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The Effect of Acute Chemical Sympathectomy on the Competence of the Canine Ureterovesical Junction*

Alan J. Wein, Joseph V. Leoni, David M. Raezer, David M. Jacobowitz, and Joseph N. Corriere, Jr.

Division of Urology, Department of Surgery, Philadelphia Veterans Administration Hospital, Hospital of the University of Pennsylvania, Philadelphia, and the Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, U. S. A.

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Summary. Selective chemical destruction of the adrenergic nerve terminals in the dog bladder with 6-hydroxydopamine does not result in vesicoureteral reflux. The sympathetic nerve supply of the bladder does not appear to play a role in maintaining the normal competence of the ureterovesical junction.

Key words: Ureterovesical junction, vesicoureteral reflux, chemical sympathectomy.

The competence of the ureterovesical junction is attributed to both passive and active forces. The passive forces preventing reflux are produced by the oblique submucosal and intramural course of the ureter which is supported by a backing of detrusor muscle fibers.

Tanagho et al. (3, 4) demonstrated ipsilateral vesicoureteral reflux following unilateral lumbar sympathectomy. They coupled this finding with the fact that the bladder is anatomically divided into the trigone, which is attached to the ureters and heavily innervated with sympathetic fibers, and the detrusor, to conclude that active contraction of the trigone may be important in preventing vesicoureteral reflux.

On the other hand, Torbey and Leadbetter (6) produced vesicoureteral reflux by sectioning the parasympathetic sacral nerve roots which supply the detrusor and failed to produce reflux after surgical sympathectomy. These authors pointed out that surgical sympathectomy is probably never complete without vascular division and felt that sympathectomy results are usually inconclusive.

This difficulty has recently been overcome by the demonstration that the drug 6-hydroxydopamine (6-OHDA) produces both an acute and chronic total chemical sympathectomy in vivo. (5, 8, 9, 7) Herein we report the effect of acute selective chemical destruction of the adrenergic nerve terminals in the canine on the competence of the ureterovesical junction.

Materials and Methods

Five adult female mongrel dogs weighing between 20 and 36 kilograms were studied. Intravenous sodium pentobarbital (12.5 mg/kg) was used for anesthesia. Prior to denervation the bladder was filled with sodium acetrizoate 30% (Cystokon^{R}, Mallinckredt Chemical Works, St. Louis, Mo.) through a 12 french Foley catheter. The radiopaque reservoir was held to a height of 50 cm, the bladder filled to capacity at that pressure, and a static x-ray performed. All cystograms were done with the animals in the supine position.

Chemical sympathectomy of the bladder was then produced by inserting a polyethylene catheter through the femoral artery so that the tip lay at or just above the aortic bifurcation and then slowly injecting into the arterial

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circulation, over a 20 min period, 1.5 mg/kg of 6-hydroxydopamine (6-OHDA) dissolved in a saline-ascorbic acid solution (0.1%) (5). We have previously shown that at this dose, the drug 6-OHDA will produce sympathetic nerve terminal destruction in the canine bladder (8).

After a four to five hour waiting period, necessary for the full pharmacologic effect of the drug and restabilization of the animal, the cystogram was repeated as previously described.

Following the final cystogram, tissue was obtained from the dome, trigone and ureterovesical junction areas of two dogs for histochemical determination of catecholamine content by our previously described method (8) to insure adequate denervation.

Results

No animal exhibited vesicoureteral reflux prior to or following the 6-OHDA treatment. Histochemical observations in the two dogs so studied showed essentially no varicose terminals remaining in proximity to the musculature of the dome, trigone or ureterovesical junction. This is in accord with our previous observations using this drug (5, 8, 9, 7) and confirms the completeness of the sympathetic nerve terminal destruction.

Discussion

This study supports Torbey and Leadbetter's (6) observations that vesical sympathectomy does not produce vesicoureteral reflux. Tanagho et al. (3, 4) based their belief that a sympathetically mediated trigonal contraction is a major contributor to ureterovesical competence in part on considerations that the trigone and ureters are an anatomic and embryologic unit separate from the detrusor, and the formerly held theory that the trigone possessed the bulk of the sympathetic innervation in this area.

