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Renal anomalies in Down syndrome

Key words: Renal anomalies – Down syndrome

Sirs,

We read with interest the comments by Ehrich [1] and by Robson and Leung [2] in this journal about renal replacement therapy and renal abnormalities, respectively, in children with Down syndrome. Since there are only a few reports, we reviewed the outpatient charts of all children with Down syndrome who were seen in the Pediatric Cardiology Clinic at James H. Quillen College of Medicine and East Tennessee State University, Johnson City, Tennessee. This report describes our findings and a review of the literature.

Fifty-four children (34 males, 20 females) aged 2 months to 24 years (median 4.5 years) with Down syndrome were seen in our clinic over the last 8 years. Clinical history and laboratory data were reviewed for any possible renal disorder. Follow-up data were obtained from the primary physician either by questionnaires or by'phone, or by both. Of the 54 patients, 40 had congenital heart disease. All had normal urinalysis. Serum creatinine and blood urea nitrogen were measured in 28 children and were normal. Thirteen children had flat plate of the abdomen immediately after cardiac catheterization to visualize the kidney, ureter, and bladder; these were normal in all.

Six children had symptoms related to their urinary tract; 3 of these, all females, had recurrent urinary tract infections. Further investigations with one or more of the following tests: voiding cystourethrography, abdominal ultrasound, intravenous pyelography, and blood urea nitrogen and serum creatinine were performed in these 3 patients, but all were within normal limits. One male child had urethral stricture that required repeated dilatations following surgical correction. This child had a normal functioning kidney as indicated by a normal blood urea nitrogen and serum creatinine. No further details are available about this child. Of the 6 patients, 2 developed acute renal failure following angiotensin converting enzyme (ACE) inhibitor therapy for cardiac failure and died. One of them had normal kidneys by gross and microscopic examination at autopsy; the other patient did not have an autopsy.

From our limited retrospective clinical data, the incidence of renal anomalies in children with Down syndrome does not appear to be higher than in the normal population. It should be noted that our series did not include fetuses, still-borns, or infants with Down syndrome who may have died in the nursery with renal disease. Hitherto, three autopsy studies have reported renal anomalies in children with Down syndrome. In 1960, Berg et al. [3] reported 4 patients with renal agenesis or hypoplasia and 1 with horseshoe kidney of 141 autopsies (2.8%) of patients with Down syndrome. In 1973, Egli and Stalder [4] reported renal anomalies in 7 of 103 autopsies (6.7%) of children with Down syndrome (cysts 2, hydronephrosis 1, hydroureter 3, ureteral stenosis 2, megacystitis 3). In 1991, Ariel et al. [5] reported renal anomalies, such as renal hypoplasia, cysts, and obstructive uropathy (4% in infants and children, 15% in still-borns and fetuses), in 124 autopsy cases of Down syndrome.

Besides these and other reports [6, 7] of congenital renal anomalies, there are few isolated reports of acquired renal disorders in children with Down syndrome, such as chronic glomerulonephritis [2], mesangiocapillary glomerulonephritis [8], and immunolactoid glomerulopathy [9]. Nonstructural renal disorders, such as hyperuricemia and a decrease in the clearance of uric acid and creatinine, are also reported in children with Down syndrome [10].

Although 6 patients in our series had signs and symptoms of renal disease, none had renal pathology except for 1 child who had urethral stricture. Two children (a 5-year-old male and a 5-month-old female) with heart failure and Down syndrome developed renal failure after ACE inhibitor therapy and died before renal replacement therapy. An association between ACE inhibitor therapy and acute renal dysfunction has been noted in patients with bilateral renal diseases such as polycystic kidney [11], bilateral renal artery stenosis, and scleroderma [12]. Neither of our 2 patients had any preexisting renal disease. Both had normal urinalysis and normal blood levels of urea and creatinine prior to ACE inhibitor therapy. One also had a normal gross and microscopic examination of both kidneys at autopsy. Nevertheless, several minor renal abnormalities, such as immature glomeruli [7], renal hypoplasia or relatively small kidney [13], maturation delay of nephrogenic zone of cortex, and persistent fetal lobulation, are reported in children with Down syndrome [13, 14]. These abnormalities may predispose to a high risk for renal failure when exposed to ACE inhibitors.

From our data and those of others [3–5], the incidence of clinically significant renal anomalies does not appear to be higher in children with Down syndrome than in the general population. We, however, recommend that caution should be exercised when using ACE inhibitors in children with Down syndrome and congestive heart failure. A larger clinical study of a similar cohort may further delineate this issue.

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Approval of cysteamine for patients with cystinosis

Key words: Cysteamine – Cystinosis – Cystagon

Sirs,

This letter is to inform readers of *Pediatric Nephrology* that cysteamine has been approved by the United States Food and Drug Administration for use in individuals with nephropathic cystinosis. The approved drug is cysteamine bitartrate capsules which are manufactured by Mylan Pharmaceuticals (Morgantown, West Virginia, USA). The trade name is Cystagon and its sole distributor in the United States is Chronimed Pharmacy which is a mail-order pharmacy in Minnetonka, Minnesota (800-444-5951). Hopefully, nephrologists presently caring for pre-transplant cystinosis patients have already been notified about Cystagon. It is important that physicians caring for transplanted cystinosis patients know about Cystagon, since we feel these patients will also benefit from this drug.

Patients who have not been receiving cysteamine should have a baseline white blood cell cystine measurement before starting the drug. Cystagon should be started at a low dose and increased over several weeks until the therapeutic dose is reached. Information concerning cystine determination can be obtained from Dr. Alice Greene (619-534-2212); information regarding dosing schedules can be obtained from Karen Clark (619-534-7966). Both can be reached by fax at 619-534-1084.

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