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ORIGINAL ARTICLE

Efficacy and safety profile of cranberry in infants and children with recurrent urinary tract infection☆

V. Fernández-Puentes[a], J. Uberos[a,*], R. Rodríguez-Belmonte[a], M. Nogueras-Ocaña[b], E. Blanca-Jover[a], E. Narbona-López[a]

[a] *Servicio de Pediatría, Hospital Universitario San Cecilio, Granada, Spain*
[b] *Servicio de Urología, Hospital Universitario San Cecilio, Granada, Spain*

Received 28 June 2014; accepted 25 August 2014
Available online 4 June 2015

KEYWORDS
Cranberry;
Urinary tract infections;
Trimethoprim;
Vesicoureteral reflux;
Antibiotic prophylaxis

Abstract
Objective: Cranberry prophylaxis of recurrent urinary tract infection in infants has proven effective in an experimental adult model. There are few data on its efficacy, safety and recommended dose in the paediatric population.
Methods: A controlled, double-blind Phase III clinical trial was conducted on children older than 1 month of age to evaluate the efficacy and safety of cranberry in recurrent urinary tract infection. The assumption was of the non-inferiority of cranberry versus trimethoprim. Statistical analysis was performed using Kaplan Meier analysis.
Results: A total of 85 patients under 1 year of age and 107 over 1 year were recruited. Trimethoprim was prescribed to 75 patients and 117 received cranberry. The cumulative rate of urinary infection associated with cranberry prophylaxis in children under 1 year was 46% (95% CI; 23–70) in children and 17% (95% CI; 0–38) in girls, with effectiveness at doses inferior to trimethoprim. In children over 1 year-old cranberry was not inferior to trimethoprim, with a cumulative rate of urine infection of 26% (95% CI; 12–41). The cranberry was well tolerated and with no new adverse effects.
Conclusions: Our study confirms that cranberry is safe and effective in the prophylaxis of recurrent urinary tract infection in infants and children. With the doses used, their efficiency is not less than that observed for trimethoprim among those over 1 year-old. (Clinical Trials Registry ISRCTN16968287).

☆ Please cite this article as: Fernández-Puentes V, Uberos J, Rodríguez-Belmonte R, Nogueras-Ocaña M, Blanca-Jover E, Narbona-López E. Eficacia y perfil de seguridad del arándano americano en lactantes y niños con infección urinaria recurrente. An Pediatr (Barc). 2015;82:397–403.

* Corresponding author.
E-mail address: juberos@ugr.es (J. Uberos).

PALABRAS CLAVE
Arándano americano;
Infección urinaria recurrente;
Trimetoprim;
Reflujo vesicoureteral;
Profilaxis antibiótica

Eficacia y perfil de seguridad del arándano americano en lactantes y niños con infección urinaria recurrente

Resumen
Objetivo: La profilaxis con arándano americano de la infección de orina recurrente infantil se ha mostrado eficaz en el modelo experimental del adulto. Existen pocos datos sobre su eficacia, seguridad y dosis recomendadas en la población pediátrica.
Métodos: Se desarrolla un ensayo clínico controlado, doble ciego en fase III en niños mayores de un mes de edad para evaluar la eficacia y seguridad del arándano americano en la infección urinaria recurrente infantil. Se parte del supuesto de no inferioridad del arándano americano frente a trimetoprima. El análisis estadístico se realiza mediante un análisis de Kaplan Meier.
Resultados: Se reclutan 85 pacientes menores de un año de edad y 107 mayores de un año. Setenta y cinco pacientes reciben arándano y 117 trimetoprima. El porcentaje acumulado de infección de orina asociado a la profilaxis con arándano en menores de un año fue de 46% (IC 95%: 23-70) en niños y del 17% (IC 95%: 0-38) en niñas, con eficacia a las dosis utilizadas inferior a trimetoprima. En los niños mayores de un año de edad el arándano se mostró no inferior a trimetoprima, con un porcentaje acumulado de infección de orina de 26% (IC 95%: 12-41). El arándano americano fue bien tolerado, no registrándose efectos adversos.
Conclusiones: Nuestro estudio confirma que el arándano americano es seguro y eficaz en la profilaxis de infección urinaria recurrente en lactantes y niños. Con las dosis utilizadas su eficacia no es inferior a la observada para trimetoprima entre los mayores de un año de edad (Clinical Trials Registry ISRCTN16968287).

Introduction

Although controversial, current evidence supports the use of long-term low-dose antibiotic treatment to control recurrent urinary tract infections (UTIs), with the number needed to treat (NNT) to prevent one UTI being 1.9.1.[1] However, one of the main problems in prescribing long-term low-dose antibiotics is the increase in bacterial resistance to antibiotics, and the effects of such treatment on the selection of multidrug-resistant bacteria in the flora. For several decades, cranberry has been used to prevent recurrent UTI in adults.[1] Most studies have focused on populations at higher risk of developing UTIs, such as pregnant women or the elderly. All of them have concluded that while the effects of cranberry seem to be beneficial, the optimal dosage is unknown, as is its potential usefulness in the paediatric age group, and there is little data on its safety in the latter population. Urinary tract infections are relatively frequent in childhood, and are found in 8% of girls and 2% of boys. The rate of recurrent UTI following pyelonephritis is of up to 20%.[2] While the effectiveness of antibiotic prophylaxis for the prevention of UTIs has not been demonstrated, the concept has biological plausibility.[3,4] Some studies[2,5] seem to show that antibiotic prophylaxis has no impact on the incidence of renal scars, even in patients with high-grade reflux, which calls its usefulness into question. Other studies[6] show that paediatric patients with recurrent UTIs undergoing prophylactic treatment with low-dose trimethoprim-sulfamethoxazole experience a 6% decrease in the risk of UTI compared to placebo (95% CI, 1–11%). On the other hand, prophylaxis with cephalosporins is associated with extended-spectrum beta-lactamase-producing or multidrug-resistant uropathogens, a fact on which some authors[7] base their recommendation of prophylaxis with trimethoprim, which is associated with a lower decrease in antimicrobial susceptibility.

Our study assessed the efficacy and safety of cranberry in the paediatric population for the prophylaxis of recurrent urinary tract infections. Our assumption was that treatment with cranberry is not inferior to other prophylactic interventions of proven efficacy, such as trimethoprim.

Methods

Our study was a randomised double-blind phase III clinical trial with two treatment arms: glucose syrup with 3% cranberry extract, and trimethoprim. For a period of two years, we recruited children from 1 month to 13 years of age that received care at the paediatric nephrology and urology departments of our hospital. The maximum duration of follow-up for the patients in the sample was one year. The trial was approved by the local ethics committee, and we obtained a written informed consent from the parents of all participants.

The inclusion criteria were a history of recurrent UTI (more than 2 episodes of infection in the past 6 months), associated or not to vesicoureteral reflux of any grade. The exclusion criteria were the concurrent presence during episodes of UTI of other infectious diseases, metabolic disorders, chronic kidney failure, kidney stones, or liver failure; allergy or intolerance to any components of cranberry or trimethoprim; the presence of blood dyscrasias; or the