

# Role of Vitamin A in Preventing Renal Scarring After Acute Pyelonephritis

Reza Dalirani, Mojtaba Yousefi Zoshk, Mostafa Sharifian, Masoumeh Mohkam, Abdollah Karimi, Alireza Fahimzad, Mona Varzandefar

Pediatric Infectious Research Center, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

**Keywords.** child, pyelonephritis, vitamin A, kidney pathology

**Introduction.** The role of vitamin A in re-epithelialization of the damaged mucosal surfaces has been documented. The aim of this study was to evaluate the role of vitamin A in preventing renal scarring after acute pyelonephritis in children.

**Materials and Methods.** This clinical trial study was conducted in children with acute pyelonephritis in Mofid Children Hospital (Tehran, Iran). Patients were randomly divided into two groups to receive ceftriaxone and vitamin A or ceftriaxone only. Dimercaptosuccinic acid (DMSA) renal scintigraphy was performed before the start of the treatment and 6 months later. Results were compared for renal scarring between the two groups.

**Results.** Seventy-six patients (11 boys and 65 girls) were enrolled. The mean age was  $25 \pm 24$  months and 54 patients (71.1%) were under 2 years old. The average vitamin A level was  $71 \pm 24$  µg/dL in the treatment group and it was  $62 \pm 18$  µg/dL in the control group. Baseline DMSA scans were comparable between the two groups in terms of scarring ( $P = .53$ ), but the second DMSA scans showed a significant change in progression of the renal injury and scarring in the control group compared to those treated with vitamin A as well as antibiotic ( $P < .001$ ).

**Conclusions.** We found administration of the vitamin A was useful in decreasing the amount of the injury and scarring following the pyelonephritis. Based on our study, vitamin A can be used in conjunction with other treatments in the management of acute pyelonephritis in children.

IJKD 2011;5:320-3  
www.ijkd.org

## INTRODUCTION

Urinary tract infection (UTI) is a common problem in pediatric population that can cause renal scarring, and eventually, chronic kidney failure. Urinary tract infection occurs in 3% to 5% of girls and 1% of boys during childhood.<sup>1</sup> Recently, the role of vitamin A in the treatment of UTI and renal scarring due to pyelonephritis has been investigated.<sup>2-6</sup> The effects of vitamin A on the infection in the respiratory system, digestive system, and other organs have

been broadly investigated.<sup>7-11</sup> This property of vitamin A was attributed to its beneficial effects on the immune system and epithelialization.<sup>4</sup> The World Health Organization recommended that children should take vitamin A capsules every 6 month, along with strategies to address vitamin A deficiency as a health problem.<sup>10</sup>

However, there have been few studies examining the influence of vitamin A on UTI.<sup>5,6,11</sup> The role of vitamin A in re-epithelialization of the damaged

mucosal surfaces has been shown, and this process probably prevents future infections and renal scarring.<sup>4,5,11</sup> Bennett and colleagues<sup>12</sup> reported that the favorable effect of vitamin A on epithelialization had a role in preventing infections. It has also been shown that the severity of renal scarring increases in those with low serum levels of vitamin A.<sup>5</sup>

The present study was conducted to evaluate the effectiveness of vitamin A in preventing renal scarring after acute pyelonephritis. Technetium Tc 99m dimercaptosuccinic acid (<sup>99m</sup>Tc-DMSA) renal scintigraphy was used as the method of choice for detection of renal scar, which can differentiate between lower and upper UTI.<sup>6,13</sup>

### MATERIALS AND METHODS

In this single-blinded clinical trial, 108 children aged between 2 months and 12 years old with a definite diagnosis of acute pyelonephritis based on clinical, laboratory, and <sup>99m</sup>Tc-DMSA renal scan findings were evaluated. This study was conducted in Mofid Children Hospital (Tehran, Iran) from 2007 to 2009. Patients with a previous history of UTI, high-grade vesicoureteral reflux, anatomical abnormality on urinary tract ultrasonography or renal scar on baseline DMSA renal scan were excluded. Consent was obtained from the parents of the eligible participants. The study was approved by the ethics committee of the Pediatric Infectious Research Center.

