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Menstrual Dysfunction in Female Patients Undergoing Dialysis

Resic H[1], Alajbegovic A[2], Sahovic V[1], Mesic E[3], Suljic E[2]
[1]Center for Haemodialysis, University Clinical Center, Sarajevo, [2]Neurology Clinic University Clinical Center, Sarajevo, [3]Clinic for Nephrology, Dialysis and Kidney Transplantation, University of Tuzla

Abstract
Uremia is associated with different endocrinologic abnormalities, which in some cases induce polyendocrinopathia. Female patients on dialysis are often subject to menstrual disorders that are variously manifested. We evaluated the etiology of menstrual dysfunctions in female dialysis patients. History, clinical and hormonal tests were performed on 25 female patients that were in chronic dialysis program 4 hours, 3 times per week. Oligomenorrhea was considered as menstrual interval between 35 and 90 days and amenorrhea as cease of menstruation in the last six months. All patients had had normal menstrual cycle before the dialysis. Mean age of patients was 42,7±9,96 years and mean dialysis duration was 75,5±62,41 months. Out of 25 patients, 10 had developed amenorrhea when beginning dialysis and 5 of them regained regular menstrual cycle after one year. 7 patients had oligomenorrhea and 8 patients had an early menopause. Prolactin concentration was significantly higher in group which developed menopause (N=8), cpr=1222,3±1013,4, amenorrhea (942,2±1061,2), oligomenorrhea (860,4±897,2), compared to the group with regular menstruation cycle (444,8±299,7). LH level in serum was increased in all groups. FSH was insignificantly higher in groups with oligomenorrhea and amenorrhea and amounted to 51,1±69,9, while β-estradiol and progesterone were in normal ranges. Haemodialysis duration influenced the prolactin level and after one year of follow up prolactin level significantly decreased in the group with amenorrhea that regained regular menstruation (cpr=596,2±297,2).
Conclusion: Different menstrual disorders develop in dialyzed patients. Hyperprolactinemia was present in our dialysis population. Significant lowering of prolactin level in 20 % of patients led to normalization of menstrual cycle.

Introduction

Uremia is associated with different endocrinologic abnormalities which, in some cases, induce multiple endocrinopathy. Symptoms of sexual function abnormalities in dialysis patients are decrease in libido, reduced frequency of sexual intercourses, galactorrhea, menstrual abnormalities, no ovular cycles, amenorrhea and infertility. The aim of our study is to evaluate the etiology of menstrual dysfunction in female patients undergoing dialysis.

Material and methods

Female patients on dialysis are often subject to menstrual disorders which are variously manifested. History, clinical and hormonal tests were performed on 25 female patients that underwent chronic dialysis program 4 hours 3 times per week. None of the patients was diabetic. Patients were allocated to different groups according to their menstrual status at the time of investigation as follows: a) patients with oligomenorrhea (menstrual interval between 35-90 days); b) patients with amenorrhea (as cause of menstruation in the last six months); c) patients with regular ovular cycles; d) patients with early menopause. Full informed consent was obtained from each patient. Patients' menstrual histories of the subjects before and during the CHD therapy were investigated. Hormonal status entailed determining the serum levels of the luteinizing hormone (LH), the follicle-stimulating hormone (FSH), prolactin (PRL), estradiol and progesterone in one-year follow-up period.
Before blood sampling, we confirmed that the patient had not received any hormone preparation during the previous three months. Levels of hormones were assayed using RIA kits. Inter-group comparisons were made by an unpaired Student's t-test.

Results

All patients had normal menstrual cycle before the dialysis. Immediately after the beginning of CHD therapy 10 females developed amenorrhea, 7 oligomenorrhea and 8 patients developed menopause. 5 of amenorrhoeic women returned to regular cycles. Table 1 presents average age of females undergoing haemodialysis, while average haemodialysis duration was 75.5±62.41 months. Table 3 summarizes the baseline characteristics of the hormonal data. The serum FSH and LH were significantly increased during a follow up period, the serum level of PRG was higher, but not significantly. Serum levels were lover in patients with menstrual disorders, as progesterone.

