The Effect of Vitamin A on Clinical Manifestations of Recurrent Pyelonephritis in Children

Parsa Yousefchajian 1, Masoud Rezagholizamenjany 2,  *, Manijeh Kahbazi 3, Mohamad Rafiei 4, Hassan Taherahmadi 3, Parisa Kaviani 2 and Ali Arjmand 3

1Department of Pediatric Nephrology, Amir Kabir Hospital, Arak University of Medical Sciences, Arak, Iran
2School of Medicine, Arak University of Medical Sciences, Arak, Iran
3Department of Pediatric, Arak University of Medical Sciences, Arak, Iran
4Department of Biostatistics, Arak University of Medical Sciences, Arak, Iran

*Corresponding author: School of Medicine, Arak University of Medical Sciences, Arak, Iran. Email: masoudrezagholi074@gmail.com

Received 2020 April 06; Accepted 2020 May 09.

Abstract

Background: Pyelonephritis as a life-threatening infection often leads to renal scarring, which presumably controls by minerals.

Objectives: The aim of this study was pyelonephritis treatment by vitamin A in children.

Methods: In the current study, 106 cases from Imam Reza pediatric clinic and Amir-Kabir Hospital, considered a study group. Children divided into groups with or without urinary incontinence. Demographic data, clinical manifestations, and urinary biomarkers were evaluated and then statistically analyzed.

Results: Our data showed that there is a statistical difference between study groups in terms of dysuria (P = 0.001), abdominal pain (P = 0.001), frequency (P = 0.003), incontinency (P = 0.001), urgency (P = 0.002), intermittency (P = 0.004) and fever (P = 0.002).

Conclusions: It has been assumed that vitamin A as a therapeutic agent could be used in children with vesicoureteral reflux induced by Pyelonephritis and congenital anomalies.

Keywords: Children, Recurrent Pyelonephritis, Vitamin A

1. Background

Pyelonephritis induced by renal parenchyma infection is considered as a potentially life-threatening condition which leads to the renal scarring (1, 2). According to pyelonephritis physiopathology, Bacteria by entering into the kidney from the blood circulation, can influence and infect the kidney. In children, most common signs/symptoms of urinary tract infection probably exert as failure to thrive, feeding difficulty, fever, and vomiting (3, 4). For pyelonephritis diagnosis, a physical and historical evaluation as well as a urinalysis are requested to perform. Antibiotics therapy is considered as the first therapeutic choice for acute pyelonephritis treatment to prevent the progression of condition (5-7). According to the previous studies, it has also been proposed that vitamin A, as a micronutrient supplementary agent, can influence pyelonephritis occurrence. Vitamin A with retinal-derived product named retinol, several pro-vitamin A carotenoids, and retinoic acid could be used in many critical conditions (8, 9). There are several reported disorders following vitamin A deficiency, particularly impaired immunity that increases the risk of urinary tract infections (10, 11).

2. Objectives

Given that the importance of Pyelonephritis and vitamin A effect on the immune system, in this study, we aimed to investigate vitamin A potential effect on pyelonephritis treatment in children.

3. Methods

3.1. Study Design and Population

This study conducted in Amir-Kabir Hospital, Arak, Iran. We selected all female children aged between 2 - 12 years who suffered from Pyelonephritis for two years, and treated with IV ceftriaxone 75 mg/kg/day and oral cefixime 8 mg/kg for 14 days. Based on previous studies, we considered 106 children in total, assigned in treatment (n = 53) and control groups. We administrated 25,000 units of vitamin A and placebo in treatment and control groups, respectively. It should also be noted that our study...
was two-sided blind. For inclusion criteria, we considered pyelonephritis patients at the ages between 2 - 12 years who have no other kidney anomalies, in addition exclusion criteria were children at the age lower than 2 years, patients or their parents who have not cooperation, the children with underlying medical conditions or recurrent urinary tract infections.

3.3. Ethical Considerations

Base on the safety of low dose vitamin A, there is no complication in this agent consumption. In addition, double publication, data fabrication, and plagiarism have been observed by the authors and approved by the Ethical Committee of Arak University of Medical Sciences.

3.4. Statistical Analysis

Data analysis was conducted by $\chi^2$ test for qualitative variables, and t-test for quantitative variables in the SPSS program and significance level ($P < 0.05$) were considered.

4. Results

Children were equal in age and mean $\pm$ SD of age in total patients were 5.02 $\pm$ 2.40 years (treatment group $= 4.60 \pm 2.60$ years, placebo group $= 5.40 \pm 2.10$ years). As shown in Table 1, there were significant statistically differences between treatment and placebo groups in terms of dysuria ($P = 0.001$), abdominal pain ($P = 0.001$), frequency ($P = 0.003$), incontinency ($P = 0.001$), urgency ($P = 0.002$), intermittency ($P = 0.004$) and fever ($P = 0.002$). Interestingly, the duration of treatment to cut off the disease-related symptoms was substantially lower in the treatment group.