The enrolled children were divided randomly into 2 groups, using a simple random method. Participants in the study group received ceftriaxone and vitamin A, and those in the control group received only ceftriaxone. Ceftriaxone was administered at a dose of 75 mg/kg for 10 days intravenously. Vitamin A was administered at 25 000 units for patient younger than 1 year old and at 50000 units for those aged 1 year or higher, through intramuscular injection during the first 3 days of admission. Before starting treatment, serum vitamin A level was measured in the two groups. <sup>99m</sup>Tc-DMSA renal scintigraphy was performed before the start of treatment and repeated 6 months later, and the two scans were compared regarding the degree of damage to the kidneys and scar formation.

All data were analyzed by the chi-square and the *t* test using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc,

Chicago, Ill, USA). A *P* value .05 was considered significant.

### RESULTS

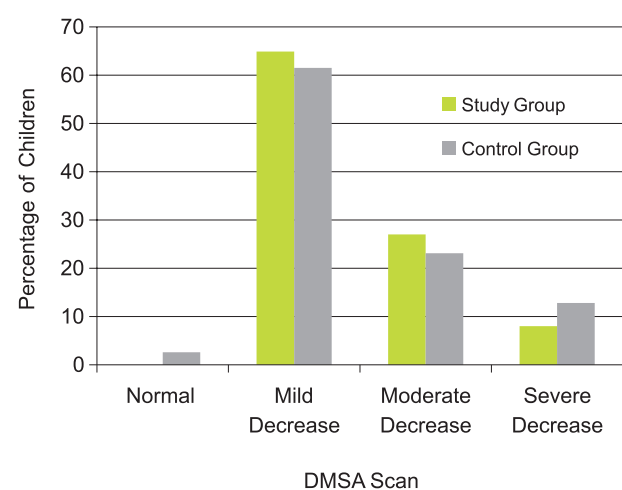
A total of 108 patients started in this study, but 32 patients were excluded from the study because of poor adherence to treatment. Therefore, 76 patients (37 in the study group and 39 in the control group) completed the study. The mean age was  $25 \pm 24$  months and the median age was 15 months. Fifty-four patients (71.1%) were younger than 2 years old. Eleven patients (14.5%) were boys and 65 (85.5%) were girls. There were no significant differences between the two groups in terms of age and gender (Table).

The mean serum vitamin A level was  $71 \pm 24$  µg/dL in the study group, and it was  $62 \pm 18$  µg/dL in the control group. Comparison of the initial DMSA scans between the two groups did not show any significant differences (*P* = .53; Figure 1); however,

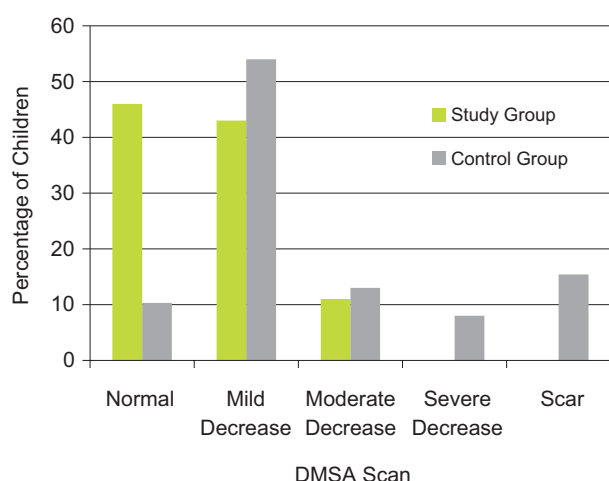
Baseline Characteristics of Children in Study and Control Groups\*

Characteristics	Study Group	Control Group
Number of patients	37	39
Gender		
Male	5 (13.5)	6 (15.4)
Female	32 (86.5)	33 (84.6)
Median age, mo	16	12
First DMSA scan		
Normal	0	1 (2.6)
Abnormal	37 (100)	38 (97.4)

\*Values in parentheses are percents.



