

Effects of Acute Dehydration on the Kidney in Solitary Kidney Rats with Chronic Partial Ureteral Obstruction

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Abstract

Aim: In this study, we evaluated the effects of dehydration on the kidney in rats with a solitary kidney subjected to experimentally induced partial ureteral obstruction.

Methods: Twenty male Wistar albino rats were randomly assigned to four groups of five animals each: Group 1, right nephrectomy (control); Group 2, right nephrectomy + dehydration; Group 3, right nephrectomy + left partial ureteral obstruction; and Group 4, right nephrectomy + left partial ureteral obstruction + dehydration. Chronic partial ureteral obstruction was induced by embedding the left ureter into the psoas muscle for four weeks. Dehydration was achieved via 48-hour water restriction.

Results: Hematocrit, urine density, and blood urea levels were significantly increased in the dehydration groups, whereas blood creatinine was significantly elevated only in Group 4 ($p=0.01$). Scintigraphic evaluation demonstrated that glomerular filtration rate decreased in all experimental groups, with the lowest value observed in Group 4 ($p=0.01$). All experimental groups showed significant prolongation of Tmax and renal perfusion time and a decrease in renal uptake compared to the control group. These changes were most pronounced in Group 4 ($p=0.01$). Histopathological examination revealed that alterations such as papillary and tubular deformities, granulocyte accumulation, and medullary edema were more pronounced in rat samples from Group 4 compared to the other groups.

Conclusions: Chronic partial ureteral obstruction in rats with a solitary kidney adversely affected renal structure and function, and the addition of acute dehydration further exacerbated this damage.

Keywords: Partial ureteral obstruction; dehydration; renal function; histopathology; kidney

1. Introduction

Urinary obstruction (UO) is an important pathological condition that can lead to kidney damage due to various anatomical, physiological, and biochemical changes resulting from impaired urine flow¹. It may present as either complete or partial obstruction and can occur in acute or chronic forms. Partial unilateral ureteral obstruction (PUUO) refers to the accumulation of urine within the kidney caused by a partial blockage of the urinary tract. In adults, the most common cause of PUUO is ureteral stones, whereas in the pediatric population, ureteropelvic junction obstruction is the predominant etiology². In unilateral UO, the contralateral kidney may exhibit compensatory hypertrophy to maintain overall renal function². However, when a kidney is anatomically or functionally absent due to congenital or acquired conditions, such as renal failure, trauma, or nephrectomy, compensatory mechanisms are impaired. Congenital solitary kidney occurs with a reported incidence of approximately 1 in 2,000 individuals³.

Obstruction leads to abrupt changes in the affected kidney, including increased intrarenal pressure, ischemia, and oxidative

stress, which trigger complex responses such as inflammation, apoptosis, and extracellular matrix accumulation⁴. Prolonged obstruction may result in tubular-interstitial fibrosis and functional loss due to epithelial cell apoptosis⁵. Biochemical and urinary findings in UO are generally nonspecific and do not reliably indicate the underlying pathology². Imaging techniques, including plain radiography, intravenous pyelography, computed tomography, and magnetic resonance imaging, are commonly employed to assess the severity and etiology of obstruction⁶. Additionally, scintigraphic evaluations are increasingly recognized as valuable tools for assessing renal anatomy and function².

Acute dehydration, resulting from reduced fluid intake or increased fluid loss (e.g., diarrhea, febrile illnesses, burns, high ambient temperature, diabetes insipidus, diabetes mellitus, chronic pyelonephritis, or diuretic use), leads to a decrease in effective circulating volume^{7,8}. Hemodynamic disturbances caused by dehydration reduce renal blood flow through contraction of mesenchymal vessels, while medullary congestion and vasoconstriction in renal arte-

rioles contribute to a decrease in glomerular filtration rate (GFR)⁹.

The aim of this study was to investigate the effects of acute dehydration on renal morphology and function in rats with a solitary kidney during experimentally-induced chronic partial ureteral obstruction.

2. Materials and Methods

2.1. Study Design and Ethical Considerations

The study protocol was approved by the Local Ethics Committee for Animal Experiments, and all experiments were carried out at the Experimental Research Center. All animal procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals and adhered to the ARRIVE guidelines. This study used 20 male Wistar albino rats (age: 8 weeks; weight: 150-180 g). The animals were housed in ventilated cages in a controlled environment (ambient temperature: 18 °C–21 °C, atmospheric humidity: 55%± 10%, and programmed 12-h light/dark cycles), with access to standard rodent feed and filtered water. The animals were randomly divided into four groups, each consisting of five rats: right nephrectomy only (Group 1, control); right nephrectomy and dehydration (Group 2); right nephrectomy + left PUUO (Group 3); and right nephrectomy + left PUUO + dehydration (Group 4).

