

RELATIONSHIP BETWEEN INFLAMMATION, SEX HORMONE PROFILE AND SEXUAL DYSFUNCTION IN FEMALE PATIENTS RECEIVING DIFFERENT TYPES OF RENAL REPLACEMENT THERAPY

Alpaslan Altunoglu¹, Demet Yavuz¹, Mujdat Batur Canoz¹, Rahman Yavuz², Latife Atasoy Karakaş³, Nilüfer Bayraktar⁴, Turan Colak¹, Siren Sezer¹, Fatma Nurhan Ozdemir¹, Mehmet Haberal⁵.

¹Baskent University Medical Faculty, Nephrology Department, Turkey, ²Ondokuz Mayıs University Faculty of Medicine, Family Medicine, Samsun, Turkey, ³Baskent University Medical Faculty, Obstetrics and Gynecology Department, Turkey, ⁴Baskent University Medical Faculty, Biochemistry Department, Turkey, ⁵Baskent University Medical Faculty, Department of General Surgery, Ankara, Turkey

OBJECTIVES

End stage renal disease (ESRD) and renal replacement therapies (RRT) tend to have a serious impact on sexual function and quality of life (QoL). ESRD is a negative condition adversely affecting patients sexual function (1). Estrogen and androgens are the main regulator hormones for the physiology of female sexual functions (2). Testosterone (TTT) is binding to albumine and sex hormone binding globuline (SHBG). The differences of SHBG changes concentrations of blood levels of free testosterone (fTTT) (3). Secretion of GnRH is decreasing in uremic women, increasing blood levels of prolactin is usually seen in ESRD women patients and increasing prolactin level causes sexual dysfunctions (4,5). The prevalence of lack of desire for sexual activity is mostly related to organic conditions but also related with the underlying presentation of depression and psychosocial factors in female dialysis patients (6). The presence of depressive symptoms, very prevalent in ESRD patients, is an independent factor of FSD in ESRD patients (7). We used the complete form of Female Sexual Function Index(FSFI), to evaluate FSD (8). We tried to explore the impact of FSD on QoL.

METHODS

A total of non-diabetic 121 female ESRD patients and 36 healthy women were recruited in this study. The study was consisted of 47 renal transplantation(RTx), 46 hemodialysis (HD), 28 continuous ambulatory peritoneal dialysis (CAPD) patients, and 36 healthy control group. All groups were evaluated with following scales; Female Sexual Function Index (FSFI) questionnaire, Short Form (SF)-36 questionnaires, Beck Depression Inventory (BDI). The FSFI scores were compared between the four groups. The patients whose FSFI score is <26.55 were accepted as FSD.

Table: BDI, SF-36 questionnaire, FSFI scores and comparison of RTx, HD, CAPD, control groups. (*Comparison of renal replacement patients and control group, * Comparison of all RRT patients.)

Patient characteristics	Transplantation (n=47)(group I)	Hemodialysis (n=46)(group II)	Peritoneal dialysis(n=28) (group III)	Control (n=36) (group IV)	P value*	P value*
BDI	8 (0-33)	10 (1-44)	10 (0-41)	6.5 (0-26)	>0.05	>0.05
SF-36 score	58 (2-91)	59 (3-89)	47 (2-91)	78 (8-92)	<0.05	>0.05
FSD (n.%)	19 (40.4)	19 (41.3)	14 (50)	6 (16.7)	<0.05	>0.05
Total FSFI score	22 (2-34.5)	22.4 (4-33.7)	18.35 (2-34.4)	29.6 (2-34.9)	<0.001	>0.05
Desire	5 (2-10)	5 (2-8)	5 (2-10)	6 (2-10)	<0.001	>0.05
Arousal	10 (0-17)	10 (0-19)	6 (0-18)	15 (5-20)	<0.001	>0.05
Lubrication	14 (0-20)	11.5 (0-20)	13.5 (0-20)	17.5 (0-20)	<0.001	>0.05
Orgasm	8 (0-15)	8.5 (0-15)	5.5 (0-15)	12 (0-15)	<0.001	>0.05
Satisfaction	9 (0-15)	9 (0-15)	7 (0-15)	13 (0-15)	<0.001	>0.05
Pain	11 (0-15)	12 (0-15)	10 (0-15)	15 (0-15)	<0.001	>0.05

