Animal Models of Partial Ureteral Obstruction (PUO) and Unilateral Ureteral Obstruction (UOO) in Renal Research

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Abstract: Urinary traction infection frequently occurs in the obstructed kidney. The ureters are the long narrow tubes in animals that carry urine from each kidney to the bladder. For human, the ureters are approximately 30 centimeters long. It exits the kidney at the hilum, comes into close contact with common iliac arteries from the aorta. The ureters pass on the lateral abdominal wall and then enters the pelvis where it joins the urinary bladder. For human, the ureters are approximately 30 centimeters long. It exits the kidney at the hilum, comes into close contact with common iliac arteries from the aorta.

Keywords: renal; complete ureteral obstruction (CUO); partial ureteral obstruction (PUO); unilateral ureteral obstruction (UUO)

Introduction
End-stage renal disease (ESRD) is a big health problem in the United States and it costs more than $30 billion each year on ESRD therapy in this country. The patients suffering from acute renal failure are even worse. The disease state arising from renal failure is the result of many factors. It is important to reveal the kidney's role in reclamation of metabolic substrates, synthesis of glutathione, freeradical scavenging enzymes, gluconeogenesis, ammoniagenesis, hormones, growth factors, and the production and regulation of multiple cytokines critical to inflammation and immunological. There is considerable drive to develop improved therapies for renal failure. It is estimated that there are over 2 million patients in USA who suffer from end-stage renal disease. About 60,000 patients in the United States are currently on the waiting list for a kidney transplant, and some patients have waited for several years before an appropriate donor can be found (Ma, et al, 2009a). Kidney is derived from the ureteric bud and metanephrogenic mesenchyme (Ma, et al, 2009b). It is important to develop the animal models in the renal research.

The ureters are the long narrow tubes in animals that carry urine from each kidney to the bladder. For human, the ureters are approximately 30 centimeters long. It exits the kidney at the hilum, comes into close contact with common iliac arteries from the aorta. The ureters pass on the lateral abdominal wall and then enters the pelvis where it joins the urinary bladder, passing a short distance into it. Obstructive nephropathy is a serious problem for many patients in the chronic kidney disease. The kidney function declined in obstructive nephropathy is associated with structural derangements, which is reparative in an attempt to overcome the kidney injury caused by the obstruction of urine flow. With sustained obstruction, a permanent loss of renal function may occur. In this problem, renal fibrosis becomes a reactive process. Partial ureteral obstruction (PUO) and unilateral ureteral obstruction (UOO) produce well documented triphasic responses in the renal hemodynamics and renal damage. This is characterized by an early increase in renal blood flow, followed by a decrease toward baseline, and later progressive profound renal ischemia. A lot studies have been performed in rodent models of unilateral urinary tract obstruction.

In a mouse model of complete PUO, the angiotensin system regulates about half of the renal interstitial fibrotic response in the obstructed kidney (Fern et al., 1999). At some stage of obstructive nephropathy, pharmacological inhibition of the angiotensin system may not be effective to reduce renal fibrosis and irreversible renal damage would ensue (Klahr and Morrissey, 1998) (Fern et al., 1999; Klahr and Morrissey, 2002). Interstitial fibrosis is a complex process involving inflammatory cell infiltration, fibroblast...
proliferation, epithelial-mesenchymal transition, excessive extracellular matrix accumulation, and reduced matrix degradation (Bohle et al., 1994). This process is a saline feature of progressive renal disease and its extent correlates with renal function deterioration in either glomerular or tubulointerstitial diseases (Bohle et al., 1994; Nath, 1992). In obstructive nephropathy, inflammatory cells appear in the interstitial space shortly after urinary tract obstruction, releasing cytokines and growth factors which stimulate the fibrotic process (Fern et al., 1999; Klahr and Morrissey, 1998). Many studies have shown that inhibition of the renin-angiotensin system or transforming growth factor-β (TGF-β) ameliorates obstruction-induced tubulointerstitial fibrosis, suggesting that angiotensin II and TGF-beta are involved in the development of fibrosis (Guo et al., 2001; Isaka et al., 2000; Klahr and Morrissey, 1998; Miyajima et al., 2000).

**Surjury propotols**

1. Partial ureteral obstruction (PUO):

   The rats are anesthetized with sodium pentobarbital (50 mg/kg, i.p.) and a low midline abdominal incision is made. Right nephrectomy is performed first. The right kidney is mobilized with minimal dissection. Two 0-0 silk ties are placed around the hilar vessels and the right kidney is removed. The left ureter is then traced to its insertion in the bladder, mobilized with minimal dissection to preserve the surrounding neurovascularure and retracted with vessel loops. The psoas muscle is split by blunt dissection to create a space which would accommodate two-thirds of the length of the ureter. The left ureter is moved into that interstice, after which the muscle is reaproximated with three interrupted 5-0 silk sutures. The abdominal wound is then closed with sutures (Figure 1). For the sham operation, the rats underwent the same surgical procedure, including right nephrectomy, but the left ureter is diverted into the psoas muscle. After recovery from anesthesia, the rats are housed individually in metal cages and given buprenorphine hydrochloride (0.02 mg/kg BW, i.m.) to relieve postoperative discomfort. One night before the surgery and clearance experiments, the rats fast but have free access to water.

2. Unilateral ureteral obstruction (UUO):

   Rats or mice are anesthetized by i.p. injection, and then shaved on the left side of the abdomen. A vertical incision is made through the skin with a scalpel and the skin is retracted. A second incision is made through the peritoneum and that skin is also retracted to reveal the kidney. Using forceps the kidney is brought to the surface and the ureter is tied with surgical silk, twice, below the kidney. The ligated kidney is placed gently back into its correct anatomical position and sterile saline is added to replenish loss of fluid. The incisions are sutured and mice are caged individually. About 6-days post ligation, the animals are placed in metabolic cages for the collection of urine. Animals are sacrificed 12-hours later and blood and tissues are collected when the sacrificing.

3. Reversal of unilateral ureteral obstruction (R-UUO) injury by mouse model

   To induce UUO injury, male C57bl/6J mice (6–8 weeks, 20–25 g) are anaesthetized with 2% inhaled isofluorane. A small left flank incision was made to access the kidney and the ureter is obstructed using a stainless steel B-1V vascular clamp (0.4–1.0 mm). Incisions are sutured and the ureter remain obstructed for 10 days before kidney collection for analysis of obstruction injury, or a second surgery to reverse obstruction and initiate repair. Surgery for R-UUO is as for the induction of UUO with the exception that the vascular clamp is carefully removed from the ureter to allow urine reflow.

**Discussion**

Complete ureteral obstruction is not a usual cause of human renal disease. PUO and UUO models are useful to examine mechanisms of tubulointerstitial fibrosis in vivo. These models can be induced in either rats or mice and other animals and there is no specific strain dependence. Partial or reversible UUO models are useful techniques in the kidney study. PUO and UUO are good models for the renal research with animals.

Kidney disease is a significant medical problem globally. In the nephrology researches, there are several other models and ways besides PUO and UUO. The following are some examples:

1) Culture renal cells in the research.
2) Glomerular and interstitial injury models
3) Vascular injury models
4) Podocyte-specific genetic models
5) HIV-associated nephropathy transgenic model
6) Alport syndrome mutation model
7) Immune-induced model
8) Non-immune induced model
9) Radiation nephropathy model
10) Puromycin aminonucleoside nephrosis and adriamycin nephropathy
11) Complete ureteral obstruction (CUO)
12) Folic acid nephropathy
13) CyA nephropathy
14) DOCA-salt nephropathy
References


