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우리나라의 학교소변검사 프로그램

영남대학교 의과대학 소아청소년과

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School Urine Screening Program in Korea

A number of kidney diseases of childhood may present as isolated proteinuria or/and hematuria, without any overt signs or symptoms. Urinalysis is a simple and inexpensive test used to evaluate various renal disorders. A school urine screening (SUS) program for kidney disease was conducted in Korea in 1998. Several research reports, including case reports and systemic reviews of SUS data, claimed that early detection and confirmatory diagnosis by renal biopsy seems to be helpful for determining the prognosis and intervention of progressive chronic renal disease. However, there is no global consensus as to whether screening for chronic kidney disease (CKD) should be undertaken in children and adolescents. This paper reviews the SUS for CKD in Korea, including the history and structure of the program, its assessment, related research, and associated problems.

Key words: School, Urine, Screening, Program

Introduction

Although screening urinalysis for CKD in adults is important [1, 2], it is still controversial in children. The primary basis for this controversy is the uncertainty as to whether early detection of renal disorders in childhood will lead to effective interventions and reduction in the number of individuals who develop end-stage renal disease (ESRD). Japanese, Taiwanese, and Korean pediatric nephrologists agree that screening programs have led to early detection and effective intervention [3-5]. However, there is no global consensus as to the role of screening for CKD. There is also controversy in its cost-effectiveness. The most common method of screening children for CKD involves the detection of hematuria and/or proteinuria in spot urine samples [3].

Even though the number of children with CKD requiring renal replacement therapy is relatively low compared to adults, CKD is the forerunner

of ESRD which cause societal burden with serious morbidity and mortality. The annual incidence of CKD was 3.68/million child population per year surveyed by the Korean Pediatric Nephrology Association in 2000 [6]. The Korean Pediatric Chronic Kidney Disease registry reported that the incidence of patients with newly developed ESRD was 3.3/million in 2009 and the leading cause of ESRD is childhood glomerulonephritis [7]. However, renal diseases usually develop without obvious symptoms and signs and can progress to CKD. Consequently, the best "treatment" for CKD and ESRD in children must be prevention. Public education, genetic screening, family counseling, prenatal diagnosis of congenital abnormalities of the kidney and urinary tract (CAKUT) and genetic renal diseases, and school screening programs can help prevent kidney disease. The success of disease prevention required the support and cooperation of the government-related organization, as well as the school board, students, families of students, and the community [8].

History of the SUS program

Regulation of the school health care program for school children by the Korean Education Ministry was enacted more than 50 years ago. Mass urine screening program was not included in these early programs and was implemented only upon each individual school's decision [5]. In 1997, this ordinance was amended to allow for annual SUS for all elementary, junior and senior high school students included in the school health care program [9]. SUS program has been conducted detect glomerulonephritis at an early stage and allow for prompt therapeutic intervention in Japan since 1974 [10]. The same has been done on a regular basis (Korea, Taiwan) or occasional basis (Philippines, Singapore and China) in Asian countries thereafter [4].

In the early enforcement period, school health-care staffs took responsibility for their SUS program with the Korean government providing full financial support. Given that more than 7 million school children, approximately over 10% of the total population were enrolled in the SUS program, the enforcement of school health care became more challenging. In addition, children, their families, physicians and communities became more aware of and concerned with renal disease [11]. Eventually, the Ministry of Education amended the SUS program regulation in 2005. SUS has been conducted during the 1st and 4th grades of elementary school, and 1st grade of junior and senior high schools instead of all students. SUS for students in other grades who were excluded from the regular health care program can still be carried out based on the individual school committee's decision. School physicians should carry out school health promotion program including SUS and schools have to continue providing full financial support [5]. This system is still being maintained to date, with approximately 5 million students screened annually. The Ministry of Educational Science & Technology reported that participants in SUS included more than 97.5% of all the students and the prevalence of proteinuria and hematuria in 2004 was 0.19% and 0.88%, respectively [7].

