTHS - 1 C-SECTIONS - 0

Recent desire change - none.

Patient has always had low desire.

Pain during intercourse - none

Arousal - normal

Orgasmic - yes

Genitals - some discharge and itching after intercourse

Sexual desire last month - absent

Frequency of intercourse - two times per week

Reported orgasm was 80% of the time.

Does not smoke. Drinks moderately.

Changes in: Change in sleep habits, appetite, mood, and weight.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: none

First injection: 07/29/02

BISF-W score: 4252 does not have low desire, but her free testosterone is below the level for testing.

Total testosterone: 20 (low) Reference range: 20-76

Patient's first injection made her very hungry, acne increased (adult acne). The effects of it lasted one week, but it took three weeks to take effect. Patient did feel an increase in desire. She has taken birth control pills for seven years prior to her pregnancy. The stressors in her life include her husband, who is a professional athlete. She frequently travels with him and has a three-year old. Patient has decided to discontinue injections of testosterone in order to get pregnant again.

PATIENT: 008

AGE: 33

ANNUAL EXAM: 05/03/02

CHIEF COMPLAINT: Low sexual desire

LMP: 04/26/02 - Not pregnant

LAST PAP SMEAR: 09/26/01

CONTRACEPTION: Husband had vasectomy

MEDICATIONS: Provera

ALLERGIES: Sulfa drugs

PREGNANCIES - 3 LIVE BIRTHS - 2 C-SECTIONS - 0

Recent desire change - since 1999

Pain during intercourse - none

Arousal - normal

Orgasmic - yes

Genitals - dryness in genital area when having intercourse

Sexual desire last month - low

Frequency of intercourse - two times per week

Reported orgasm was 80% of the time.

Does not smoke. Drinks moderately.

Changes in: no change in sleep, appetite, mood or weight

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: none

First injection: 05/03/02

BISF-W score: Did not want to take

Total testosterone: 14 (low) Reference range: 15-70

Free testosterone: 1.60 Reference range: 1-27

Patient was on oral contraceptives for ten years. After her first injection she reported that she did feel an effect from it, but it took one week, not strong. Subsequent injections after that, a three-month interval, she has reported that she felt a desire level that has risen and if her beginning desire level was on continuum from 1-6, one being the lowest and six being the highest, she was at one when she started out with the injections and now is at a four. Continues to have injections, given to her by her friend, not done through the office. This was done because she lost her job, was looking for a job, and this was a more inexpensive way to get the testosterone injections.

PATIENT: 009

AGE: 39

ANNUAL EXAM: 09/24/02

CHIEF COMPLAINT: Very low sexual desire

LMP: 09/24/02 - Not pregnant

LAST PAP SMEAR: 09/11/02

CONTRACEPTION: Barrier method

MEDICATIONS: None

ALLERGIES: NKDA

PREGNANCIES - 2 LIVE BIRTHS - 2 C-SECTIONS - 0

Recent desire change - last three years, none

Pain during intercourse - yes

Arousal - not happening

Orgasmic - never

Genitals -

Sexual desire last month - absent

Frequency of intercourse - none

Reported orgasm was 0% of the time.

Does not smoke. Drinks wine and beer weekly.

Changes in: no change in sleep, appetite, mood, or weight

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: none

First injection: 10/10/02

Second injection: Missed injection due to busy holiday season.

BISF-W score: -5 (very low)

Total testosterone: 26 Reference range: 20-76

Free testosterone: 4 (very low) Reference range: 1-21

The patient states that her family has been in financial problems for awhile. She says her relationship is good but not great. I have referred this patient for marital counseling. I think something else is going on besides the low testosterone level, although she does have a low testosterone level, physiologically.

PATIENT: 010

AGE: 47

ANNUAL EXAM: 04/15/02

CHIEF COMPLAINT: Low sexual desire

LMP: hysterectomy at age 31, but ovaries are intact

LAST PAP SMEAR: 01/25/02

CONTRACEPTION: hysterectomy

MEDICATIONS: Premarin and Zoloft

ALLERGIES: dust, pollen, and fragrances

PREGNANCIES - 2 LIVE BIRTHS - 2 C-SECTIONS - 0

Recent desire change - two years ago, more severe in last six months

Pain during intercourse - yes, suggested use of lubricant

Arousal - not good

Orgasmic - not at all

Genitals - dry, cracking, and burning upon intercourse

Sexual desire last month - absent

Frequency of intercourse - none

Reported orgasm was 0% of the time.

Does not smoke. Drinks moderately.

