

AASCIT Journal of

Health



Keywords

Herbal Therapy, Recurrent Urinary Tract Infections, Blubbery, Infections, Bacteria

Received: March 25, 2017 Accepted: May 5, 2017 Published: November 25, 2017

Patients with Recurrent Urinary Tract Infection Using Bilberry

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Citation

Hakan Sezgin Sayiner, Zeynep Biyik, Sadik Akgun, Mehmet Selim Sahin, Meral Celiker. Patients with Recurrent Urinary Tract Infection Using Bilberry. *AASCIT Journal of Health*. Vol. 4, No. 3, 2017, pp. 22-26.

Abstract

We retrospectively examined 7 patients with recurrent urinary tract infections complaint who applied to Adiyaman University Training and Research Hospital, infectious disease clinic and frequently took antibiotic and also tried herbal products for solution. Ethnobotany and folk medicine are re-gaining popularity since last decade. Although their possible complications, interactions and side effects are repeatedly explained in the media, popularity seems to be increasing. Adiyaman city has a 800.000 population, almost 60% are living in rural areas. In this report, we would like to explain our observations on how patients overcame their recurrent urinary tract infections (validated by hematological, urinary and urinary microbial culture parameters) via consuming blueberry capsule, tea or blueberry fruit itself besides their routine antibiotic therapy. In our study, we examined our patients with recurrent urinary tract infection which used blueberry, is a scientifically researched herbal product, and we have presented to draw attention to the use of herbal products.

1. Introduction

Urinary tract infections (UTI), which commonly caused by Escherichia coli in all ages are hard to treat. UTI is more common in women than in men due to anatomically shorter urethrae. In addition, anomalies like neurological bladder or kidney stones may also provoke recurrent urinary system infections in both sexes. Nearly each infection require antibiotic treatment that eventually creates highly antibiotic resistant bacteria like enlarged spectrum beta lactamase (ESBL) *E.coli* [1-5].

In our clinics, it was observed that some patients with recurrent urinary tract infections were almost hospitalized once in a month receiving parenteral antibiotic treatment and this therapy seems to work less each time. These patients, without asking us, seeked alternative therapy in addition to standard antibiotics according to their wills. It was noticed improvement in their situation and was asked whether they were used any other alternative method, those patients closely monitored by their urine culture, haematological parameters and detailed biochemical investigations of their urine in each month. In this paper, Health status of 7 patients after at least one year continuous consumption blueberry, as tea, fruit or capsules in comparison to their initial visits were reported.

2. Material and Methods

We retrospectively examined 7 patients with recurrent urinary

tract infections complaint who applied to Adiyaman University Training and Research Hospital, infectious disease clinic and frequently took antibiotic and also tried herbal products for solution. These patients were three women and four men.

The first case takes diabetic therapy and he has one kidney. Second one has double j stent since more than 1 year because of kidney stone. Third one has cystofix for three years after a traffic accident. Fourth one was followed due to heart failure and there was no risk factor for fifth one. The sixth patient had diabetes and the seventh patient had dementia and diabetes (health status of the cases and their urine culture results before and after usage of blueberry during 1 year were given in Table 1).

Table 1. Risk factors an	d urine culture results	s before and after use of	<i>blueberries in one year.</i>
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Case	Age/sex	RiskFactor	duration of complaints	growing bacteria	Bacterial growth on track	Usage	Usage time
1	64/E	One kidney Diabetes	>1 year	$E.coli^a$	No growth	blueberries capsule	1 year
2	71/E	Double j catheter	>1 year	E. cloacae ^b	E. cloacae ^b	Dried blueberries	>1 year
3	40/E	cystofix catheter	>1 year	ESBL E.coli ^c	E.faecium ^d C.albicans ^e	Dried blueberries	>1 year
4	40/K		1 month	ESBL E.coli ^c	No growth	Dried blueberries	1 year
5	34/K		1 month	ESBL E.coli ^c	No growth	Dried blueberries	1 year
6	45/K	Diabetes	6 month	ESBL E.coli ^c	No growth	Dried blueberries	1 year
7	65/E	Dementia, Diabetes	1 year	ESBL E.coli ^c	No growth	Dried blueberries	1 year

^aE.coli, ^bEnterobacter cloacae, ^cExtente Spectrum Beta Lactamase Escherichia coli, ^dEnterococcus faecium, ^eCandida albicans

All the patients have taken antibiotic against bacterial growth in recent urine culture which was taken in their complaint period and they have started to use blueberries when there is no growth in their urine cultures (Hematological and biochemical examination results, which were done before using blueberries and one year after using blueberries by patients, were given in Table 2).

 Table 2. Haematological and biochemical examination results before using blueberries and after 1 year using blueberries by patients.