**Figure 1.** Baseline technetium Tc 99m dimercaptosuccinic acid (DMSA) renal scans in children of the study and control groups. Scan results are categorized as normal and mild, moderate, and severe decrease in kidney cortical function.



**Figure 2.** Secondary technetium Tc 99m dimercaptosuccinic acid (DMSA) renal scans in children of the study and control groups. Scan results are categorized as normal; mild, moderate, and severe decrease in kidney cortical function; and scar presentation.

the second DMSA scan showed a significant change in progression of kidney injury and scarring in favor of vitamin A administration ( $P < .001$ ; Figure 2).

## DISCUSSION

Vitamin A is a micronutrient essential for immunity, cellular differentiation, and maintenance of epithelial surfaces.<sup>14</sup> Several experimental studies on rat showed that the severity of renal scarring increased in those with low serum vitamin A level, and administration of the vitamin A was useful in decreasing the amount of the injury and scarring following pyelonephritis.<sup>4,5,12</sup> Previous studies demonstrated the inhibitory effects of antioxidant and anti-inflammatory agents such as vitamin A, vitamin E, glucocorticoids, and pentoxifylline on renal scarring in animal models.<sup>15-19</sup> However, a few studies showed failure of vitamin A to prevent kidney damage.<sup>20</sup> In our study, of 37 patients with primary abnormal DMSA scans in the study group, none of the children were demonstrated to have renal scar on their second scans 6 months after the hospital discharge. Among the 39 patients in the control group, the results of renal DMSA scans were significantly different as shown by the second renal scans, in which 6 patients were revealed to have renal scar.

Ayazi and colleagues showed that of 25 patients with primary abnormal DMSA renal scan in the their case group, only 5 children had abnormal scans on the second DMSA 3 months after the

initial scan, and in the control group, 17 patients had abnormal findings on the second renal scan. The difference between the two groups was significant ( $P = .001$ ).<sup>6</sup> The differences between results of second DMSA renal scan in our patient may be related to the time that scan was performed (6 months after initial scan). Another reason for different rates of scar formation in our study may be related to the higher dose of vitamin A that we administered to the patients.

## CONCLUSIONS

Vitamin A deficiency is an important health problem. Vitamin A is required for the development and preservation of all epithelial tissues of the body. Administration of vitamin A is useful in decreasing the amount of the injury and scarring following the pyelonephritis. Based on our study, vitamin A can be used in conjunction with other treatments in the management of UTI. However, this exciting new approach has to be explored further in order to find the true effect of vitamin A in management of UTI.

## ACKNOWLEDGMENTS

This study was originally a thesis conducted at Mofid Children's Hospital, supported by the Pediatric Infectious Disease Research Center of Shahid Beheshti University of Medical Sciences and Health Services. We would like to thank Dr Rouhollah Yousefi Zoshk; physicians, nurses, and staff of pediatric nephrology ward; colleagues at the Pediatric Infectious Disease Research Center; and Mrs Sabouri and Mrs Gholikani for their collaboration in this project.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Elder JS. Urinary tract infections. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, editors. *Nelson textbook of pediatrics*. 18th ed. Philadelphia: Saunders;2007. p. 2223-8.
2. Bahat E, Yilmaz GG, Akman S, et al. Effect of vitamin A supplementation on recurrent urinary tract infections in children [abstract]. *Pediatr Nephrol*. 1998;12:C129.
3. Yilmaz A, Bahat E, Yilmaz GG, Hasanoglu A, Akman S, Guven AG. Adjuvant effect of vitamin A on recurrent lower urinary tract infections. *Pediatr Int*. 2007;49:310-3.
4. Kavukcu S, Soyulu A, Turkmen M, Sarioglu S, Buyukgebiz