Correspondence to: Halima Resic, Center for Haemodialysis, University Clinical Center, Sarajevo

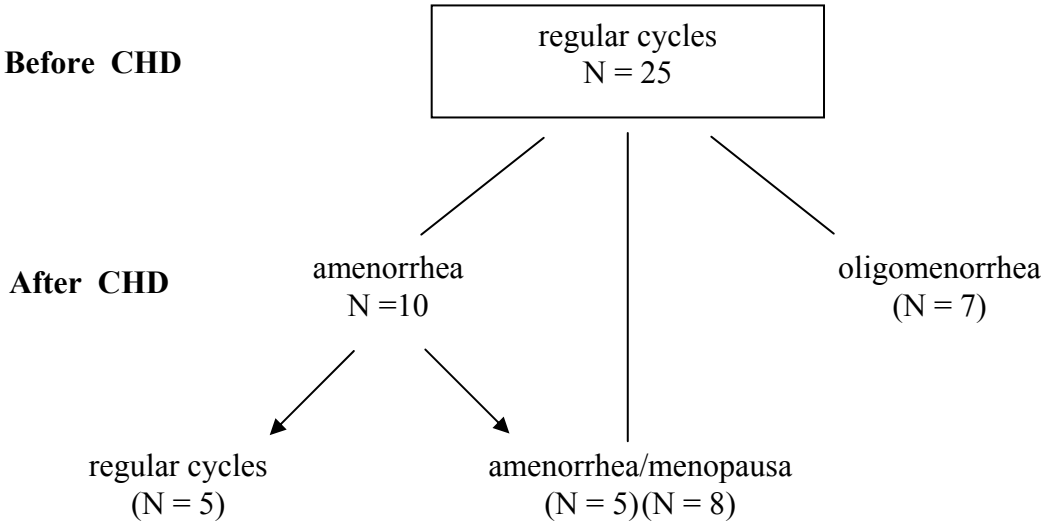

Fig. 1 Menstrual histories of the female patients undergoing dialysis.

Table 1. Avarage age of females undergoing haemodialysis

Diagnosis	Number of patients	Age (years)	Standard error
Total	25	46.7± 9.96	2.03
Amenorrhea	5	47.0± 3.28	1.47
Oligomenorrhea	7	49.2± 4.18	1.71
Normal menstruation	5	47.2± 3.71	1.51
Menopause	8	49.8± 5.29	187

Table 3. Hormone status in patients undergoing haemodialysis

Hormones	First finding	Second Fnding	Differentiation	T-test
FSH	74.0± 81.3	96.7±80.3	22.7±50.3	p<0.05
LH	66.5± 72.0	94.1±69.2	27.6±56.4	p<0.05
Estradiol	407.8±472.1	442.3±555.3	34.5±387.6	n.s.
Progesteron	6.04±6.14	6.22±5.79	0.18±6.82	n.s.
Prolactin	959.5±889.7	740.3±564.1	219.2±695.4	n.s.

Table 4a. Avarage hormone values (FSH)

Diagnosis	First finding	Control finding	Differentiation	p-value
Amenorrhea	51.1 ± 69.9	108.9 ± 71.5	57.8 ± 52.5	p < 0.07
Oligomenorrhea	55.5 ± 74.8	87.45 ± 80.3	31.9 ± 57.3	n. s.
Normal menstruation	84.4 ± 98.5	75.4 ± 88.1	-9.0 ± 18.1	n. s.
Menopause	98.9 ± 71.7	111.2 ± 75.8	12.3 ± 35.3	n. s.

Table 4a summarizes characteristics of the FSH level in different groups during a follow up period; FSH was significantly higher in groups with oligomenorrhea and amenorrhea. Serum LH levels were markedly elevated in all groups (Table 4b). Serum estradiol levels were lower in patients with menstrual disorders (Table 4c). Table 4e summarizes characteristics of the serum prolactin level which remained low.