Case	Glucose mg/dL	Urea mg/dL	Creatinine mg/dL	Hb mg/dL	HTC %
1	162/136	52/42	1.76/1.25	14.3/15.6	42.02/46
2	88/85	43/41	1.1/1.1	13.03/13.5	37.76/39
3	91	19/19	0.7/0.7	16.9/16.1	53/54.6
4	-	22/24	0.5/0.5	13.4/13	38.08/38
5	89/93	19/16	0.6/0.6	13.9/14.6	39.9/41
6	140/135	35/33	0.9/0.9	12.3/12.09	37.6/41.2
7	159/154	22/23	1.19/1	12.59/13.02	38.3/37.6

The first case has taken an oral antibiotic due to urinary tract infection four times a year and *E. coli* growth has occurred in the last culture which was taken before starting of the using blueberry. Creatinine level was measured as 1.76 mg/dl. There was no growth in his urine culture once he used the capsule form of blueberries in the morning and evening, and his creatinine level reduced to 1.2 mg/dl. There was no growth in urine culture for 1 month, after he left the using of capsule form after 3 months and his creatinine level reduced to 1.5 mg/dl. After complaints of urinary tract infections resolve, the patient began to eat 5-7 times per day dried blueberries and after 8 months there was no growth in the urine cultures and creatinine level reduced to 1.27 mg/dl.

Second case has double j stent since more than 2 years because of kidney stone. When he took parenteral antibiotic at the hospital due to positive urine culture with *Enterobacter cloacae*, after starting up taking the form of dried blueberries 5-7 per day, then in spite of the *E. Cloacae* growth there was no complaint during one year antibiotic cure has not started.

Third case had an accident 3 years ago and he had cystofix, his hospitalization was frequently due to ESBL *E.coli.* growth when he took parental therapy after starting to eat dried form of blueberry and after 1 year of follow up, there were 2 times *Enterococcus faecium* and 1 time *Candida albicans* growth have been detected in urine culture and there has not spotted any growth in control cultures with oral cure.

Fourth case was followed due to heart failure and there was a growth of ESBL *E.coli* in urine culture many times which were taken during 1 month. After treatment, there was no growth in the control urine culture of the patients who had eaten 5 dried blueberries per day.

There was no risk factor for the fifth case and there were ESBL *E.coli* growth in 2 urine cultures which were taken during a month. There was no growth in the urine cultures of the patient, who was eaten 5 dried form of blueberry per day for 3 months, during 1 year.

The sixth patient was diabetic and had *E. coli* recurrence in urine culture 3 times in the last 6 months and *E. coli* returned to ESBL form in the final culture. The patient did not complain after 4 to 5 times a day started to eat blueberries and no urine cultures were observed in the controls of the patient.

The seventh patient was male, with dementia and diabetes, and ESBL *E. coli* was found in the urine culture. There was no growth in control urine cultures after eating blueberries.

3. Result and Discussion

Due to the high anthocyanin content in the blueberry fruit, it has a great interest in the world. Anthocyanins are flavonoids like flavonol glycosides, flavan-3-ol and proanthocyanidins [6, 7]. Flavonoids and other phenolic compounds are reported to have many biological effects which includes antioxidant, antimutagenic, anticarcinogenic, anti-inflammatory, antiproliferative and antimicrobial effects [8-11].

Howell et al. reported that proanthocyanidins in the blueberries and cranberries responsible for preventing uropathogenic P-fimbriated *E. coli* from adhering [12].

Zafiri et al. reported that the hemagglutinating activity of *E. coli* was inhibited by MR adherence by cranberries and blueberries juice cocktail [13].

Ofek et al. [14]. which were assessed 7 fruit juices and reported that only blueberry and cranberry, types of vaciinium have an Anti-adhesive activity against to *E.coli*. It inhibits adhesion between P-fimbriated uropathogenic *E.coli* and urothelial cells which is the first step of infection process [15, 17]. If bacteria can not connect to the bladder wall, bacteria does not proliferate and urinary tract infection will not progress [18]. This mechanism doesn't kill bacteria but robust bacteria strain's opportunity reduces [19].

Polymeric inhibition of *E. coli* adhesion in fruit juices, one of them was also obtained from blueberry, was tested at study of Nowack et al and it was shown that blueberry fruit juice had prevented *E. coli* adhesion and also it was shown, this inhibitory effect at urinary *E. coli* isolates was more than out of urinary (fecal) *E. coli* isolates [20].