Considerations of SUS

1. Examination of the urine

Urine containers were distributed to students the day prior to testing to ensure appropriate specimen collection. Children were instructed to completely empty the bladder the night before, and the first morning voided specimens were tested using the dipstick method to detect urinary protein and occult blood. Dipstick test was performed by a school primary care physician, although it was done at school by the school health-care staff during the early days. Female adolescents were instructed to avoid urinalysis during menstruation and to provide a urine sample for dipstick test at least 1 week after menstruation has ended.

A positive result was defined as +1 or higher in protein or occult blood during the 1st screening test. If the 1st test was positive, a second test was performed in the same manner. In cases with positive result, urinalysis with microscopic examination and/or other laboratory tests related to renal function as well as detailed history

and physical examination were conducted at a hospital of the student's choice. If urinary abnormalities persisted or any abnormal history, symptoms, signs or any associated urinary anomalies were found in the evaluation at the primary care clinic, the child was strongly recommended to visit a pediatric nephrologist for further evaluation (Table 1) [5]. Unfortunately, this process may not be carried out properly during its implementation.

2. Assessment of the SUS' result

The Korean Education Development Institute proposed guidelines for assessing SUS results. If hematuria and/or proteinuria in the 1st SUS were combined with signs and symptoms of renal disease such as previous renal disease history, hypertension, edema, or oliguria, an underlying renal disease should be suspected and further evaluation was recommended at the 2nd examination (Table 2). Microscopic examination can rule out the occurrence of false-positive hematuria. Hematuria was defined as an erythrocyte excretion rate of over 5 red blood cells per high-power field in the centrifuged urine. Regular follow-up urinalysis and noninvasive renal function tests were performed for those with persistent isolated microscopic hematuria.

The type of proteinuria was classified into transient proteinuria, orthstatic proteinuria and persistent nonorthostatic proteinuria. Transient proteinuria was characterized by the disappearance of urinary protein following one or more positive tests. Heavy exercise, history of significant illnesses, fever, and significant heat or cold stress are some clues for the diagnosis of transient proteinuria. Orthostatic proteinuria, the most common manifestation of isolated proteinuria, present only when the patient is in upright position and is not associated with abnormal renal function or hypertension. Recumbently collected urine specimens are negative for proteins by dipstick whereas urine collected in the upright position is positive. Orthostatic proteinuria became a less likely diagnosis if the total daily urinary protein content exceeded 1 g/d or if there was any degree of associated hematuria. Persistent nonorthostatic proteinuria of any

Table 1. Consideration for Proteinura and/or Hematuria in the 2nd Examinations for the Positive in the 1st SUS (The Korean Education Development Institute)

Proteinuria		Hematuria	
Asymptomatic isolated proteinuria	· Repeat U/A · Rule out 'orthostatic proteinuria'.	Microscopic examination	For evaluate the false positive (hemoglobinuria, myoglobinuria, etc.)
Proteinuria(-) by accurate method	No further test	Isolated microscopic hematuria	Regular U/A and noninvasive kidney function tests.
Persistent proteinuria at repeated urinalysis	Refer to the hospital for further examinations.	Persistent hematuria and suspected renal disease	Refer to the hospital for further examinations.
Proteinuria is accompanied by hematuria, Suspicious renal disease	Refer to the pediatric nephrologist	Hematuria is accompanied by proteinuria and Suspicious renal disease	Refer to the pediatric nephrologist

Table 2. Assessment of the result of SUS according to guideline (The Korean Education Development Institute)

Method of tests	Tests	Results	Marks
Early morning urine sample,	Proteinuria	Negative	Normal
1. Early morning urine sample		Trace	
2. Dipsticks		Positive (1+, 2+, 3+, 4+)*	Asymptomatic isolated proteinuria
3. Recheck if positive at first test		Positive with symptoms of renal disease†	Proteinuria with suspicious renal disease
	Hematuria (Occult blood)	Negative	Normal
		Trace	
		Positive (1+, 2+, 3+, 4+)*	Asymptomatic isolated hematuria
		Positive, both†	Hematuria with suspicious renal disease
	Proteinuria & Hematuria		Hematuria is accompanied by proteinuria, Suspicious renal disease

*Subjects of 2nd. examination.
†Symptoms of renal disease: previous renal disease Hx., hypertension, edema, oliguria, etc.
Keywords School urine screening, Hematuria, Proteinuria, Korea.

degree was indicative of some form of underlying renal disease and were more thoroughly evaluated.