RESULTS

The mean age of the above-mentioned groups were similar ($p > 0.05$). Half of the patients (56.7%) had 6 years or more ESRD duration and similarly most of the patients (68.1%) received dialysis treatment for more than 6 years. Overall, total FSFI scores and ranges of women in groups RTx, HD, CAPD and controls were 22 (2-35), 22.4 (4-34), 18.35 (2-34) and 29.6 (2-35) respectively. The mean total FSFI score was not different in patients receiving different kinds of RRT ($p > 0.05$) while they were significantly worse than the control group ($p < 0.001$). On regression analysis, age was significantly associated with FSD ($\beta = -0.14$, $p = 0.001$). In addition, physiological health domain of SF-36 was significantly better in control groups ($p < 0.001$). FSD score was negatively correlated with BDI ($r = -0.371$, $p < 0.001$); whereas positively correlated with mental-physical component score of SF-36 ($r = -0.423$, $p < 0.001$ and 0.494 , $p < 0.001$, respectively) in all RRT patients. Among to the hormones of the patients, there was a significant difference between RTx and HD, CAPD groups in dihydroepiandrosterone sulfate (DHEAs) ($p < 0.001$), RTx and HD in prolactin ($p < 0.001$), RTx and CAPD in fTTT ($p < 0.001$).

CONCLUSIONS

This study demonstrated that FSD was increased in all kinds of RRT patients than control group. In addition, patients were observed to have significantly lower desire, arousal, orgasm, sexual satisfaction, and lubrication and higher pain compared to the healthy control group. Whereas there was no significant difference between RTx, HD, and CAPD patients. The QoL following RTx was significantly increased, but FSD remains a problem for many post-transplant cases in our study. Peng et al. (7) studied female HD patients and reported that they had significantly lower sexual FSFI score compared with the control group. In a study carried out by Guan et al. (9), it was reported that more ESRD patients have FSD, decreased libido, less frequent orgasm, and sexual displeasure compared with the healthy controls, which is in line with the results of the present study. The risk factors associated with FSD were age, low educational level, depression, uremia, sexual violence, history of a sexually transmitted disease, and physical health status (1). Age is the most important one among these factors (1). Iacovides et al. (10) reported a significantly positive relationship between age and sexual dysfunction in dialysis patients. Similarly, Peng et al. (7) reported a positive correlation between age and sexual dysfunction in HD patients. These findings were in accordance with the results of the present study. Potential problems experience body image deteriorations that may also cause sexual dysfunction (11). Toorians et al (6) reported that 100 % of the female HD patients, 67 % of the female CAPD patients, 31% of the RTx patients had lack of sexual desire and sexual fantasy. In the present study, no significant difference was observed between HD, CAPD, and RTx patients in terms of sexual dysfunction sub-scales; however, significant differences were observed between the study groups and the control group. Kettaş et al. (1) reported that patients who undergo pelvic or abdominal surgery are at more risk of developing sexual dysfunction. Although successful RTx increases the QoL as well as improved sexual dysfunction in ESRD patients (6) it was observed in the present study that RTx patients experienced sexual dysfunction similar to the HD and CAPD patients, which may be attributed to the major surgery they experienced, glucocorticoid treatment used in renal graft survival (RGS) resulting in decreasing testosterone biosynthesis, or CsA and tacrolimus (12) treatments potentially affecting the leydig cells (12). In the present study CsA were widely used in RTx patients. The CsA therapy may be the potential risk of high incidence of FSD in our RTx patients. Betablockers, diuretics, antihypertensive drugs affecting the central nervous system have negative effects on sexual intercourse (13,14). In our both RTx and HD, CAPD groups had multiple anti-hypertensive regimens. As the assessment of hormonal profiles of the patients, there was no significant difference between patients in TSH, FSH, LH, fTTT, estradiol, SBG levels. But we found ameliorating levels of DHEAs in RTx group. Dehydroepiandrosterone and its sulfated active form DHEAs play an important positive role in human systems including sexual dysfunctions (15). However, the normal laboratory cut-off levels of DHEAs may not be associated with clinical efficacy of RTx hosts. There are limited studies assessed the inverse relationship between the CRP levels and the FSFI score. Esposito K, et al. reported that higher CRP levels might be speculated reduced nitric oxide activation which tend to play a major role in the prevalence of FSD in chronic disease progress (16). In the study higher circulating levels of CRP was evaluated in both patient groups which may intrigues the complexity of FSD.