Table 4b. Avarage hormone values (LH)

Diagnosis	First finding	Control finding	Differentiation	p-value
Amenorrhea	48.2 ± 64.7	97.5 ± 53.6	49.3 ± 63.5	n. s.
Oligomenorrhea	59.7 ± 80.8	99.4 ± 88.5	39.7 ± 72.0	n. s.
Normal menstruation	72.0 ± 82.2	73.9 ± 81.1	1.9 ± 4.4	n. s.
Menopause	79.6 ± 58.3	100.6 ± 47.3	21.0 ± 47.8	n. s.

Table 4c. Avarage hormone values (estradiol)

Diagnosis	First finding	Control finding	Differentiation	p-value
Amenorrhea	493.4± 276.4	163.4± 65.2	-330.1± 245.4	p< 0.05
Oligomenorrhea	553.5± 781.0	537.5± 686.2	-160.0± 328.7	n. s.
Normal menstruation	444.8± 299.7	611.0± 578.7	166.2± 363.2	n. s.
Menopause	222.0± 198.5	439.7± 535.5	217.7± 346.8	n. s.

Table 4d. Average hormone levels (progesterone)

Diagnosis	First finding	Control finding	Differentiation	p-value
Amenorrhea	3.42 ± 1.09	2.74 ± 1.50	- 0.68 ± 1.74	n. s.
Oligomenorrhea	3.20 ± 1.45	4.65 ± 2.42	1.45 ± 1.43	p<0.05
Normal menstruation	11.62 ± 9.68	11.86 ± 9.49	0.24 ± 13.4	n. s.
Menopause	6.37 ± 4.48	6.03 ± 2.38	- 0.34 ± 4.31	n. s.

Table 4e. Average hormone levels (prolactin)

Diagnosis	First finding	Control finding	Differentiation	p-value
Amenorrhea	860.4± 796.9	897.2± 887.2	36.8± 97.6	n. s.
Oligomenorrhea	942.2± 1061.0	596.2± 297.2	346.0± 1176.0	n. s.
Normal menstruation	711.6± 225.2	530.0± 122.3	-181.6 ± 203.1	p<0.001
Menopause	1222.3 ± 013.4	902.1± 551.2	- 320.2 ± 543.1	p<0.001

Discussion

The main causes of endocrine dysfunctions in uremia are intoxication not adequately corrected by current treatments, nutritional deficiencies, electrolyte abnormalities and mineral metabolism acidosis.

In this study all patients with regular menstruation before dialysis developed amenorrhea once dialysis started. In our study amenorrhea persisted in five women, while five returned to regular cycles. Three out of 5 women with regular cycles had anovulatory menstruation what suggests that dialysis had long-term effects on ovaries function. Primson et al examined the metabolic processing of the luteinizing hormone – releasing hormone (LH – RH) and they noted reduced MCR and prolonged half-life in patients with renal failure. Therefore, abnormalities in gonadotropin (LH and FSH) secretion arise in patients undergoing dialysis inducing ovarian dysfunction (3). The influence of dialysis on the MCR of LH – RH may result in a continuous increase of the LH level (2). The serum FSH levels were neither elevated nor lowered. Endocrinologic findings of gonodotropins in patients undergoing dialysis are consistent with those reported by several investigators (4,5). The prolactin level (PRL) in our group with amenorrhea, oligomenorrhea and menopause was significantly higher than the one in group with regular menstrual cycle. Many investigators have reported that hyperprolactinemia contributes to ovarial dysfunction in women undergoing CHD (5,6). Therefore, hyperprolactinemia might be an important cause of ovarial dysfunction. Menstruation recovered in 5 out of 10 patients who developed amenorrhea during dialysis. This can be explained by the erythropoietin effect which was administered to women with regular menstrual cycles.

Conclusion

Patients undergoing dialysis developed different menstrual disorders. Specific endocrine differences between the group with regular menstrual cycle and the group with menstrual disorders were present in the prolactin level. Significant lowering of the prolactin level in 20% of patients led to normalization of menstrual cycle. Long term dialysis might improve menstrual disorders in such patients.

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