However, on the basis of neurophysiology and pharmacologic responses to autonomic agents, the bladder has since been found to functionally be more appropriately divided between its body and base than between the trigone and detrusor (1). The bladder base, which includes both the trigone and the detrusor muscle, circumferentially distal to the ureterovesical junction, appears to be uniformally innervated and works physiologically and pharmacologically as a unit (2).

The only objection that could be raised to our model is whether a period of time must elapse after the sympathectomy for the reflux to occur. In Tanagho's series (5) of five dogs on whom unilateral sympathectomy was performed, none of the immediate postoperative cystograms showed reflux. Ipsilateral reflux appeared subsequently in all dogs from five to twenty-two days postoperatively, and, in two dogs, on the contralateral side as well. We have followed a series of four dogs whose bladders were kept sympathectomized by biweekly intraperitoneal injections of 6-OHDA (10). At three months one ureter in one animal exhibited grade one reflux; we feel it is very questionable whether this can be attributed to the drug induced sympathetic terminal destruction, considering the fact that the other seven ureters did not show reflux at this time. Why sectioning of the lumbar sympathetics by Tanagho et al. (3) resulted in reflux remains obscure. Perhaps the reflux was secondary to physical changes or inefficient detrusor function created by the surgical procedure rather than the primary result of the supposed denervation.

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References

1. Raezer, D.M., Wein, A.J., Jacobowitz, D., Corriere, J.N., Jr.: Autonomic innervation of the canine urinary bladder, Urology 2, 211 (1973)
2. Raezer, D.M., Greenberg, S., Benson, G., Jacobowitz, D., Corriere, J.N., Jr.: The innervation of the trigonal area of the canine urinary bladder. Urology (in press)
3. Tanagho, H.A., Hutch, J.A., Meyers, F.H., Rambo, O.N., Jr.: Primary vesicoureteral reflux: Experimental studies of its etiology. J. Urol. 93, 165 (1965)
4. Tanagho, E.A., Meyers, F.H., Smith, D.R.: The Trigone: Anatomical and physiological considerations. 1. In relation to the ureterovesical junction. J. Urol. 100, 623 (1968)
5. Thoener, H., Tranzer, J.P.: The pharmacology of 6-hydroxydopamine. Ann. Rev. Pharmacol. 13, 169 (1973)
6. Torbey, K., Leadbetter, W.F.: Innervation of the bladder and lower ureter: Studies on pelvic nerve section and stimulation in the dog. J. Urol. 90, 395 (1963)
7. Wein, A.J., Leoni, J.V., Gregory, J.G., Schoenberg, H.W., Jacobowitz, D.M.: The effect of 6-hydroxydopamine on canine ureteral contractility: Further evidence in favour of a non-neurogenic theory of ureteral function. J. Urol. 108, 402 (1972)
8. Wein, A.J., Jacobowitz, D.M., Corriere, J.M., Jr., Murphy, J.J.: Chemical sym-

pathectomy with 6-hydroxydopamine: A useful research tool. Surg. Forum 24, 560 (1973)
9. Wein, A.J., Gregory, J.G., Cromie, W. J., Corriere, J.N., Jr., Jacobowitz, D.M.: Sympathetic innervation and chemical sympathectomy of the canine urinary bladder. Urology 4, 27 (1974)
10. Wein, A.J., Gadbois, W.F., Raezer, D.M., Benson, G.S., Jacobowitz, D., Corriere, J.N., Jr.: The effect of long-term chemical sympathectomy on the function of the canine urinary tract. (in preparation)

Alan J. Wein, M.D.
Suite W-310
Hospital of the University
of Pennsylvania
3400 Spruce Street
Philadelphia, PA 19104
U.S.A.

Responsible for the text: Prof. Dr. F. Truss, Urolog. Klinik und Poliklinik für Urologie der Univ. Göttingen.
Responsible for advertisements: L. Siegel, D-1000 Berlin 15, Kurfürstendamm 237.
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