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The effect of renal transplantation and hemodialysis on fertility in uremic men

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Male infertility is a serious problem, especially in young patients. Advances in kidney transplantation technology allow patients with kidney failure to survive after receiving a transplanted organ. Herein, the study evaluated the effect of renal transplantation on fertility in uremic men on hemodialysis. In this study, we compared two groups comprised of 20 patients in each group. Group one includes 20 patients on hemodialysis at least 2 years that compared with group two consist of 20 kidney recipients with 2 years of successful graft function. Evaluation between two groups was done in testis biopsy, semen analysis, and gonadotropin hormones. Then we assessed the effect of transplantation on fertility. The mean age of men on hemodialysis was 37.35 ±10.58 years and the mean age of transplanted men was 34.75 ± 6.82. In hemodialysis group from 20 biopsies, 11 (55%) had normal spermatogenesis and interstitium and 9 (45%) abnormality were seen. In transplanted group from 20 performed biopsies 16 (80%) had normal spermatogenesis and interstitium and Leydig and Sertoli cells and in 4 (20%) abnormality were observed semen analysis indices in quality and quantity had improvement after transplantation, since improvement in volume, count, motility, live ratio, morphology were statistically significant (P= 0.0001). Luteinizing hormone mean on hemodialysis was 12.49± 7.28 and after transplantation was 7.05 ±3.02 (P= 0.004), follicle-stimulating hormone mean on hemodialysis was 13.15± 32.27 and after transplantation was 6.5 ±7.07 (P= 0.377). Prolactin mean on hemodialysis was 41.93± 65.87 and after transplantation was 13.73 ±5.77 (P= 0.064). Thyroid stimulating hormone mean on hemodialysis was 1.8± 0.99 and after transplantation was 1.7 ±0.9 (P= 0.89). The present study showed that renal transplantation is more effective to correct histologic and endocrinologic abnormalities and also quality and quantity of semen compared to hemodialysis.

INTRODUCTION

Male infertility is a serious problem especially in young patients (1). Spermatogenesis is now known to be an extremely sensitive process and can be depressed, temporarily or permanently, by various factors apart from the primary disease of endocrine glands (2); among these are heat, radiation, severe malnutrition and chronic debilitating disease such as chronic renal failure, diabetes mellitus, and tuberculosis (3,4). However exact mechanism leading to impaired Spermatogenesis in end-stage renal disease (ESRD) and hemodialysis, is unknown (5). Cross-sectional studies about Spermatogenesis and fertility in men with ESRD demonstrated that semen quality in men on hemodialysis is poor and only successful renal transplantation can restore spermatogenesis (6). Spermatogenesis will be impaired in uremia even with favorable hemodialysis. (7) ESRD and hemodialysis have adverse effects on all levels of the hypothalamic-pituitary-testicular axis (7,8). There are many documents that ESRD causes a microinflamation state with high levels of active cytokines and oxidative stress (9). Oxidative stress results in peroxidative damage on testis and sperm which will end to infertility in men (10). Advances in kidney transplantation technology allow patients with renal failure to survive longer after transplantation. Therefore it becomes important for both clinical investigators and transplant recipients to know the effects of transplantation on patient fertility and ability to be fathered after the procedure (6). Since up to 40% of men receiving kidney transplantation are younger than 50 years, male fertility with kidney transplantation is a major concern. In contrast to results in kidney transplantation in women, less investigation has been done in men kidney transplanted fertility (11). The aim of this study was to assess the effect of renal transplantation and hemodialysis on fertility in uremic men.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of Urmia University of Medical Sciences, West Azarbaijan, Iran (code: IR.UMSU.REC.1389.732). We obtained informed consent from all patients. Patients were evaluated in two groups including hemodialysis and kidney transplanted patients. Each group consists of 20 patients. Patient with a history of infertility and other causes resulting in infertility such as a history of mumps or cryptorchidism or trauma to testis were excluded. The first group consisted of end-stage renal failure patients who were on hemodialysis at least two years, time of initiation of dialysis and numbers per week was recorded. This group included patients candidate for renal transplantation and testis biopsy performed just before the time of kidney transplantation. The second group consisted of patients who were transplanted minimally two years before the study, with a successful graft function. This group had hemodialysis