Patients with persistent proteinuria or hematuria should be referred to a hospital for further examination. Furthermore, patients with combined proteinuria and hematuria or family history, symptoms or signs of renal disease should be referred to a pediatric nephrologist (Table 1) [5, 9]. Each medical institution to conduct SUS must notify the students or parents and the head of each school of the urine test results within 15 days of completion of the examination. In addition, these results should be retained by the medical facilities for 5 years in accordance with the regulation of health examination [12].

3. Cost-effectiveness

Dipstick urinalysis for the first SUS and second dipstick test or microscopic examination for children with positive of proteinuria or occult blood at first SUS has been performed in most countries. Nevertheless, comparison of the cost-effectiveness in each countries is not easy because of different medical fees including indirect cost such as personnel time, cost and data analysis. The screening strategy involved a cost per dipstick test of $3.05 included supply items and labor expense in U.S [13]. And the direct cost of screening test was $0.22-0.39.per person in Shanghai, China [8]. Meanwhile, it is difficult to calculate cost of SUS in Korea because it is a part of school health examination program and should be carried out according to a contract with each medical clinics. By the way, the cost of dipstick test examination is 990 won by National Health Insurance Act.

Studies for SUS

A few small-scale systematic SUS programs for the regional communities were attempted in Seoul since 1973. According to these reports, the prevalence of proteinuria was reported at 2.04-4.21% [14, 15]. Mass SUS based on elementary, junior and senior high school children for early detection of proteinuria and glucosuria by the Seoul Office of Education Department has been performed since 1981. The Committee of Children Health of the Korean Pediatric Association did an analysis of SUS for 4 million elementary, junior and senior high school children over an 8-year period (1987-1994) in Seoul and found that the prevalence of asymptomatic proteinuria was 0.28%. The distribution of proteinuria by type was transient proteinuria (19%), orthostatic proteinuria (55%), persistent proteinuria (6%) and proteinuria with hematuria (20%). Pathologic findings in 80 students with asymptomatic proteinuria were IgAN (38.9%), membranoproliferative glomerulonephritis (MPGN) (10.0%), and membranous nephropathy (7.5%) [16]. Unfortunately, only a few systematic SUS programs were undertaken in other provinces during this period.

Organized nationwide annual SUS was established by law on Dr. B. S. Cho's effort in 1997. Since that time, over 7 million students have been screened annually. Cho reported on 452 children with abnormal urinary findings between 1998 and 2000 who visited the Pediatric Kidney Center of the Kyung-Hee University Hospital. Results of the SUS were divided into three groups: isolated hematuria (50.4%), isolated proteinuria (21.7%), and combined hematuria and proteinuria (17.5%). Among the biopsied cases, IgAN comprised 11.3%, while mesangial proliferative glomerulonephritis comprised 21.9%. The combined hematuria and proteinuria group had more frequent CKD (57.7%) [9]. And other nationwide multicenter-study reported a survey of 1,044 referred children with hematuria and/or proteinuria after a SUS in 2005 [11]. These children had isolated hematuria (60.1%), isolated proteinuria (26.4%: transient, 19.6%; orthostatic, 4.9%; persistent, 1.9%) or combined hematuria and proteinuria (13.5%). Renal biopsies were performed on 113 children who showed severe proteinuria, hypertension, abnormal renal function, family history of chronic renal disease, systemic diseases or persistent hematuria and/or proteinuria for more than 12 months. IgAN and thin basement membrane nephropathy (TBMN) were the most common causes in the combined hematuria and proteinuria group and isolated hematuria group, respectively. Accordingly, they insisted that children with

isolated hematuria and isolated low-grade proteinuria were likely to have favorable histopathological changes. As a result, these conditions do not warrant aggressive diagnostic procedures such as a renal biopsy, but do require periodic follow-up examination [9].