2.2 Unilateral Nephrectomy and PUUO Procedures

All surgical procedures were performed under spontaneous respiration following intramuscular administration of 50 mg/kg ketamine hydrochloride (Ketalar®, Eczacıbaşı, Istanbul, Turkey) and 5 mg/kg xylazine hydrochloride (Rompun®, Bayer, Germany). After the rats were placed in the supine position, a midline incision was made under sterile conditions to perform laparotomy. The renal artery, vein, and ureter of the right kidney were ligated together using 5/0 nylon sutures (Prolene®, Ethicon, Edinburgh, UK), and right ne-

phrectomy was performed. This procedure was applied to all animals.

PUUO was induced in Groups 3 and 4. The exposed left ureter was placed into a 2–3 mm longitudinal slit created in the psoas major muscle, and the muscle edges were approximated using 7/0 nylon sutures (Prolene®, Ethicon, Edinburgh, United Kingdom).

2.3. Induction of Dehydration

Dehydration was induced in the experimental animals four weeks after the unilateral nephrectomy and PUUO procedures. Dehydration was induced by restricting water intake for 48 hours while maintaining the rats at room temperature. During this period, the animals had free access to standard laboratory chow. The degree of dehydration was assessed by measuring hematocrit levels from blood samples obtained via skin puncture and urine specific gravity from samples collected by suprapubic compression.

2.4. Scintigraphic Studies

Scintigraphic evaluation was carried out in all experimental groups after the dehydration protocol was applied to the animals in Groups 2 and 4. Scintigraphic evaluations were performed at the Nuclear Medicine Department using a digital gamma camera equipped with a single-hole collimator and a computer system (Toshiba 901SA, Tokyo, Japan). The radiopharmaceutical agent technetium-99m-labeled diethylenetriamine pentaacetic acid (Tc-99m DTPA) was administered intravenously via the femoral vein at a dose of 1 mCi. The acquired images were analyzed using renogram and GFR software programs. Renal concentration (Tmax/min) and perfusion (Tmax/sec) values were quantitatively obtained from the renogram curves. Subsequently, technetium-99m-labeled dimer-captosuccinic acid (Tc-99m DMSA) was administered subcutaneously at a dose of 100 MBq/kg, and imaging was performed 12 hours post-injection. DMSA uptake measurements were obtained using a radiocamera.

Table 1

Mean hematocrit, urine specific gravity, serum urea, and serum creatinine values in the study groups

Parameters	Group 1 (Control)	Group 2 (Dehydration)	Group 3 (PUUO)	Group 4 (PUUO+Dehydration)
Hematocrit (%)	37.8 ± 1.4	43.8 ± 1.9 ^a	37.8 ± 1.4	51.0 ± 1.0 ^a
Urine specific gravity	1011 ± 4.1	1028 ± 2.7 ^a	1015 ± 3.5	1029 ± 2.2 ^a
Serum urea (mg/dL)	65.4 ± 7.7	101.4 ± 9.9 ^a	64.4 ± 21.8	182 ± 38.1 ^a
Serum creatinine (mg/dL)	0.84 ± 0.2	0.86 ± 0.5	0.87 ± 0.1	1.64 ± 0.8 ^b

PUUO: partial unilateral ureteral obstruction

^aStatistically significant difference with control group (p=0.001).

^bStatistically significant difference with control, dehydration and PUUO groups (p=0.001).

p-value less than 0.05 was considered statistically significant

Table 2

Mean GFR, Tmax, renal perfusion, and radionuclide uptake according to groups

Parameters	Group 1 (Control)	Group 2 (Dehydration)	Group 3 (PUUO)	Group 4 (PUUO+Dehydration)
GFR (mL/min/100 g)	2.1 ± 0.2	1.7 ± 0.1	1.8 ± 0.2	1.4 ± 0.2 ^a
Tmax (min)	1.22 ± 0.1	3.6 ± 1.5 ^a	9.9 ± 2.6 ^a	13.7 ± 1.2 ^a
Mean renal perfusion (mL/min/100 g)	4.2 ± 0.7	10.8 ± 2.3 ^a	5.7 ± 1.1	13.0 ± 2.2 ^a
Radionuclide uptake (%)	30.5 ± 2.8	24.6 ± 2.1 ^a	21.4 ± 2.7 ^{a,b}	17.8 ± 3 ^{a,b}

PUUO: Partial ureteral obstruction; GFR: Glomerular filtration rate; Tmax: Time to maximum concentration.