- B, Gure A. The role of vitamin A in preventing renal scarring secondary to pyelonephritis. *BJU Int*. 1999;83:1055-9.
5. Kavukcu S, Turkmen M, Sevinc N, Soylu A, Derebek E, Buyukgebiz B. Serum vitamin A and beta-carotene concentrations and renal scarring in urinary tract infections. *Arch Dis Child*. 1998;78:271-2.
  6. Ayazi P, Moshiri SA, Mahyar A, Moradi M. The effect of vitamin A on renal damage following acute pyelonephritis in children. *Eur J Pediatr*. 170:347-50.
  7. Brown KH, Gaffar A, Alamgir SM. Xerophthalmia, protein-calorie malnutrition, and infections in children. *J Pediatr*. 1979;95:651-6.
  8. Stansfield SK, Pierre-Louis M, Lerebours G, Augustin A. Vitamin A supplementation and increased prevalence of childhood diarrhoea and acute respiratory infections. *Lancet*. 1993;342:578-82.
  9. Kjolhede CL, Chew FJ, Gadowski AM, Marroquin DP. Clinical trial of vitamin A as adjuvant treatment for lower respiratory tract infections. *J Pediatr*. 1995;126:807-12.
  10. [No authors listed]. Vitamin A and malnutrition/infection complex in developing countries. *Lancet*. 1990;336:1349-51.
  11. Kavukcu S, Turkmen MA, Soylu A. Could the effective mechanisms of retinoids on nephrogenesis be also operative on the amelioration of injury in acquired renal lesions? *Pediatr Nephrol*. 2001;16:689-90.
  12. Bennett RT, Mazzaccaro RJ, Chopra N, Melman A, Franco I. Suppression of renal inflammation with vitamins A and E in ascending pyelonephritis in rats. *J Urol*. 1999;161:1681-4.
  13. Mohkam M, Maham S, Rahmani A, et al. Technetium Tc 99m dimercaptosuccinic acid renal scintigraphy in children with acute pyelonephritis: correlation with other imaging tests. *Iran J Kidney Dis*. 4:297-301.
  14. Atadzhanov UZ, Utegenov NU. Structural functional damage to cellular membrane in deficiency of vitamin A, E, B2, B6 in children with calculus pyelonephritis. *Urologia*. 2003;35-41.
  15. Sommer A. Xerophthalmia: clinical classification and diagnosis. In: Sommer A, editor. *Vitamin A deficiency and its consequences*. 3rd ed. Geneva: World Health Organization;1955. p. 8-13
  16. Sadeghi Z, Kajbafzadeh AM, Tajik P, Monajemzadeh M, Payabvash S, Elmi A. Vitamin E administration at the onset of fever prevents renal scarring in acute pyelonephritis. *Pediatr Nephrol*. 2008;23:1503-10.
  17. Haraoka M, Matsumoto T, Takahashi K, Kubo S, Tanaka M, Kumazawa J. Suppression of renal scarring by prednisolone combined with ciprofloxacin in ascending pyelonephritis in rats. *J Urol*. 1994;151:1078-80.
  18. Sharifian M, Anvaripour N, Karimi A, et al. The role of dexamethasone on decreasing urinary cytokines in children with acute pyelonephritis. *Pediatr Nephrol*. 2008;23:1511-6.
  19. Yagmurlu A, Boleken ME, Ertoyl D, Ozsan M, Gokcora IH, Dindar H. Preventive effect of pentoxifylline on renal scarring in rat model of pyelonephritis. *Urology*. 2003;61:1037-41.
  20. Soylu A, Kavukcu S, Sarioglu S, Astarcioğlu H, Turkmen M, Buyukgebiz B. The effect of vitamin A on the course of renal ablation nephropathy. *Pediatr Nephrol*. 2001;16:472-6.

Correspondence to:

Reza Dalirani, MD

Mofid Children's Hospital, Shariati Ave, Tehran, Iran

Tel: +98 21 2288 7529

Fax: +98 21 2222 0254

E-mail: rdalirani@yahoo.com

Received December 2010

Revised April 2011

Accepted May 2011