Moreover, Table 2 showed the results of urine culture in two groups. As described in Table 2, positive U/C was 22.5% in vitamin A group and 15% in the placebo group 48 h after treatment ($P = 0.001$). We also took another urine culture test, 7 to 10 days after treatment. Our findings showed that positive U/C were 5.5% and 13% in vitamin A and placebo group, respectively, which implicated a statistically significant difference between two groups ($P = 0.012$).

5. Discussion

Immunological effects of vitamin A may affect the infection state in our body; therefore, in this study, we evaluated the effects of vitamin A on clinical manifestations of urinary tract infections. Notably, the results of some clinical studies were consistent with our study. For example, Yang et al. (12), evaluated the therapeutic effect of vitamin A in measles. According to their results, it could not find any significant reduction in the mortality rate in groups with vitamin A administration for children with measles (12). Another study conducted by Semba et al. (8), also assessed the efficacy of vitamin A on mortality rate in HIV-infected subjects. According to the reported results, they found that vitamin A was able to decreases the mortality rate in HIV-infected children (8).

Furthermore, Aguayo et al. (13), declared that vitamin A deficiency considered as the main risk factor in children’s survival rate. In this line, another clinical study performed on 141 severely anemic children showed that the administration of vitamin A (100000 or 200000 IU depending on age) significantly decreased the erythropoietin concentration as well as inflammation responses (14). Regarding the vitamin A effect on immune responses and clinical outcomes, there was not considerable evidence to present any desirable effect (15). A review study conducted by Wiysonge et al. (10) showed that it was about vitamin A by modulation of the immune system that could reduce the risk of transmission of HIV infection from mother-to-child. Regarding the dietary supplements mechanism of action on immune response, it has been clarified that vitamin deficiency as a malnutrition in children might have long-term effects on health, because the immune system is relatively inactive from the first hours after birth (16). The evaluation of the long-term vitamin A deficiency showed that vitamin A deficiency could be affected by poor nutrition and public health programs (17). In a case-control study, the levels of vitamin D in the study group, including 82 children with urinary tract infection (UTI) and 64 healthy participants, have been compared. The results showed that vitamin D deficiency could be one of the major risk factors for UTI in children (18). Moreover, the effect of vitamin C on urinary oxalate and pH showed that vitamin C increased the oxalate excretion as well as calcium oxalate crystallization (19). Meanwhile, it has been reported that vitamin D deficiency occurred in kidney diseases can instigate the renal inflammation (20).

5.1. Study Limitation

Limitation of our study were: (1) parental incompatibility who were convinced enough after further explanation about the importance of the issue; (2) inability of pain
Table 1. Cut Off Time of Clinical Manifestations (Days) in Children with Pyelonephritis After Treatment with Vitamin A in 14 Days Period

| Variables             | Groups                               | P Value |
|-----------------------|--------------------------------------|---------|
|                       | Vitamin A                           | Placebo |         |
| Fever                 | 2.20 ± 1.70                         | 4.30 ± 2.00 | 0.002   |
| Dysuria               | 0.43 ± 0.86                         | 3.20 ± 2.40 | 0.001   |
| Frequency             | 0.45 ± 0.91                         | 4.01 ± 2.70 | 0.001   |
| Abdominal pain        | 1.20 ± 0.60                         | 3.54 ± 2.60 | 0.001   |
| Urgency               | 0.05 ± 0.41                         | 3.32 ± 2.60 | 0.002   |
| Urination incontinence| 0.00 ± 0.00                         | 3.20 ± 2.50 | 0.001   |
| Intermittency         | 0.00 ± 0.00                         | 2.58 ± 2.40 | 0.004   |

*Values are expressed as mean ± SD.

Table 2. Urine Culture in Children after Treatment with Vitamin A

| Urine Culture                  | Groups                               | P Value |
|--------------------------------|--------------------------------------|---------|
| 48 hours after treatment induction | Vitamin A | Placebo |         |
| Positive                       | 12 (22.5)                            | 8 (15)  | 0.001   |
| Negative                       | 41 (77.5)                            | 45 (85) |         |
| 7-10 days after ends of treatment | Vitamin A | Placebo |         |
| Positive                       | 3 (5.5)                              | 7 (11)  | 0.012   |
| Negative                       | 50 (94.5)                            | 46 (87) |         |

*Values are expressed as No. (%).

assessment with quantitative scale; (3) Limited financial resource detained us to perform radiological investigation.

Overall, we recommend further studies to resolve these restrictions. In addition, despite several clinical studies carried out concerning the impact of different factors on urination management, further studies will be needed to discover any possible correlation.

5.2. Conclusions

Based on fewer side effects and higher efficacy of vitamin A, it has been suggested that vitamin A as a potential therapeutic agent could be used to treat urinary tract infection, particularly in children with vesicoureteral reflux and congenital anomalies.

Footnotes

Authors’ Contribution: All Authors were equal in manuscript preparation and submission.

Clinical Trial Registration Code: Our study was register with IRCT code as IRCT2014091013366N3.

Conflict of Interests: The authors declared no competing interests.