The antimicrobial activity of the pure phenol which contains phenolic acid and flavonoids was measured against to Gram-positive and Gram-negative bacteria types of selected 8 pulps of common Finnish fruits. The myricetin does not affect in the Salmonella strains in spite of inhibition of growing all lactic acid bacteria which was obtained from human gastrointestinal system flora. Generally it was displayed, fruit extracts have not inhibited growing of Grampositive bacteria but it has inhibited growing of Gramnegative bacteria [21]. There was growth of Enterobacter in urine of 1 patient and E. coli in 4 patients before using of blueberry and after the using of it, there was no growth of E. coli. During this time, there was occasionally growth of Enterococci in our cystofix patient and oral antibiotic was given. But complaint that leaving usage of blueberry after 3 months, there was E. coli growth in the urine culture. For one year later there is no clinical symptom while Enterobacter still growing.

It was reported there is antimicrobial effect on *E. coli*, and there is no effect on candidiasis in the study the mechanism and antimicrobial activity of 12 Nordic berry phenolic pulps,

which one of them was blueberry [22]. There was candida albicans growth in urine culture, when our patient had urinary complaint after he or she started to use blueberry [22].

Anthocyanin components show high antioxidative capacity both in vivo and in vitro and also inhibit LDL oxidation. It has also been shown to possess vasoprotective antiinflammatory activity and it contributes as radical scavengers, to inhibit of nitric oxide production, in reducing oxidative stress and sustaining of normal physiological functions [23].

Kalt et al. [24] reported that the abundance of flavonoidbased Anc-derived products in the gastrointestinal tract could contribute to the health benefits of Anc-rich berries. Rodrigo et al. [25] reported that blueberry (poly) phenols were absorbed and extensively metabolized by phase II enzymes and by the gut microbiota, leading to a whole array of metabolites after blueberry consumption.

5 obese and weak Zucker rats (OZR and LZR) were fed with isocaloric control diet or enriched blue berry diet for 15 weeks in one study. For p38MAPK phosphorylation's TLR4, cytokine and ERK, gene and protein expression levels were measured. Kidney redox statue and urine albumin levels were measured. Renal pathology was assessed histologically. Control OZR showed low glucose tolerance, intensified renal function parameters and increased oxidative stress. TLR4 gene and protein expression levels have increased and this increment is together with deterioration of comprehensive albuminuria and OZR antioxidant levels, and growing renal pathology. In addition, OZR ERK and p38MAPK phosphorylation have increased. It was shown that in comparison with OZR, blueberry fed OZR's have created important recovery for all parameters [26].

Serious kidney damage in rats was induced by giving a potent nephrotoxic agent, potassium bromate, earlier and serum BUN and creatinine levels caused to increase. It was shown that turned to normal levels serum BUN and creatinine levels of rats which were given 50, 100 and 200 mg/kg blueberry extract orally for 5 days. A dose-response relationship was mentioned in the study [27]. Thus, 0.99 mg/dl creatinine value at basal, has increased to 2.22 mg/dl after potassium bromate. For given 50 mg/kg blueberry extract to rat, creatinine level had reduced to 1.6 mg/dl, for 100 mg/kg, creatinine level had reduced to 1.3 mg/dl, for 200 mg/kg, creatinine level had reduced to 1.2 mg/dL. Additionally, in the study it was shown that reduction of kidney malondialdehyde, nitric oxide and xanthine oxidase levels and recovery of oxygen radical absorbance capacity of kidney. These finding shown that blueberry extract had a protective impact with free radical cleaning activity and lipid peroxidation inhibition effect [27].

After urinary tract infection, glomerular filtration speed gradually has turned previous levels in almost all patients in a study which researched episodic urinary tract infection that effects to long period renal functions [28]. With the patients under study, in addition to the antioxidant effect of blueberries, urinary tract infection treatment had contributed to recovery of GFR.

Nilubowicz et al. and Hannan et al. studies were related to bacteriuria's, a global common infection, and predicted that the costs of treatment could be 2.500000000-3500000000\$. It was predicted that treatment cost is high in Turkey but actually it is not known absolutely [29, 30].

4. Conclusion

Nearly each infection requires antibiotic treatment that eventually creates highly antibiotic resistant bacteria like enlarged spectrum beta lactamase (ESBL) E.coli. Besides the high cost of treating patients with recurrent urinary tract infection due to resistance which have developed by bacteria against antibiotics, there is almost no option for oral antibiotics. Especially in patients with urinary problems, this condition is often repeated and the days of hospitalization are long. Both requirement of long hospitalization in hospital for using of parenteral antibiotics and increasing resistance to parenteral antibiotics causes requirements of other solutions search for patients. These findings may create solutions from time to time. However, sometimes it may cause unwanted results. In order to prevent this, it is important to be made the scientific studies of product used and to evaluate the compliance with the scientific aspects of the disease. It was shown that blueberry fruit juice had prevented E. coli adhesion. In the study, the patients with recurrent urinary tract infection which used blueberry, is a scientifically researched herbal product, and the aim is to draw attention to the use of herbal products.

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