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Table 1 The mean of baseline characteristics of both groups

Group	Hemodialysis (n=20)	Transplanted (n=20)	P-value
Age	37.35	34.75	0.36
ESRD duration	29	21	0.31
Hb	9.82	13.82	0.0001
Hct	30.66	42.24	0.0001
BUN	113.56	37.42	0.0001
Cr	9.74	1.4	0.0001

***Abbreviations**: ESRD, end-stage renal disease; Hb, haemoglobin; Hct, hematocrit; BUN, blood urea nitrogen; Cr, creatinine*

Table 2 Comparison of semen analysis indices in both groups (mean ± SD)

Variable	Hemodialysis group (n=20)	Transplanted group (n=20)	P-value
Liquefaction (Minute)	46.50±5.6	43.25±6.9	0.0001
Semen Analysis pH	7.29±0.1	7.42±0.6	0.3
Volume (cc)	3.405±0.6	3.940±0.5	0.008
Count (Million)	35±14.04	72.50±27.40	0.0001
Min. Motility	14.91±32.25	19.62±52	0.001
Max. Motility	15.42±42	20.34±61.75	0.001
Min. Live Ratio	15.37±31.25	20.32±44.50	0.02
Max. Live Ratio	15.68±41	21.52±56.5	0.01
Min. Morphology	14.51±30	6.12±56.75	0.0001
Max. Morphology	14.31±39.50	6.12±66.75	0.0001

Table 3 Comparison of endocrine indices in both groups

Group	Transplanted (n=20)	Hemodialysis (n=20)	P-value
LH	3.02 ±7.05	7.28±12.49	0.004
FSH	7.07 ± 6.5	13.15±32.27	0.37
PRL	13.73± 5.77	41.93± 65.87	0.64
TSH	1.7±0.9	1.8± 0.99	0.89

***Abbreviations**: LH, luteinizing hormone; FSH, follicle-stimulating hormone; PRL, prolactin; TSH, thyroid stimulating hormone*

at mean 21 months before transplantation. Kidney transplantation times were recorded and biochemistry blood tests were obtained for each patient. After primary assessment such as physical examination, age, occupation and end-stage renal disease etiology, patients in each group were evaluated about fertility. The checklists containing patient data consist of testis biopsy result, semen analysis result, haemoglobin (Hb), hematocrit (Hct), blood urea nitrogen (BUN), creatinine (Cr), thyroid stimulating hormone (TSH), prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), were completed for each patient. All evaluations were done by the single urologist and pathologic samples also were evaluated by the single pathologist who was blinded of patient's information.

Statistical analysis

The analysis was done by SPSS software version 18. Data were sampled in two groups and for comparison of quantitative variables we used t-test (if normal variables) and Chi-square test, Fisher exact test for qualitative variables.

RESULTS

The present study evaluated men with end-stage renal disease on hemodialysis minimally two years and men who had normal function and transplanted kidney at least for two years. The mean age of men on hemodialysis was 37.35 ±10.58 years and the mean age of transplanted men was 34.75 ± 6.82. Comparing two groups in means of end-stage renal disease duration revealed that the hemodialysis group had 29 months and transplanted group patients had 21 months history of hemodialysis before transplantation (Table 1). From 20 patients on hemodialysis, 1(5%) once weekly, 3(15%) twice weekly and 16(80%) third weekly and from 20 transplanted patients 3(15%), and 17(85%) third weekly became hemodialysis. Hb and Hct mean on hemodialysis group was 9.82±1.7 and 30.66±5.37 and after transplantation was13.82±2.1and 42.24±5.33 respectively (P= 0.0001). BUN and Cr mean on hemodialysis group was 113.56±33.27 and 9.74±3.9 and after transplantation was 37.42±15.03 and 1.4±0.24 respectively (P= 0.0001).