Since then, several studies have analyzed the clinical implications of isolated hematuria, isolated proteinuria and combined proteinuria and hematuria [17-24]. Recently, another larger cohort study showed that chronic glomerulonephritis was detected in 25% of all visiting subjects. The most common findings in renal biopsies were IgAN in 38.97%, mesangial proliferative GN in 24.29%, and thin basement membrane nephropathy in 13.13%. However, renal biopsies performed in 26.8% of isolated hematuria cases to date, have revealed only benign pathologic findings [25]. Another study reported that IgAN discovered after a SUS showed milder proteinuria when compared to clinically manifested IgAN [26] and MPGN type I detected after a SUS which were more frequently found in children with combined hematuria and proteinuria rather than isolated proteinuria or hematuria [27]. In addition, several unusual glomerular diseases and renal disorder-related syndromes were reported from SUS [28-36].

Problems of SUS as screening test for student's health care

The controversy with SUS looking for CKD is the uncertainty as to whether early detection of urine abnormalities in childhood will lead to effective interventions and reduction in the number of individuals who develop ESRD. The problems with SUS are false negatives and false positives. First morning urine collection, close communication with the parents of children with abnormal results and system of appropriate consultation with a pediatric nephrologist are important. Another important issue is the cost-effectiveness of Korean SUS in meeting the goals of a school screening program for CKD. It is clear that there is no global consensus as to whether screening for CKD should be undertaken in children and adolescents even though mass screening programs are well established in Asian countries [3, 37].

Conclusion

Although it is debatable whether SUS programs are cost-effective, the detection and management of patients in the early stages of CKD may prove helpful, as interventions are aimed at preventing or delaying its progression. Because screening programs have to be accurate, practical, and economical, efforts should be made to get the support and cooperation of the local health and education department, as well as the school board, students, families of students, and the community as a whole. Furthermore, screening programs should be backed by an institution to ensure continuity. Even though the prevalence of ESRD has slightly decreased since the beginning of a nationwide mass SUS, the effectiveness of SUS should be assessed by long term follow-up epidemiologic studies such as cohort study. The programs can be tailored according to the specific needs of the community with practicality and cost-effectiveness strongly considered. Solutions to help reduce the false-positive rate are needed to reduce creating anxiety in children and families, while decreasing the need for unnecessary diagnostic procedures. Unfortunately, some administrations have attempted to cut the SUS budget on account of cost-effectiveness. Increased testing accuracy will raise the cost-effectiveness of the program primarily by slowing renal disease progression, while reducing both the morbidity and mortality associated with renal diseases in Korea.

한글요약

소아들의 여러 신장 질환 특히 만성신장병은 초기에는 뚜렷한 증세나 징후를 나타내지 않고 단독 단백뇨 또는 현미경적 혈뇨로만 나타나는 경우가 많다. 이런 신장 질환을 발견하기 위하여 소변검사는 여러 장단점에도 불구하고 간단하고 비용이 적게 드는 검사로서 선별검사에 이용하게 되었다. 우리나라에서는 신장 질환의 조기 발견을 위한 학교 집단소변검사가 1998년에 개정된 학교신체검사규칙에

근거하여 전체 초·중·고등학생을 대상으로 실시되었다. 그 이후에 많은 연구와 보고들이 학교 집단소변검사가 만성신질환의 조기 발견에 유용할 것이라고 하였지만 아직도 여기에 대한 이견이 있을 뿐만 아니라 비용 효과 등에 대하여서도 충분한 의견 일치를 얻지 못하였기에 코호트 연구 등의 장기적인 관찰적 역학 연구가 반드시 필요하다. 이를 위하여서는 신장학자들의 지속적인 연구뿐만 아니라 제도 개선 및 개발들이 반드시 동반되어야 할 것이다.

