

Bölüm 3

OBSTRÜKTİF BÖBREK HASARINDA BİYOBELİRTEÇLER

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GİRİŞ

Üroloji pratiğinde en sık karşılaşılan sorunlardan biri üriner sistemin herhangi bir yerinde gelişen obstrüksiyon ve buna sekonder idrar stazıdır. Bu obstrüksiyon, üreteropelvik bileşke darlığı, taş, tümör, benign prostat hiperplazisi, üretra darlığı gibi anatomik nedenlere veya vezikoüreteral reflü, konjenital megaüreter, nörojenik mesane gibi fonksiyonel nedenlere bağlı olabilir. Obstrüksiyonun lokalizasyonu, tamamen veya kısmi obstrukte etmiş olması veya obstrüksiyonun süresi gibi faktörler oluşan hasar ile çoğu zaman ilintilidir. Örneğin infravezikal obstrüksiyonlarda nihai hasar çoğu zaman bilateral böbreklerde görülmekteyken, supravezikal ve unilateral olan patolojiler genelde ipsilateral böbreği etkiler. Genel olarak üriner sistem obstrüksyonlarının sebepleri konjenital ve edinsel olarak iki ana başlığa ayrılabilir. Konjenital ve edinsel sebeplerin detayı Tablo 1'de verilmiştir. Hidronefroz ise böbreğin toplayıcı sisteminin, kalıkslerinin ve pelvisinin genişlemesini ve kapasite artışını tanımlayan anatomik bir terimdir. Obstrüktif nedenlerle olabileceği gibi non-obstrüktif hidronefroz sebepleri de mevcuttur. Obstrüktif üropati, idrar yolunun herhangi bir seviyesinde idrar akışının fonksiyonel veya anatomin obstrüksiyonunu ifade eder. Obstrüktif nefropati ise obstrüksiyonun fonksiyonel veya anatomin renal hasara neden olduğu durumlarda ortaya çıkar¹.

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ortaya çıkmaktadır. Şu ana kadar obstrüktif böbrek hasarında yeterince tatmin edici duyarlı ve özgül bir biyobelirteç yoktur ancak son zamanlarda yapılan panel ve kombinasyon çalışmaları umut verici sonuçlar vermektedir.

KAYNAKLAR

1. Wiener SV, Stoller ML. Pathophysiology of Renal Obstruction. In: Chapple CR, Steers WD, Evans CP, eds. Urologic Principles and Practice. Cham: Springer International Publishing; 2020:185-200.
2. Murakumo M, Nonomura K, Yamashita T, et al. Structural changes of collagen components and diminution of nerves in congenital ureteropelvic junction obstruction. *The Journal of urology* 1997;157:1963-8.
3. Wang Y, Puri P, Hassan J, et al. Abnormal innervation and altered nerve growth factor messenger ribonucleic acid expression in ureteropelvic junction obstruction. *The Journal of urology* 1995;154:679-83.
4. Kajbafzadeh AM, Payabvash S, Salmasi AH, et al. Smooth muscle cell apoptosis and defective neural development in congenital ureteropelvic junction obstruction. *The Journal of urology* 2006;176:718-23; discussion 23.
5. McGuire EJ. Physiology of the lower urinary tract. *American journal of kidney diseases : the official journal of the National Kidney Foundation* 1983;2:402-8.
6. McGuire EJ, Woodside JR, Borden TA, et al. Prognostic value of urodynamic testing in myelodysplastic patients. *The Journal of urology* 1981;126:205-9.
7. Whitaker RH. Clinical assessment of pelvic and ureteral function. *Urology* 1978;12:146-50.
8. Drumond MC, Kristal B, Myers BD, et al. Structural basis for reduced glomerular filtration capacity in nephrotic humans. *The Journal of clinical investigation* 1994;94:1187-95.
9. Moody TE, Vaughn ED, Jr, Gillenwater JY. Relationship between renal blood flow and ureteral pressure during 18 hours of total unilateral urethral occlusion. Implications for changing sites of increased renal resistance. *Investigative urology* 1975;13:246-51.
10. Yared A, Kon V, Ichikawa I. Mechanism of preservation of glomerular perfusion and filtration during acute extracellular fluid volume depletion. Importance of intrarenal vasopressin-prostaglandin interaction for protecting kidneys from constrictor action of vasopressin. *The Journal of clinical investigation* 1985;75:1477-87.
11. Gobet R, Bleakley J, Cisek L, et al. Fetal partial urethral obstruction causes renal fibrosis and is associated with proteolytic imbalance. *The Journal of urology* 1999;162:854-60.
12. Klahr S, Morrissey J. Obstructive nephropathy and renal fibrosis. *American journal of physiology Renal physiology* 2002;283:F861-75.
13. Strimbu K, Tavel JA. What are biomarkers? *Curr Opin HIV AIDS* 2010;5:463-6.
14. Biomarkers Definitions Working G. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. *Clin Pharmacol Ther* 2001;69:89-95.
15. Radmayr C, Bogaert G, Dogan HS, et al. EAU Guidelines on Paediatric Urology 2020. European Association of Urology Guidelines 2020 Edition. Arnhem, The Netherlands: European Association of Urology Guidelines Office; 2020.
16. Cortes D, Jorgensen TM, Rittig S, et al. [Prenatal diagnosed hydronephrosis and other urological anomalies]. *Ugeskrift for laeger* 2006;168:2544-50.
17. American Society of N. American Society of Nephrology Renal Research Report. *Journal of the American Society of Nephrology : JASN* 2005;16:1886-903.