Ethical Approval: Our study was approved in Ethical Committee of Arak University of Medical Sciences ethical code as IRCT20130518013366N12.

Funding/Support: Our study were funded by Arak University of Medical Sciences. Also this work was performed in partial fulfillment of the requirements for Dr. Parisa Kaviani, in School of Medicine, Arak University of Medical Sciences, Arak, Iran.

Informed Consent: We have taken informed consent from all cases.

References

1. Morello W, La Scola C, Alberici I, Montini G. Acute pyelonephritis in children. Pediatric Nephrology. 2016;31(8):1253–65. [PubMed: 26238274].

2. Yousefchajjan P, Rezagholizamenjany M, Dorreh F, Rafiei M, Taherahmadi H, Niyakan Z, et al. Comparison of development indicators, according to ages and stages questionnaires in children with pollakuria compared to healthy children. Nephro-Urol Mon. 2020;12(3):e103278. 3

3. Yousefchajjan P, Rezagholizamenjany M, Rafiei F, Taherahmadi H, Rafiei M. The Relationship between Blood Biomarkers Level and the Prognosis of Nephrotic Syndrome in the Children. International Journal of Pediatrics. 2016;4(9):3469–97. [PubMed: 26238274].

4. Shaikh N, Borrell JL, Evron J, Leelang MM. Procalcitonin, C-reactive protein, and erythrocyte sedimentation rate for the diagnosis of
acute pyelonephritis in children. The Cochrane Library. 2015. [PubMed: 25603480].
5. Rezagholi-Zamnjany M, Yousefichaijan P. An overview on peritoneal dialysis. Annals of Research in Dialysis. 2016;1(1).
6. Strohmeyer Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. The Cochrane Library. 2014. [PubMed: 25066627].
7. Yousefichaijan P, Dorreh F. Bartter’s syndrome type 5; a case report. Journal of Renal Injury Prevention. 2017;6(4):244–6. doi: 10.15171/jrip.2017.46.
8. Semba RD, Ndugwa C, Perry RT, Clark TD, Jackson JB, Melikian G, et al. Effect of periodic vitamin A supplementation on mortality and morbidity of human immunodeficiency virus-infected children in Uganda: a controlled clinical trial. Nutrition. 2005;21(1):25–31.
9. Irlam JJ, Visser MM, Rollins NN, Siegfried N. Micronutrient supplementation in children and adults with HIV infection. The Cochrane Library. 2005. [PubMed Central: PMC1315220].
10. Wiysonge CS, Shey M, Kongnyuy EJ, Sterne JA, Brocklehurst P. Vitamin A supplementation for reducing the risk of mother-to-child transmission of HIV infection. The Cochrane Library. 2005. doi: 10.1002/14651858.CD003648.pub2.
11. Yousefichaijan P, Rezagholizamenjany M, Dorreh F, Rafiei M, Taherahmadi H, Arjin A, et al. Serum zinc levels in children with and without nephrolithiasis. Current Pediatric Research. 2017;21(4).
12. Yang HM, Mao M, Wan C. Vitamin A for treating measles in children. The Cochrane Library. 2005.
13. Aguayo VM, Baker SK. Vitamin A deficiency and child survival in sub-Saharan Africa: a reappraisal of challenges and opportunities. Food and nutrition bulletin. 2005;26(4):348–55. [PubMed: 16465981].
14. Cusick SE, Tielsch JM, Ramsan M, Jape JK, Sazawal S, Black RE, et al. Short-term effects of vitamin A and antimalarial treatment on erythropoiesis in severely anemic Zanzibari preschool children. The American journal of clinical nutrition. 2005;82(2):406-12. [PubMed: 16087986].
15. Villamor E, Fawzi WW. Effects of vitamin A supplementation on immune responses and correlation with clinical outcomes. Clinical microbiology reviews. 2005;18(3):446-64. [PubMed: 16020684].
16. Cunningham-Rundles S, McNeely DF, Moon A. Mechanisms of nutrient modulation of the immune response. Journal of Allergy and Clinical Immunology. 2005;115(6):1199-28. [PubMed: 1594021].
17. Seal AJ, Creeke PI, Mirghani Z, Abdalla F, McBurney RP, Pratt LS, et al. Iron and vitamin A deficiency in long-term African refugees. The Journal of nutrition. 2005;135(4):808-13. [PubMed: 15795439].
18. Tekin M, Konca C, Celik V, Almis H, Kahramaner Z, Erdemir A, et al. The association between vitamin D levels and urinary tract infection in children. Hormone Research in Paediatrics. 2015;83(3):198-203. [PubMed: 25612848].
19. Baxmann AC, De OG Mendonca C, Heilberg IP. Effect of vitamin C supplements on urinary oxalate and pH in calcium stone-forming patients. Kidney international. 2003;63(3):1066-71. [PubMed: 1263089].
20. Zehnder D, Quinkler M, Eardley KS, Bland R, Lepenies J, Hughes SV, et al. Reduction of the vitamin D hormonal system in kidney disease is associated with increased renal inflammation. Kidney international. 2008;74(10):3343-51. [PubMed: 18784644].