Changes in: change in sleep and appetite

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: hysterectomy - 1985 with ovaries intact

First injection: 09/11/02

Second injection: 12/09/02 200 mg

Third injection: 02/12/03 100 mg, Depo-testosterone

BISF-W score: 18

Total testosterone: 23 Reference range: 15-70

Free testosterone: Did not test

The patient is a professional banker, who has had an adult daughter return with a baby into her home. Her husband has been very supportive, but the family dynamics have been strained. The patient reported that after her first injection it took one month to take effect, but then had one week of heightened sexual interest and desire in intercourse did increase. After the second injection she explained that her desire level increased and this lasted a shorter amount of time, probably less than one week. Patient reported no side effects after third injection other than some facial hair and that is why the dosage was cut down to 100 mg. It was noted on her chart that she was receiving more estrogen, which is good and will probably help relieve the dryness and cracking in her vaginal area during intercourse. The patient should probably have an FSH test, probably is experiencing the beginning of menopause.

PATIENT: 011

Patient took testosterone testing. Testosterone level was considered low. In talking with the patient, it was recommended that she and her husband have marital counseling because there was probably more going on than just drop in desire.

PATIENT: 012

Patient complained of low desire level. Offered testosterone therapy and initially said she wanted to be a part of the study, but a health crisis in her family precipitated withdraw before her first injection. She did take the BISF-W and actually scored very normal in that test, so she probably would not have been a good candidate for the study.

PATIENT: 013

Patient initially started with testosterone, but did not want to take the test. She was having side effects of acne and facial hair. Patient also needed marital counseling and was referred to marital counseling. I did counseling with her for several months. Her husband also attended counseling sessions and worked with them on other issues having to do with sexual functioning in their marriage. Patient was given sexual function and history assessment and signed the adult consent form, but dropped out because she decided she wanted to get pregnant.

PATIENT: 014

Patient started testosterone therapy. She did not take the BISF-W test Patient was referred to couples counseling and so dropped out of study.

PATIENT: 015

AGE: 42

ANNUAL EXAM: 04/26/02

CHIEF COMPLAINT: low sexual desire

LMP: hysterectomy with ovaries intact - not pregnant

LAST PAP SMEAR: 04/26/02

CONTRACEPTION: hysterectomy

MEDICATIONS: Wellbutrin, Celexa, Adoral

ALLERGIES: NKDA

PREGNANCIES - 2 LIVE BIRTHS - 2 C-SECTIONS - 0

Recent desire change - started about two years ago

Pain during intercourse - none

Arousal - very slow to arouse

Orgasmic - yes

Genitals - no problems

Sexual desire last month -

Frequency of intercourse - two times per week.

Reported orgasm was 100% of the time.

Does not smoke or drink.

Changes in: Had a change in mood swings and medications.

No chronic diseases, STD's, PID, GYN cancer, or breast cancer.

Surgeries: laparoscopic surgery 08/15/02

Total testosterone: 48 Reference range: 20-76

Free testosterone: 4 (low) Reference range: 1-21

BISF-W score: Did not take

First injection - 06/28/01

Second injection - 09/09/02

Third injection - 12/18/02, lowered dose to 100 mg

I did counseling with this patient and have been counseling with her for at least six months. We had her on testosterone injections since she was in the very low range. After her first injection she reported that there was a difference in her sexual desire. After her second injection she reported that she felt very sexual all of the time, but her thoughts and fantasies were about sexual encounters. She and her husband seemed to have reached a period where they have some placidity in their relationship. This patient is struggling with recently losing her job and having to really change her life. The patient is doing very well and finding some direction in her life.

Because of the three different medications that she is on, it is difficult not to see why this would interfere with testosterone since one of the medications is an anti-depressant. She, again, seems to be doing very well. Both of her teenage sons live at home and she is involved in helping them with their school life, as well as some other struggles that they have had, one of them with drugs. This patient has a lot of exciting things and challenges ahead of her, but she seems to be able to take them with good spirit. It was interesting to have her in the study because she was very verbal and gave some good anecdotal material for the testosterone study.

CHAPTER 3

DISCUSSION

Introduction

The purpose of the study was to find an office protocol to relieve the symptoms that are the criteria for the DSM-IV-TR Hypoactive Sexual Desire Disorder. “Sexual desire appears to arise from the interplay of neurocircuits, hormones and psychological factors. The limbic system, hypothalamus, and temporal lobes seem to be particularly important in sexual drive ... the sexual desire phase has no characteristics and readily measurable physiological response pattern.” (Arnett, Prosen & Toews 1986) The ovary produces three classes of sex steroids estrogen, progestin, and androgens. Fifty percent (50%) of testosterone comes from the ovaries and fifty percent (50%) comes from the adrenal glands. Some of the things that affect the levels of testosterone in women are, estrogen preparations and anti-depressive medications.