18. Wasilewska A, Taranta-Janusz K, Debek W, et al. KIM-1 and NGAL: new markers of obstructive nephropathy. *Pediatric nephrology* 2011;26:579-86.
19. Karabay E, Yucetas U, Aytac Ates H, et al. Neutrophil gelatinase-associated lipocalin is an early marker of renal damage in lower urinary tract obstruction in rats. *Arch Esp Urol* 2020;73:554-60.
20. Flower DR. The lipocalin protein family: structure and function. *The Biochemical journal* 1996;318 (Pt 1):1-14.
21. Kuwabara T, Mori K, Mukoyama M, et al. Urinary neutrophil gelatinase-associated lipocalin levels reflect damage to glomeruli, proximal tubules, and distal nephrons. *Kidney international* 2009;75:285-94.
22. Yavas H, Sahin OZ, Ersoy R, et al. Prognostic value of NGAL staining in patients with IgA nephropathy. *Renal failure* 2013;35:472-6.
23. Haase M, Haase-Fielitz A, Bellomo R, et al. Neutrophil gelatinase-associated lipocalin as a marker of acute renal disease. *Curr Opin Hematol* 2011;18:11-8.
24. Jin Y, Shao X, Sun B, et al. Urinary kidney injury molecule1 as an early diagnostic biomarker of obstructive acute kidney injury and development of a rapid detection method. *Molecular medicine reports* 2017;15:1229-35.
25. Xue W, Xie Y, Wang Q, et al. Diagnostic performance of urinary kidney injury molecule-1 and neutrophil gelatinase-associated lipocalin for acute kidney injury in an obstructive nephropathy patient. *Nephrology* 2014;19:186-94.
26. Olvera-Posada D, Dayarathna T, Dion M, et al. KIM-1 Is a Potential Urinary Biomarker of Obstruction: Results from a Prospective Cohort Study. *Journal of endourology* 2017;31:111-8.
27. Qian S, Xia W, Wu Y, et al. Urinary kidney injury molecule-1: a novel biomarker to monitor renal function in patients with unilateral ureteral obstruction. *Int Urol Nephrol* 2020;52:2065-72.
28. Karakus S, Oktar T, Kucukgergin C, et al. Urinary IP-10, MCP-1, NGAL, Cystatin-C, and KIM-1 Levels in Prenatally Diagnosed Unilateral Hydronephrosis: The Search for an Ideal Biomarker. *Urology* 2016;87:185-92.
29. Dong Y, Zhang Q, Wen J, et al. Ischemic Duration and Frequency Determines AKI-to-CKD Progression Monitored by Dynamic Changes of Tubular Biomarkers in IRI Mice. *Front Physiol* 2019;10:153.
30. Han WK, Alinani A, Wu CL, et al. Human kidney injury molecule-1 is a tissue and urinary tumor marker of renal cell carcinoma. *Journal of the American Society of Nephrology : JASN* 2005;16:1126-34.
31. Kennedy WA, 2nd, Butyan R, Garcia-Montes E, et al. Epidermal growth factor suppresses renal tubular apoptosis following ureteral obstruction. *Urology* 1997;49:973-80.
32. Lucarelli G, Mancini V, Galleggiante V, et al. Emerging urinary markers of renal injury in obstructive nephropathy. *BioMed research international* 2014;2014:303298.
33. Grandaliano G, Gesualdo L, Bartoli F, et al. MCP-1 and EGF renal expression and urine excretion in human congenital obstructive nephropathy. *Kidney international* 2000;58:182-92.
34. Bartoli F, Penza R, Aceto G, et al. Urinary epidermal growth factor, monocyte chemotactic protein-1, and beta2-microglobulin in children with ureteropelvic junction obstruction. *Journal of pediatric surgery* 2011;46:530-6.
35. Koyner JL, Vaidya VS, Bennett MR, et al. Urinary biomarkers in the clinical prognosis and early detection of acute kidney injury. *Clinical journal of the American Society of Nephrology : CJASN* 2010;5:2154-65.
36. Pavlaki A, Printza N, Farmaki E, et al. The role of urinary NGAL and serum cystatin C in assessing the severity of ureteropelvic junction obstruction in infants. *Pediatric nephrology* 2020;35:163-70.