References

1) Narva A: Screening is part of kidney disease education. Clin J Am Soc Nephrol 2007;2:1352-4.
2) Brown WW, Collins A, Chen SC, King K, Molony D, Gannon MR, Politoski G, Keane WF. Identification of persons at high risk for kidney disease via targeted screening: The NKF kidney early evaluation program. Kidney Int 2003;63(Suppl 83): S50-S55.
3) Hogg RJ. Screening for CKD in Children: A Global Controversy. Clin J Am Soc Nephrol 2009;4:509-15.
4) Yap HK, Quek CM, Shen Q, Joshi V, Chia KS. Role of urinary screening programmes in children in the prevention of chronic kidney disease. Ann Acad Med Singapore 2005;34:3-7.
5) Lee CG, Moon JS, Park HW, Lee HK. A Study for the development of guidelines for the school health screening program. 2008;29.
6) Kim KS. Chronic renal failure in children: a nationwide survey in Korea. J Korean Soc Pediatr Nephrol 2000;4:92-101.
7) Ha IS. Current Status of Pediatric Renal Replacement therapy in Korea. S-11-1, ACPN 2011.
8) Zhai YH, Xu H, Zhu GH, Wei MJ, Hua BC, Shen Q, et al. Pediatr Nephrol 2007;22:2073-9.
9) Cho BS, Kim SD, Choi YM, Kang HH. School urinalysis screening in Korea: prevalence of chronic renal disease. Pediatr Nephrol 2001;16:1126-8.
10) Murakami M, Yamamoto H, Ueda Y, Murakami K, Yamauchi K. Urinary screening of elementary and junior high-school children over a 13-year period in Tokyo. Pediatr Nephrol 1991;5:50-3.
11) Park YH, Choi JY, Chung HS, Koo JW, Kim SY, Namgoong MK, et al. Hematuria and proteinuria in a mass school urine screening test. Pediatr Nephrol 2005;20:1126-30.
12) Shin HI. The current status of the Korean Student Health Examination. Korean J Pediatr 2013;56:313-22.
13) Sekhar DL, Wang L, Hollenbeak CS, Widome MD, Paul IM. A Cost-effectiveness Analysis of Screening Urine Dipsticks in Well-Child Care. Pediatrics 2010;125;660.
14) Oh HS, Kim IH. Proteinuria in Korean healthy children. J Korean Pediatr Soc 1973;16:9-15.
15) Kim US, Ko KW. Study of school urine screening. J Korean Pediatr Soc 1981;24:13-22.
16) Lee CG, Lee DW, Yang SW, Cha SH, Hong CH, Choi YM, et al. Analysis of urinary mass screening for elementary, junior and high school children over a 8-year period in Seoul. J Korean Pediatr Soc 1997;40:1347-59.
17) Kim YK and Lee CG. A study of diagnostic significance of simultaneous examination of proteinuria and hematuria in the urinary mass screening. J Korean Soc Pediatr Nephrol 1999;3:57-63.
18) Kang HS, Lee CG. Analysis of urinary mass screening for elementary, middle and high school children over a 3-year period (1995-1997) in Seoul. J Korean Soc Pediatr Nephrol 1999;3:161-9.
19) Kim SK, Kim YK, Park YW, and Lee CG. Analysis of urinary mass screening for second grade of elementary school children in Paju City. J Korean Soc Pediatr Nephrol 2001;3:156-63.
20) Kim CM, Hahn HW, Lee BS, Park YS. Analysis of isolated proteinuria on schoolurinary mass screening. J Korean Soc Pediatr Nephrol 2002;6:61-7.
21) Oh DH, Kim JS, Park JK, Chung WY. Analysis of isolated proteinuria on school urinary mass screening test in Busan and Kyungsangnam-do province. J Korean Soc Pediatr Nephrol 2003;7:142-9.
22) Cho MH, Jang YC, Kim YC, Ko CW, Koo JH. Asymptomatic primary hematuria in children. J Korean Soc Pediatr Nephrol 2004;8:166-75.
23) Yum MS, Yoon HS, Lee JH, Hahn HW, Park YS. Follow-up of children with isolated microscopic hematuria detected in a mass school urine screening test. J Korean Pediatr Soc 2006; 49:82-6.
24) Lee YM, Baek SY, Kim JH, Kim DS, Lee JS, Kim PK. Analysis of renal biopsies performed in children with abnormal findings in urinary mass screening. Acta Pædiatrica 2006;95:849-53.
25) Cho BS, Hahn WH, Cheong HI, Lim IS, Ko CW, Kim SY, et al. A nationwide study of mass urine screening tests on Korean school children and implications for chronic kidney disease management. Clin Exp Nephrol 2012;Epub ahead of print.
26) Kim SY, Lee SS, Lee JM, Kang SJ, Kim YJ, Park YH. The Characteristics of IgA nephropathy when detected early in mass school urine screening. J Korean Soc Pediatr Nephrol 2013; 17:49-56.
27) Choi JY, Park MY, Lee YJ, Ha IS, Cheong HI, Choi Y, et al. The characteristics of membranoproliferative glomerulonephritis I detected from school urine screening. J Korean Soc Pediatr Nephrol 2006;10:152-61.
28) Kim SH, Roh HK, Lee YM, Kim TH, Kim PK, Hong SW, et al. Membranous glomerulopathy showing asymptomatic isolated microscopic hematuria only. J Korean Soc Pediatr Nephrol