In hemodialysis group from 20 performed biopsies, 11(55%) had normal spermatogenesis and interstitium and Leydig and Sertoli cells and in 9(45%) abnormality were observed including incomplete spermatogenesis in all tubules (one case), thinning of germinal cell lining in most tubules and decrease in spermatid/spermatozoa and Leydig cells (one case), hypospermatogenesis in about half of tubules with thickening of tubular basement membrane (3 cases), hypospermatogenesis and decrease in Leydig cells (3 cases), mostly only Sertoli cells and spermatogenesis arrest in some tubules and also decrease in Leydig cells (one case).

In transplanted group from 20 performed biopsies 16(80%) had normal spermatogenesis and interstitium and Leydig and Sertoli cells and in 4(20%) abnormality were observed including hypospermatogenesis (2 cases), mostly Sertoli cells with hypospermatogenesis and reduced Leydig cells (one case), thickening of tubular basement membrane with interstitial edema (one case).

The analysis of the semen in both groups and the comparison made indicated a significant difference; increase in sperm count (p=0.008) and morphology (p=0.001). Indices of the live ratio, motility and semen volume indicated considerable improvement, as well. Details are seen in Table 2.

LH mean on hemodialysis was 12.49± 7.28 and after transplantation was 7.05 ±3.02 (P= 0.004) also FSH mean on hemodialysis was 13.15± 32.27 and after transplantation, it was 6.5 ±7.07 (P=0.377) (Table 3; Figure 1). In our study, prolactin levels on hemodialysis were relatively

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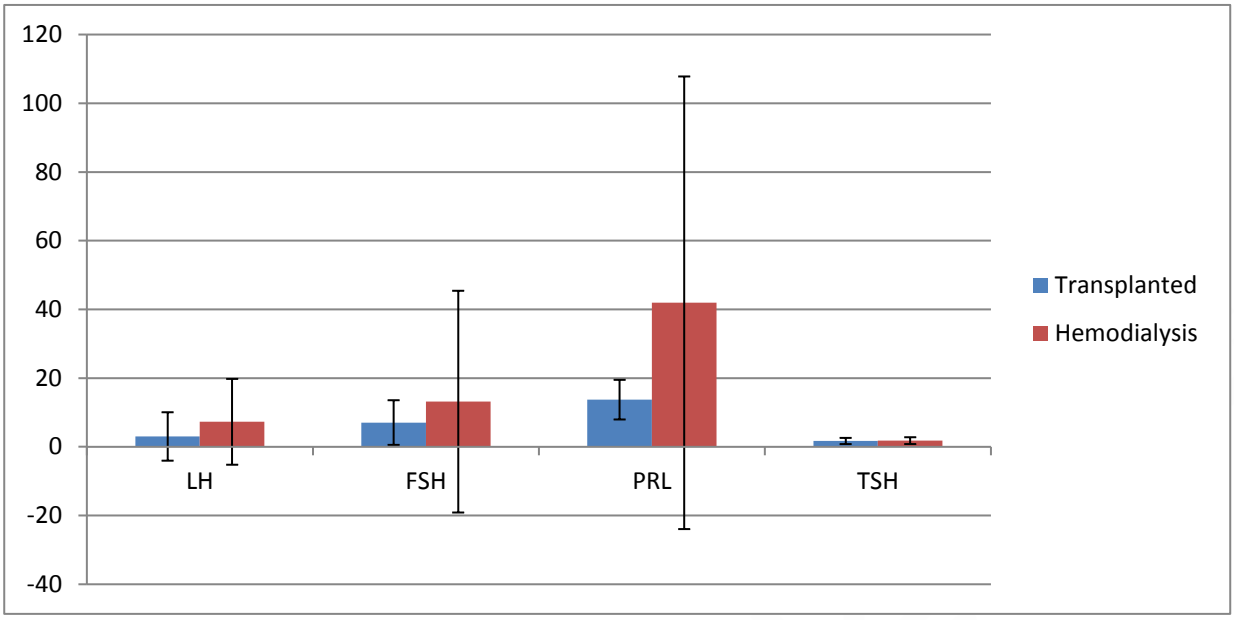

Figure 1 Comparison of endocrine indices in both transplanted and hemodialytic groups.
***Abbreviations**: LH, luteinizing hormone; FSH, follicle-stimulating hormone; PRL, prolactin; TSH, thyroid stimulating hormone*

high (mean: 41.93), which decreased considerably after transplant to 13.73 ng/mL; however, this reduction was not statistically significant (p-value = 0.64). In the comparison of TSH in two groups, mean TSH in hemodialytic men was 1.8±0.99 and after transplantation, it was 1.7±0.9. The significant difference was not seen in two groups (p=0.89).