^aStatistically significant difference with control group (p=0.001).

^bStatistically significant difference with group 2 (p=0.001).

P value less than 0.05 were considered statistically significant.

2.5. Sample Collection and Histopathological Examination

After the scintigraphic procedures, laparotomy was performed under anesthesia to collect blood samples from the inferior vena cava in order to determine serum urea (mg/dl) and creatinine (mg/dl) levels. In the same session, the left kidneys of the rats were removed for histopathological examination. The collected kidneys were bisected along their longitudinal axis and examined macroscopically. Histopathological evaluation of the sections included the assessment of papillary deformation, dilatation of the tubular or collecting ducts, presence of granulocytes within the tubular or collecting ducts, degenerative and inflammatory changes in the renal parenchyma, interstitial fibrosis, and medullary hemorrhage. At the end of the study, the rats were euthanized under general anesthesia by cervical dislocation.

2.6. Statistical Analysis

All statistical analyses were conducted using SPSS for Windows, Version 28.0.1.1 (SPSS Inc., IL, USA). Categorical variables are presented as counts and percentages, and continuous variables as mean ± standard deviation (SD) or, when appropriate, median (range). Due to a sample size <30 and the ordinal or interval nature of the data, comparisons among three or more independent groups were performed using the Kruskal-Wallis test, while differences between two groups were assessed with the Mann-Whitney U test. A p value < 0.05 was considered statistically significant.

3. Results

Examination of blood and urine samples from the subjects (Table 1) revealed significantly higher hematocrit values and urine density in the dehydrated groups (Groups 2 and 4) (p=0.01). However, the analysis showed no significant difference between the dehydrated groups in terms of hematocrit and urine density (p=0.08). Blood urea levels increased significantly in the dehydrated groups (p=0.01). Blood creatinine levels, reflecting progressive renal failure, were significantly higher in Group 4 (p=0.01).

DTPA scintigraphy demonstrated significant dilatation of the renal pelvis and proximal ureter in all rats in the PUUO groups. The scintigraphic evaluation of renal function (Table 2) revealed a decrease in GFR in all groups except the control group. Notably, Group 4 exhibited a significantly lower mean GFR compared to the other groups (p=0.01). Tmax increased significantly in all experimental groups compared to the control group (p< 0.05).

Figure 1

Macroscopic appearance of kidneys in each group at the end of the four-week experimental period

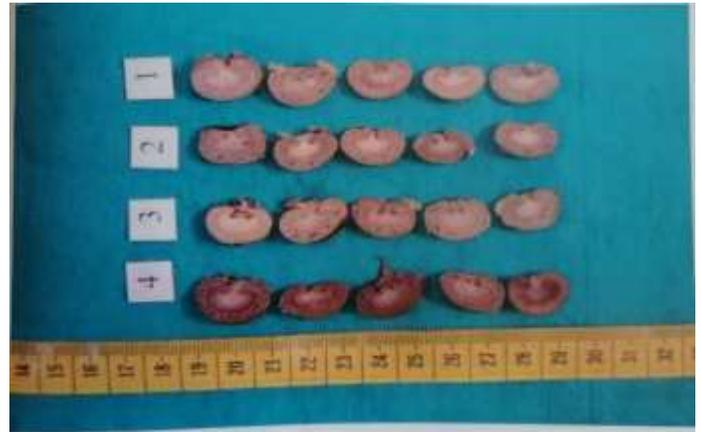
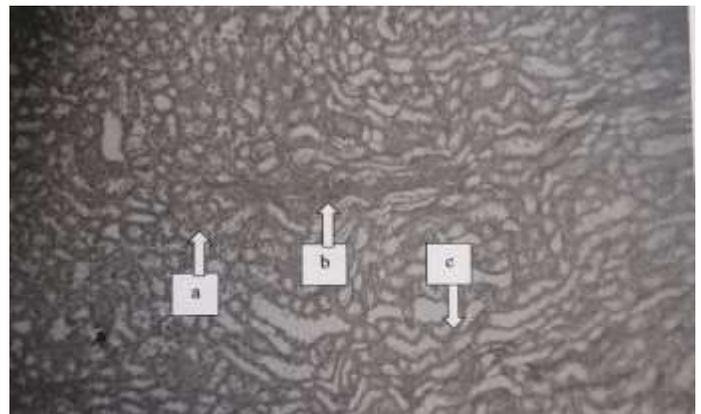