2001;5:196-205.

29) Lee TJ, Choi MS, Lee YM, Kim PK, Jeong HJ. A case of lupus nephritis with positive antiphospholipid antibodies, initially detected through analysis of urinary mass screening. J Korean Soc Pediatr Nephrol 2001;5:219-24.

30) Park S, Lee JW, Cho SJ, Yoo ES, Lim HS, Song SH, et al. A case of oligomeganephronia of the solitary kidney, presented with isolated proteinuria. J Korean Soc Pediatr Nephrol 2002; 6:92-6.

31) Choi IK, Kim SA, Kim JH, Kim PK, Lee JS, Jeong HJ, et al. A case of Fraley's syndrome with benign hematuria. J Korean Soc Pediatr Nephrol 2002;6:97-101.

32) Ham JY, Koo NH, Pai KS, Lim HY, Kim KH. A four-year follow up case of oligomeganephronia detected early by school screening urinalysis. J Korean Soc Pediatr Nephrol 2003;7:223-8.

33) Kim YB, Baek SC, Yoo HJ, Kim CH, Lee HH, Kim PK, et al. A case of nutcracker syndrome presenting with orthostatic proteinuria. J Korean Soc Pediatr Nephrol 2004;8:74-9.

34) Lee EJ, Ha TS. Mesangial hypercellulality in a patient with nutcracker syndrome and orthostatic proteinuria. J Korean Soc Pediatr Nephrol 2006;10:83-8.

35) Yoon SJ, Song JE, Shin JI, Jeong IC, Lee JS, Shin HS, et al. Diagnosis of systemic lupus erythematosus during medical follow-up after urinary screening. J Korean Soc Pediatr Nephrol 2008;12:227-32.

36) Kim HJ, Kwak SO, Bae JU, Kim KS, Lim SD. A case of thype II membranoproliferative glomerulonephritis detected by school urinary screening tests. J Korean Soc Pediatr Nephrol 2010;14:79-83.

37) Jin DS. Development research of new guideline of school health examination in Annual report of Korean Education Development Institute. Seoul. Daehan Print, 2009:81-89.