37. Mao W, Liu S, Wang K, et al. Cystatin C in Evaluating Renal Function in Ureteral Calculi Hydronephrosis in Adults. *Kidney Blood Press Res* 2020;45:109-21.
38. Madsen MG, Norregaard R, Palmfeldt J, et al. Epidermal growth factor and monocyte chemoattractant peptide-1: potential biomarkers of urinary tract obstruction in children with hydronephrosis. *Journal of pediatric urology* 2013;9:838-45.
39. Kamijo-Ikemori A, Sugaya T, Matsui K, et al. Roles of human liver type fatty acid binding protein in kidney disease clarified using hL-FABP chromosomal transgenic mice. *Nephrology* 2011;16:539-44.
40. Xie Y, Xue W, Shao X, et al. Analysis of a urinary biomarker panel for obstructive nephropathy and clinical outcomes. *PLoS One* 2014;9:e112865.
41. Parmaksız G, Noyan A, Dursun H, et al. Role of new biomarkers for predicting renal scarring in vesicoureteral reflux: NGAL, KIM-1, and L-FABP. *Pediatric nephrology* 2016;31:97-103.
42. Noyan A, Parmaksız G, Dursun H, et al. Urinary NGAL, KIM-1 and L-FABP concentrations in antenatal hydronephrosis. *Journal of pediatric urology* 2015;11:249 e1-6.
43. Furuhata N, Shiba K, Nara N. [N-acetyl-beta-D-glucosaminidase]. *Nihon rinsho Japanese journal of clinical medicine* 1995;53:1267-76.
44. Price RG. Measurement of N-acetyl-beta-glucosaminidase and its isoenzymes in urine methods and clinical applications. *European journal of clinical chemistry and clinical biochemistry : journal of the Forum of European Clinical Chemistry Societies* 1992;30:693-705.
45. Carr MC, Peters CA, Retik AB, et al. Urinary levels of the renal tubular enzyme N-acetyl-beta-D-glucosaminidase in unilateral obstructive uropathy. *The Journal of urology* 1994;151:442-5.
46. Fahmy N, Sener A, Sabbisetti V, et al. Urinary expression of novel tissue markers of kidney injury after ureteroscopy, shockwave lithotripsy, and in normal healthy controls. *Journal of endourology* 2013;27:1455-62.
47. Skalova S, Rejtar P, Kutilek S. Increased urinary N-acetyl-beta-D-glucosaminidase activity in children with hydronephrosis. *International braz j urol : official journal of the Brazilian Society of Urology* 2007;33:80-3; discussion 4-6.
48. Bartucci R, Salvati A, Olinga P, et al. Vanin 1: Its Physiological Function and Role in Diseases. *Int J Mol Sci* 2019;20.
49. Hosohata K, Washino S, Kubo T, et al. Early prediction of cisplatin-induced nephrotoxicity by urinary vanin-1 in patients with urothelial carcinoma. *Toxicology* 2016;359-360:71-5.
50. Washino S, Hosohata K, Oshima M, et al. A Novel Biomarker for Acute Kidney Injury, Vanin-1, for Obstructive Nephropathy: A Prospective Cohort Pilot Study. *Int J Mol Sci* 2019;20.
51. Hosohata K, Jin D, Takai S, et al. Vanin-1 in Renal Pelvic Urine Reflects Kidney Injury in a Rat Model of Hydronephrosis. *Int J Mol Sci* 2018;19.
52. Fugmann T, Borgia B, Revesz C, et al. Proteomic identification of vanin-1 as a marker of kidney damage in a rat model of type 1 diabetic nephropathy. *Kidney international* 2011;80:272-81.
53. Sen CK. Cellular thiols and redox-regulated signal transduction. *Current topics in cellular regulation* 2000;36:1-30.
54. Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. *Clinical biochemistry* 2014;47:326-32.
55. Kasuno K, Nakamura H, Ono T, et al. Protective roles of thioredoxin, a redox-regulating protein, in renal ischemia/reperfusion injury. *Kidney international* 2003;64:1273-82.
56. Xu ZM, Li MJ, Tao C. Serum and urinary thioredoxin concentrations are associated with severity of children hydronephrosis. *Clinica chimica acta; international journal of clinical chemistry* 2017;466:127-32.