Laboratory Testing

The first test that was given to each patient in the study was an assay blood test that measures total testosterone. Then that is broken down to the measurement of weakly bound and free. The free testosterone is what is available in a woman's system to fuel her drive to want sex. The problem with this is if there is too much SHBG in the system it binds with the free testosterone that is bioavailable. What causes too much SHBG? Estrogen. A study by Raisz et al. with postmenopausal women showed that when they were given oral estrogen at a dose of 1.25 mg. per day for nine weeks their SHBG levels increased and their testosterone decreased.

The many other studies done on post menopausal women demonstrate this. As you can see by all the test results in the protocol group, there were ten women who had low levels of free testosterone. Even the women who dropped out had low free testosterone levels. Two of the women in the group of ten had levels so low they could not be detected by that test. Five of the women took birth control pills for over ten years. Two of the women were on an estrogen preparations. One was using a birth control patch and two were using birth control pills. Again all of this is inferred.

Office Sexual Assessment and History

A sexual assessment and history was taken. That gave us more information. There were items picked up on this assessment that lead us to inquire further about medications. Several anti-depressants affect the levels of testosterone bioavailability for a person. Sometimes there was a discovery of a major stressor in a relationship such as a marital separation. Those people were not included in the study. Three women were on some form of anti-depressant. Every respondent told the nurse in the office she had a good relationship with her partner on the sexual assessment. When the staff sex-therapist called to go over the protocol study, she discussed four areas with the patient: 1) Did they understand what the study was about? 2) Did they have any questions about the testosterone treatment? 3) What would happen at the end of the study? 4) Are you having any problems in your relationship? The last question would usually elicit a more honest answer if there were problems. Marital problems are part of the everyday landscape for couples. Divorce and separation are too stressful for someone to be concerned about following through on a study. So those women were excused from the study. What started out with twenty-five is now down to fifteen.

After the telephone screening took place, treatment began. The nurse had already discussed with the women the side-effects and then given them a prescription for testosterone.

There were patients who did not choose to continue. If they still wanted to be treated they were told to bring their testosterone vial to the office and the injection would be given.

Preceding the first injection, each patient was asked to take the Brief Index of Sexual Functioning Test and to sign an adult consent form. They were told if they felt uncomfortable with any of the questions they could leave it blank. It consists of twenty-two questions that explore the sexual functioning level and desire component of the individual woman. They were given the test in an empty office with the door closed. It was thought that this would assure them that we valued their time and privacy. When they finished the test, they placed it in an envelope and sealed it. There was only their patient number on it. It took around twenty minutes. One person did not want to take the test they were not excluded. Of the original group of ten, nine scored below twenty-one, which was rated low on the scale of respondents. The patients are then given their first injection of 200IM of testosterone.

The current literature, what little bit there was, reported that it usually takes two to three days of the IM treatment for the testosterone to take effect. Of the ten that stayed with the study, only one woman gave that report. Seven said it took three weeks minimum. All of the women in this study except two reported that their desire level increased as well as their sexual activity with their partners. One woman joked that when she came into her office with her vial of testosterone in a brown bag she told everyone it was her "balls". Another reported that she felt like she was on a second honeymoon. The two that reported no increase had both stated to the staff sex therapist during the de-briefing that they had had low desire or no desire their entire life. Both indicated that their relationships were strained because of it. Both were seeking something to alleviate this problem of low desire. One was seen in counseling with her partner. One person was being treated for hypothyroidism. There was not a sustained physiological state that could be maintained with these injections. Two of the women did report an increase in energy and a sense of well-being.

Other anecdotal material that would be discussed upon de-briefing was the fact that all the women discussed the lower desire levels they had when they had their children. All the women in this study had children. Some had children that were grown and others had babies. Eight of the women discussed that when they were just starting their sex lives they had desire and energy. Those same eight discussed the joy they received from this activity and the grief they felt when it was no longer something they enjoyed or even thought about. As one respondent stated, "I did not want to put up with this." Ten of the women talked about the impact this low level of desire had on their relationships. Not one wanted to stay as they were, including the two who had life long desire problems. They were looking for a positive change.

While testosterone would seem to be a panacea for low sexual desire in women it has its pitfalls. As with any investigation into its uses there are more questions than answers. Because there are no medically approved protocols for the treatment of women with this hormone it is difficult to find anyone who will share information about it. This researcher interviewed Dr. Norman Mazer, a prominent researcher in this field of testosterone replacement for women and men. He stated that there were several transdermal patches being developed but that it would be two years before they would be marketed. He emailed an interesting article he wrote on protocols. It shows some of the over the counter remedies as well as other therapies now used. (Appendix 7) It was difficult for this researcher to find physicians in the United States that wrote about their protocols for this perimenopausal group. The literature that is out there would suggest there are at least 40% of women who have the problem of low levels of desire in this age group. The women in this protocol group were perimenopausal. It was very difficult to find information about this group. Most studies and research is done on menopausal women. Yet the statistics say only 20% of menopausal women have a lack of sexual desire. It is understood that for both women and men testosterone is necessary for people to have the desire

to have sex. Yet there is disagreement on at what level. One study said 1/10th another said 1/20 of what is given to men. Hypogonadal men are given 5 mg. a day. Healthy premenopausal women produce 300 ug of testosterone per day or 5% of the daily production in men. Men make about 5 mg. per day. There was not a written standard that this researcher could find that said what dosing level to start at.