DISCUSSION

Chronic renal injury is associated with testicular injury and compromised spermatogenesis, often resulting in infertility (12,13). Tissue changes in testes include reduced spermatogenetic activity and principal changes in hormone-related steps of spermatogenesis. The number of spermatocytes decreases and there may be little evidence of sperm maturation (14). Other findings include injury of seminiferous tubules, interstitial fibrosis, and calcification. Factors influencing testicular injury remain to be fully understood.

Palmer et al. (15) investigated sexual dysfunction in uremia and observed that the level of pituitary gonadotropin LH rises in uremic men. This rise develops at the beginning of renal failure and aggravates increasingly as renal function drops. The increased level of LH appears to be due to of reduced release of testosterone from Leydig cells. Moreover, metabolic clearance of LH is compromised as a result of reduced renal clearance. FSH secretion increases in men with chronic renal failures, although with varying degrees, thus increasing the LH/FSH ratio. The highest levels of FSH are observed in patients with severe damage to seminiferous tubules and the lowest levels of inhibin. In our study, the LH level decreased from 12.49 to 7.05 after transplant, indicating a significant difference. A fall in FSH from 13.15 to 6.54 was observed following transplant, which was not significant.

High prolactin levels are often observed in patients undergoing dialysis, which is due to increased prolactin synthesis since the kidney has little role in catabolizing this hormone. Prolactin secretion in chronic renal failure appears to be autonomous and is resistant to stimulating or inhibiting maneuvers (16). Severe hyperprolactinemia is reportedly associated with infertility, reduced libido (17), low testosterone levels, and low LH levels (18). The overall reduction in body stores of zinc may have an etiologic role in uremic hyperprolactinemia (16). In our study, prolactin levels on hemodialysis were relatively high (mean: 41.93), which decreased considerably after transplant to 13.73 ng/mL; however, this reduction was not statistically significant. One study (19) showed that transplant patients showed a significant improvement in sexual activity, a return of testosterone to normal, and a significant fall in LH levels. Fertility, as assessed by sperm count, was improved in 50% of transplant patients. Thus while renal transplantation may restore reproductive function in men with chronic renal failure maintenance hemodialysis has no effect.

Hamdi et al. (20) suggested that endocrine secretions of Leydig and Sertoli cells are differently impacted by dialysis, kidney transplant and immunosuppressive regimen raising new issues to explore. The impairment of testicular function seen in advanced uremia is not reversible by maintenance hemodialysis. In contrast, after successful transplantation, steroidogenic function became almost normal while the spermatogenic function showed a striking if incomplete recovery (21). Although sperm morphology and density did not improve after renal transplantation, there were highly significant changes in sperm motility. Hormonal levels in patients on hemodialysis improved after transplantation and returned to nearly normal; sexual function was also significantly better. Further studies are needed to confirm these results (22).

For hemodialysis patients, male fertility and quality of semen are significantly poorer than in healthy and infertile men, although some fertility improvement occurs after renal transplantation (23). It has been shown previously that there is a correlation between semen volume, motile spermatozoa, and oligo- or complete azoospermia in men with end-stage renal disease (CKD 5), (24). The researches have shown that hemodialysis doesn't improve the hypothalamic-pituitary-testicular axis (25), but that renal transplantation could reverse the uremic damage to testicular function (19,26). Although sufficient and appropriate hemodialysis and renal transplant are both considered therapy options for renal failure, our study indicates that only successful renal transplant is able to salvage fertility indices and hemodialysis fails in this regard.

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CONCLUSION

The study showed that renal transplantation was more effective to correct histologic and endocrinologic abnormalities and also quality and quantity of semen compared to hemodialysis. However, future studies with a more patients and various areas are needed that confirmed the present results.

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Renal transplantation, Fertility, hemodialysis, Semen Analysis, Testis biopsy

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Conflict of interest

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