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57. Tokuc E, Urkmez A, Can U, et al. Evaluation of dynamic thiol-disulphide homeostasis in obstructive uropathy. *Int Urol Nephrol* 2020;52:821-8.
58. Laborde E. Glutathione transferases as mediators of signaling pathways involved in cell proliferation and cell death. *Cell Death Differ* 2010;17:1373-80.
59. Bienias B, Sikora P. Potential Novel Biomarkers of Obstructive Nephropathy in Children with Hydronephrosis. *Dis Markers* 2018;2018:1015726.
60. Madsen MG, Norregaard R, Palmfeldt J, et al. Urinary NGAL, cystatin C, beta2-microglobulin, and osteopontin significance in hydronephrotic children. *Pediatric nephrology* 2012;27:2099-106.
61. Spaggiari E, Faure G, Dreux S, et al. Sequential fetal serum beta2-microglobulin to predict postnatal renal function in bilateral or low urinary tract obstruction. *Ultrasound Obstet Gynecol* 2017;49:617-22.
62. Xie Y, Sakatsume M, Nishi S, et al. Expression, roles, receptors, and regulation of osteopontin in the kidney. *Kidney international* 2001;60:1645-57.
63. Kaneto H, Morrissey J, McCracken R, et al. Osteopontin expression in the kidney during unilateral ureteral obstruction. *Mineral and electrolyte metabolism* 1998;24:227-37.
64. Kajbafzadeh AM, Elmi A, Talab SS, et al. Urinary and serum carbohydrate antigen 19-9 as a biomarker in ureteropelvic junction obstruction in children. *The Journal of urology* 2010;183:2353-60.
65. Lopes RI, Denes FT, Bartolamei MG, et al. Serum and Urinary Values of CA 19-9 and TGFss1 in a Rat Model of Partial or Complete Ureteral Obstruction. *European journal of pediatric surgery : official journal of Austrian Association of Pediatric Surgery [et al] = Zeitschrift fur Kinderchirurgie* 2015;25:513-9.
66. Palmer LS, Maizels M, Kaplan WE, et al. Urine levels of transforming growth factor-beta 1 in children with ureteropelvic junction obstruction. *Urology* 1997;50:769-73.
67. Furness PD, 3rd, Maizels M, Han SW, et al. Elevated bladder urine concentration of transforming growth factor-beta1 correlates with upper urinary tract obstruction in children. *The Journal of urology* 1999;162:1033-6.
68. El-Sherbiny MT, Mousa OM, Shokeir AA, et al. Role of urinary transforming growth factor-beta1 concentration in the diagnosis of upper urinary tract obstruction in children. *The Journal of urology* 2002;168:1798-800.
69. Madsen MG. Urinary biomarkers in hydronephrosis. *Danish medical journal* 2013;60:B4582.
70. VanderBrink BA, Asanuma H, Hile K, et al. Interleukin-18 stimulates a positive feedback loop during renal obstruction via interleukin-18 receptor. *The Journal of urology* 2011;186:1502-8.
71. Gerber C, Harel M, Lynch ML, et al. Proximal tubule proteins are significantly elevated in bladder urine of patients with ureteropelvic junction obstruction and may represent novel biomarkers: A pilot study. *Journal of pediatric urology* 2016;12:120 e1-7.
72. Ozkuvancı U, Donmez MI, Ziyylan O, et al. Can urinary biomarkers detect obstruction defined by renal functional loss in antenatal hydronephrosis? *Journal of pediatric urology* 2020;16:844 e1- e7.
73. Yu L, Zhou L, Li Q, et al. Elevated urinary lipocalin-2, interleukin-6 and monocyte chemoattractant protein-1 levels in children with congenital ureteropelvic junction obstruction. *Journal of pediatric urology* 2019;15:44 e1- e7.
74. Kostic D, Beozzo G, do Couto SB, et al. The role of renal biomarkers to predict the need of surgery in congenital urinary tract obstruction in infants. *Journal of pediatric urology* 2019;15:242 e1- e9.