Review Article

Effects of Progesterone on the Urinary Tract

S. E. Swift and D. R. Ostergard
Division of Urogynecology, Department of Obstetrics and Gynecology, University of California, Irvine, Long Beach Memorial Women’s Hospital, Long Beach, California, USA

Abstract: The effects of progesterone on the urinary tract are not thoroughly discussed in the literature except with respect to hydronephrosis of pregnancy. This article is a comprehensive review of the effects of progestational agents on the ureter, bladder and urethra and the possible clinical uses of this hormone. From the data in the literature, it appears that progesterone brings about relaxation of smooth muscle in the urinary system, which may be important clinically in managing menopausal women on hormone replacement, as well as younger women using oral contraception.

Keywords: Bladder; Progesterone effects; Urethra; Ureter

Introduction

The data on the effects of progesterone on the urinary tract stem mainly from observations during pregnancy, when there is a relative increase in progesterone. The well recognized physiologic hydroureter of pregnancy, an increased bladder capacity, and an increased incidence of genuine stress incontinence during pregnancy, are all felt to be due in some degree to the effects of progesterone. These changes in structure and function are attributed to the relaxative effect of progesterone on the smooth muscle of the urinary system.

The Ureter

There is some disagreement in the literature as to the cause of the physiologic hydroureter of pregnancy, whether it is due to mechanical obstruction or hormonal causes or both. Roberts, in a review article, presents strong evidence for a predominantly obstructive cause:

1. The absence of hydronephrosis when the ureter does not cross the pelvic brim, i.e. those patients with pelvic kidneys or ileoceocuts.
2. The finding that dilatation and elevated ureteral pressures can be decreased by elevating the pregnant uterus off the ureters with positional changes.
3. That hydronephrosis of pregnancy does not occur in quadrupeds, where the uterus hangs away from the ureters.
4. That neither peristaltic activity nor compliance of the ureter is changed with in vivo studies of human or animal ureters, and this effect is only noted with in vitro studies where very high non-physiologic doses of progesterone are used [1].

These arguments have been echoed by several other authors, who agree that the hormonal influence on the physiologic hydroureter of pregnancy is negligible [2,3].

However, there are several studies that contradict some of the points in Roberts’ article and suggest some effect of progesterone on the ureter. In a classic study by Van Wagenen et al., they were able to demonstrate the development and maintenance of a hydroureter in rhesus monkeys after the removal of the fetus, where the hormonal effect was maintained by leaving the placenta in situ [4]. Their study involved eight monkeys. In two, the fetus was removed prior to the development of a hydroureter, and in both cases the subjects went on to develop ureteral dilatation. In five of the six
remaining monkeys, ureteral dilatation persisted after removal of the fetus, thus suggesting a role for the hormonal milieu of pregnancy in bringing about the hydronephrosis. Using ultrasound to measure renal calyces in rabbits, Ishihara et al. demonstrated increasing dilatation throughout pregnancy, beginning in the first trimester. They found hydronephrosis in progesterone-treated ovariectomized rabbits as well, and concluded that early in pregnancy, ureteral dilatation was due to hormonal influences [5]. Lubens et al. evaluated the effects of progesterone and estrogen on postpartum patients with physiologic hydronephrosis documented by IVP. They were able to maintain or increase the degree of ureteral dilatation in 5 of 6 patients who received progesterone, and demonstrated regressive changes in 5 of 6 patients receiving estrogen. Six patients that served as controls, and received neither estrogen nor progesterone, showed slight regression or no change at all [6]. Although the problem with this study was the small number of patients, they noted an increase in the degree of ureteral dilatation only in those patients who received progesterone.

Hundley and Diehl measured the peristaltic activity in the ureters during pregnancy and noted that activity steadily decreased, starting in the first months of pregnancy and continuing through the 9th month, where they noted almost complete atony [7]. In cases of mechanical ureteral obstruction, there tends to be an initial increase in the peristaltic activity of the ureter as it attempts to overcome the obstruction. Then, as the ureters dilate, they eventually become somewhat atonic. However, they did not note increased activity at any point during the course of pregnancy to suggest an early mechanical obstruction, and therefore postulated a hormonal cause. In 1945, they evaluated the effects of prolonged exposure to progesterone and estrogen on the ureter in non-pregnant females. The subjects received 9–10 weeks of either oral estrogen or I.M. and oral progesterone. In those patients receiving estrogens, there was an increase in the peristaltic activity and in those patients receiving progestational agents, there was a gradual decrease in peristalsis to complete atonia, similar to that noted in their previous study on pregnant women [8]. Marchant and Miller also noted a decrease in ureteral peristalsis in females receiving large doses of hydroxyprogesterone (1000 mg per week), but noted no changes with lower doses of norethynodrel (5–30 mg per week) [9]. One explanation for this may be that norethynodrel may have different effects on the GU smooth muscle as it is a nor-androgen (C19 compound). Studies on ureters in vitro obtained at the time of nephrectomy have also demonstrated a decrease in the spontaneous peristaltic activity when exposed to progesterone. Similar responses of gastric and colonic smooth muscle to progesterone have also been demonstrated, [10]. Other investigators have likewise come to the conclusion that progesterone leads to relaxation of the ureters, and does play a role in the hydronephrosis of pregnancy [11].

The physiologic hydronephrosis of pregnancy arises from a combination of both mechanical and hormonal factors. How much effect is contributed by each is still unknown, and not the purpose of this discussion. However, from the studies mentioned, it does appear that progesterone causes some degree of relaxation of the smooth muscle of the ureter, both in vitro and in vivo under physiologic conditions (Fig. 1).

**The Bladder**

The data on the effects of progesterone on the bladder again come mainly from observations during pregnancy. Langworthy and Brach noted in the course of experiments on the nervous influence of vesical activity in cats, that they needed to exclude pregnant felines from their study because their bladders were able to hold unusually large volumes at low pressures. They then measured the capacity in pregnant rabbits and in rabbits artificially induced to ovulate. It was noted that in both states, there was at least a 50% increase in the bladder capacity over pretreatment or prepregnant values [12]. Muellner did 86 cystometrograms on 50 women during pregnancy, and noted that bladder capacity increased throughout pregnancy, beginning at 3 months and lasting through 6–8 weeks postpartum. They noted maximum bladder capacities up to 1300 ml in the third trimester, and showed a decrease in the filling pressures during the cystometrograms [13]. However, there was no increase in the postvoid residuals, as would be expected if these changes were due to an obstruction of the outlet by the enlarging uterus. Therefore, they attributed the changes in bladder capacity and tone to progesterone. Youssef confirmed these studies in 1956 [14]. He performed supine cystometrograms on 10 women throughout pregnancy, and noted increased maximal capacity (patients tolerated up to 1200 ml) and decreased absolute intravesical pressure as pregnancy progressed. These changes were noted from the early