Upon further inquiry it was discovered that two women in the study had a primary desire disorder. They had always had a low level of desire. Their testosterone tests were low. One was so low it could not be detected on the assay test. The other person on further inquiry had some sexual identity issues to resolve. Secondary desire disorder usually follows a period of higher interest. The other eight would fit that category .

Written Assessment Tests

BISF-W

There are written test that can assess the level of sexual functioning and desire. The BISF-W is one that was used in many clinical trials but usually on a larger number than fifteen.

ASEX

I also was given another test that is even shorter and easier to take in an office setting: The Arizona Sexual Experience Scale (ASEX) developed by McGahuey, Glenberg, Laukes, Moreno and Delgado in 2000. They actually used the BISF-W to develop the test. It takes less than five minutes and can be scored right away. There is one just for women. It is easier to take and finds the same level of sexual functioning and desire that the BISF-W did with only six questions. The ASEX would be more effective with time being a problem and then expense for someone to score it. A physician's office is more time managed then ever before. All of these women were busy and not inclined to want to spend their time taking a test and being interviewed for an hour about their desire level or the lack of it.

After conducting this protocol study, it is clear that there are changes that need to be made for women having to do with their sexual health. The managed care atmosphere today really sets women patients up for limited evaluations. If they have a problem, it has to be dealt with either by their primary care physician or OB-GYN. If the office exam or visit uses more than the time allotted by the patients insurance company will not pay. Going to a sex therapist is a luxury. There were fifteen women in this study with only ten finishing it. It took at least a week of interviews and telephone calls before the final ten were parsed out for the study. Imagine in a practice of 5,000 women how you would do that? Staffing alone would take a bite out of the operating budget. Yet the self-reports of these women in the study were reinforced by the blood assay test as well as the written sexual functioning test. Kaplan spoke of the reluctance of health care personnel who discounted the self-report of women regarding desire. Why is it always in a woman's head?

Protocol Suggestions

Here are some suggestions based on this limited protocol study as to how to best serve the woman who is experiencing low levels of desire.

1. Believe her when she tells you that she is experiencing a low level of desire. Hearing that there are other women who have this problem reassures her that she is not alone. Tell her there are things that can be done to help her.
2. Make sure she has a blood assay test that has total testosterone as well as the free and weakly bound testosterone levels. It also should contain SHBG analysis with the albumin level. There should be a standard assay test that would have the same reference range. In this study we had four different tests to use for analysis.
3. If possible give the ASEX test since it is so brief and does show levels of sexual

functioning and desire. It takes less than five minutes and can be done during the waiting period in the lobby.

4. There needs to be a sexual assessment and history taken on each woman in a medical practice. It has so much information for understanding her total overall sexual health. Much of the information is already available in the medical file.

5. Refer this woman out if the above evaluations prove to not present what the complaint is about. A skilled therapist can usually elicit good information on the emotional and psychological health of this person. Give the therapist, with the patient's permission, a copy of the sexual health assessment and history.

The Future

There is hope for the future in testosterone treatment for women with low sexual desire. There is testing of a transdermal patch for women that mimics the normal fluctuations of testosterone. It will take two years before all the tests and approvals allow it to be marketed as reported to this researcher by Dr. Norman Mazer of Watson Laboratory. In June of 2001, an international panel of experts met in Princeton, New Jersey, to discuss the female androgen deficiency syndrome (FADS). Here is the consensus of the diagnosis:

- global loss of sexual desire (libido)
- decreased sensitivity in the nipples and clitoris
- decreased arousability and capacity for orgasm
- loss of muscle tone
- diminished vital energy (fatigue)
- thinning and loss of pubic hair
- blunted motivation, lack of well being

There was discussion on the cut-off level for the normal range of testosterone. There was disagreement on assay tests used and standardization and sensitivity to what is bioavailable in the testosterone measured. The SHBG that binds with testosterone was discussed as being so different in many women and can be affected by different drugs as well as diseases. Several of the authors of the literature in this study (Davis and Mazer) were on the panel. A published report is still pending but a participant from the panel put an unofficial report for educational purposes online (www.medscape.com). It would seem from all that is out there now that this is what the future holds for women who suffer from hypoactive sexual desire disorder.

Women have had their sexual liberation as long as the pill has been out, yet this very thing might be one of the reasons they have given up sex!

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