Figure 2

Histopathological features of a specimen from the PUUO + dehydration group (Group 4), showing granulocytes in the tubules (a), fibrotic focus in the medulla (b), and tubular deformities (c), stained with hematoxylin and eosin (H&E) at ×40 magnification



Among the experimental groups, Tmax increased most in Group 4, was moderate in Group 3, and was lowest in Group 2. Groups 2 and 4 showed a significant prolongation of mean renal perfusion time compared to the control group (p=0.01). Tc-99m DMSA imaging demonstrated significantly lower renal radionuclide uptake in all experimental groups compared to the control group (p=0.01). While DMSA uptake was significantly lower in Groups 3 and 4 compared to Group 2 (p=0.01), the analysis revealed no statistically significant difference between Groups 3 and 4 (p=0.12).

Macroscopic examination of the kidneys from rats revealed that Groups 3 and 4 exhibited the most pronounced hydronephrotic changes (Figure 1). Histopathological examination of the specimens showed no pathological findings in the control group. Two specimens from Group 2 showed tubular deformation was observed in two specimens from Group 2, while papillary and tubular deformation, as well as medullary edema, were observed in one specimen each. In Group 3, all specimens exhibited papillary deformation and the presence of granulocytes within the tubules. Additionally, tubular deformation and lymphocytic infiltration of the cortex were ob-

Table 3

Distribution of histopathological lesions across groups

Lesion Type	Group 1	Group 2	Group 3	Group 4
Papillary deformation	0	1	5	5
Tubular deformation	0	1	1	5
Granulocytes in tubules	0	2	5	5
Cortical lymphocytic infiltration	0	0	1	2
Medullary edema	0	1	0	5
Medullary calcification	0	0	0	2
Medullary hemorrhage	0	0	0	2
Pelvic hyperplasia	0	0	0	2
Total number of lesions	0	5	12	28

Note: Values represent the number of subjects exhibiting each lesion in the respective group.

served in one specimen each. Examination of Group 4 specimens revealed papillary and tubular deformation, granulocytes within the tubules, and medullary edema in all specimens (Figure 2). Lymphocytic infiltration, medullary calcification, medullary hemorrhage, and pelvic hyperplasia were observed in the cortex of two specimens each. Histopathological changes by group are summarized in Table 3.

4. Discussion

In cases of PUUO with both kidneys present, the contralateral kidney takes over as a compensatory mechanism, thereby maintaining overall urinary function¹⁰. Therefore, our study aimed to identify changes that may occur in a single kidney in the absence of compensatory effects from the contralateral kidney. In an experimental study comparing the effects of hydronephrosis on the kidney, no significant differences were observed in measurements between the fourth and ninth weeks¹¹. Consequently, we limited our study to four weeks. In our study, all rats in the PUUO groups exhibited significant dilatation of the renal pelvis and proximal ureter, confirming the effectiveness of the technique and its consistency with previous studies.

Experimental studies of chronic PUUO have focused primarily on normovolemic studies. Studies of unilateral PUUO reported that no changes in serum urea and creatinine levels are observed due to the compensatory effect of the contralateral kidney¹². In our study, blood urea and creatinine levels did not increase significantly in PUUO subjects who were not exposed to dehydration.

Acute dehydration is a state of negative fluid balance resulting from the rapid loss of total body fluid. It can occur due to factors such as inadequate fluid intake, diarrhea, vomiting, sepsis, or nephrotic syndrome.⁸ Previous experimental studies reported significant increases in serum urea and creatinine levels in rats after 24 and 48 hours of dehydration^{13,14}. In the present study, serum urea levels increased significantly in dehydrated subjects, whereas creatinine levels increased significantly only in Group 4 compared to the other groups. Furthermore, statistically significant increases in hematocrit and urine density in the dehydrated groups confirm the adequacy of the dehydration protocol. These findings suggest that rats with a single kidney can tolerate either acute dehydration or chronic PUUO alone; however, the coexistence of both conditions significantly compromises renal function.

In chronic UO, renal blood flow and GFR decrease¹⁵. In two separate studies in which the right kidney was preserved and PUUO was induced on the left side, significant and persistent reductions in GFR were observed in the obstructed kidney in the third, ninth, and fifteenth weeks^{16,17}. Similarly, Ozturk et al.¹⁸ reported an approximately 68% decrease in GFR over three weeks in a unilateral PUUO model where the right kidney was preserved. In our study, scintigraphic evaluations at the end of the four-week experimental period showed an 18% decrease in GFR in the dehydration group, a 23.3% decrease in the PUUO-only group, and a 33% decrease in the PUUO + dehydration group.