References

1. Kettaş E, Cayan F, Akoy E, Kykim A, Cayan S. Sexual dysfunction and associated risk factors in women with end-stage renal disease. *J Sex Med.* 2008;5(4):872-7.
2. McKenna K. The brain is the master organ in sexual function: central nervous system control of male and female sexual function. *Int J Impot Res.* 11(Suppl 1):S48-S53. March 1999;82:1492-1496.
3. Paulaitis WA, Beck SG, Handa RJ. Mechanisms of action of androgen in the brain. In: *Andrology in the 21st century: proceedings of the 7th international congress of andrology, Montreal, Medmond Medical Publications, Englewood* (2001).
4. Ginsburg ES, Owen FR Jr. Reproductive endocrinology and pregnancy in women on hemodialysis. *Semin Dial.* 6: 105-116, 1993.
5. Toorians AW, Jansson E, Laan E, Gooren LJJ, Gillay EJ, Oe PL, Donker AJM, Everaerd W. Chronic renal failure and sexual functioning: Clinical status versus objectively assessed sexual response. *Nephrol Dial Transplant.* 12 : 2654-2663, 1997.
6. Palmer BF. Sexual dysfunction in uremia. *J Am Soc Nephrol.* 1999;10(6):1381-8.
7. Peng YS, Chiang CK, Kao TW, Hung KY, Lu CS, Chiang SS, Yang CS, Huang YC, Wu KD, Wu MS, Lien YR, Yang CC, Tsai DM, Chen PY. Sexual dysfunction in female hemodialysis patients: a multicenter study. *Kidney Int.* 2005; 68(2):760-5.
8. Wegel M, Meison C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. *J Sex Marital Ther.* 2005; 31(1):1-20.
9. Guan J, Fan JM, Zheng WD, Luo H, Li Z, Peng GH, Zhou L, Wang W. Sexual dysfunction in female patients with chronic renal insufficiency. *Shichuan Da Xue Xue Bao Yi Xue Ban.* 2005; 36(4):555-8.
10. Iacovides A, Fountoulakis KN, Balaskas E, Manika A, Markopoulou M, Kaprinis G. Relationship of age and psychosocial factors with biological ratings in patients with end-stage renal disease undergoing dialysis. *Ageing Clin Exp Res.* 2002; 14(5):354-60.
11. Stewart M. Narrative literature review: sexual dysfunction in the patient on hemodialysis. *Nephrol Nurs J.* 2006 Nov-Dec; 33(6):631-41; quiz 642.
12. Schmidt A. Sexual hormone abnormalities in male patients with renal failure. *Nephrol Dial Transplant.* 2002; 17(3):368-71.
13. Manolis A, Doumas M. Sexual dysfunction: the prima ballerina of hypertension-related quality-of-life complications. *J Hypertens.* 2008; 26(11):2074-84.
14. Doumas M, Tsioltras S, Tsakiris A, Douma S, Chounta A, Papadopoulos A, Kanellopoulou K, Giannarellou H. Female sexual dysfunction in essential hypertension: a common problem being uncovered. *J Hypertens.* 2006 Dec; 24(12):2387-92.
15. Trush AM. Dihydroepiandrosterone-a precursor steroid or an active hormone in human physiology. *J Sex Med.* 2015; 11(1):2960-82.
16. Esposito K, Cirotola M, Marfella R. Sexual dysfunction in women with the metabolic syndrome. *Diabetes Care.* 2005; 28(3):