Previous clinical studies conducted under normovolemic conditions reported that UO prolongs the time to T_{max} on the renogram curve^{19,20}. Similarly, in our study, T_{max} values increased significantly in the experimental groups compared to the control group. This increase was most pronounced in Group 4.

Previous studies demonstrated that the use of vasodilatory agents such as captopril and L-arginine in models of PUUO resulted in relatively preserved renal perfusion after three weeks (59% and 64%, respectively)¹⁸. In the present study, no pharmacological agents that could enhance renal perfusion were administered. Nev-

ertheless, renal perfusion delay in Group 2 was approximately 2.5-fold higher than in the control group at the end of the fourth week. In Group 3, the delay was 1.5-fold, while in Group 4, it reached approximately 3-fold compared to controls. These findings indicate that dehydration markedly impairs renal perfusion, and this effect becomes even more pronounced when chronic left partial ureteral obstruction coexists.

Experimental studies in which unilateral PUUO was created showed a decrease in ^{99m}Tc-DMSA uptake in the obstructed kidney^{20,21}. Similarly, in the present study, the obstructed kidneys showed reduced uptake rates, and this reduction was statistically significant. These findings indicate that chronic PUUO causes more pronounced renal damage than dehydration, and the kidney sustains the greatest degree of injury when both conditions are present simultaneously.

In normovolemic experimental models, kidneys subjected to PUUO were reported to exhibit various histopathological alterations, including papillary deformities, widespread dilatation of collecting and convoluted tubules, and localized inflammatory and degenerative lesions^{22,23}. In the present study, histopathological examination of kidneys from the control group revealed no pathological changes. In rats that were only dehydrated, papillary deformity, tubular deformity, and medullary edema were observed in one sample each. Additionally, granulocytes were detected in the tubules of two samples. In the chronic PUUO group, all specimens exhibited papillary deformities and granulocyte accumulation in the collecting tubules, while dilatation of the collecting ducts and medullary fibrosis were each observed in one specimen. These results indicate that chronic PUUO exerts a more pronounced impact on renal histology than acute dehydration alone. Notably, in the group subjected to both PUUO and dehydration, all specimens displayed papillary deformity, collecting duct dilatation, and tubular convolution. We also observed interstitial lymphocyte infiltration within the cortex. Additionally, we observed medullary lymphocyte infiltration, medullary edema, and microcystic hyperplasia of the pelvic epithelium in two specimens. Taken together, these histopathological findings indicate that dehydration may exacerbate and accelerate the deleterious effects of ureteral obstruction on the kidneys.

4.1. Limitations

The limitations of this study include the small sample size, which may restrict the generalizability of the results. Additionally, the use of a rat model and the short duration of the experiment limit the direct applicability of the findings to humans. Only specific biochemical and imaging parameters were evaluated, while the effects of different degrees of obstruction and sex were not examined. Future studies with larger sample sizes and long-term follow-up are warranted to further validate these findings.

5. Conclusion

This study demonstrates that the detrimental effects of chronic PUUO alone on renal function and structure are more pronounced than those induced by acute dehydration. Furthermore, the addition of acute dehydration to chronic obstruction exacerbated renal injury and often caused irreversible damage. In patients with a solitary kidney affected by chronic PUUO, maintaining adequate hydration is critically important for preserving renal function and preventing further renal damage.

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Statement of ethics

The study was approved by the Local Ethics Committee for Animal Experiments of Harran University and was supported by the Harran University Scientific Research Projects Office (2002/9). All animal procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals and adhered to the ARRIVE guidelines

genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

This article is derived from the medical specialty thesis entitled "Kronik Parsiyel Üreter Obstrüksiyonlu Tek Böbrekli Sıçanlarda Akut Dehidratasyonun Böbrek Üzerine Etkileri," completed at the Faculty of Medicine, Harran University, in 2004, and registered in the National Thesis Center of the Council of Higher Education (Yükseköğretim Kurulu Ulusal Tez Merkezi) under registration number 156436.

URL:

<https://tez.yok.gov.tr/UlusalTezMerkezi/tezDetay.jsp?id=BNG-DqUCxOxYOSc-tTi7aOg&no=Pq8Yr-UhY0sZNRxZpp3cA>.

Author contributions

Concept, Design, Supervision (ASB, MK); Data Collection and/or Processing (ASB); Analysis and/or Interpretation (ASB, MK); literature review (ASB, ÇAA); writer (ASB), critical review (ASB, ÇAA); All authors have read and approved the final manuscript.

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