

The Efficacy and Safety of Uractiv Control in Overactive Bladder Treatment

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The aim of this study is to evaluate the efficacy and safety of Uractiv Control as an alternative treatment with no side effects in Overactive Bladder (OAB). We performed a prospective study over a period of 15 months (May 2018- September 2019) in Department of Urology from Târgu-Mureş. We included 165 patients diagnosed with OAB wet (129 patients) and dry form (36 patients) which were fully evaluated over a 3-month period of treatment. 48 patients were treated with placebo 1 month and were evaluated by the same parameters like Uractiv Control group. The frequency of micturition during the day and night after the treatment with Uractiv Control was improved compared to placebo group ($p=0.0001$) and also the loss of urine episodes ($p=0.03$). Patients did not report any significant side effects of the treatment. Uractiv Control represents a safe treatment option with no side effects and improvement of the storage in OAB.

Keywords: overactive bladder, OAB, natural extract, pumpkin, alternative treatment

Overactive Bladder Syndrome (OAB) is defined according to International Continence Society (ICS) as urinary urgency with or without urge incontinence usually associated with frequency and nocturia, in the absence of pathologic conditions or causative infection and suggestive of underlying detrusor overactivity [1]. Urgency is defined as the sudden compelling desire to urinate, a sensation that is difficult to defer [2]. Urgency urinary incontinence is urinary leakage associated with urgency. Urinary frequency is defined as voiding 8 or more times in a 24-hour period [3]. The term OAB has been adopted by the US Food and Drug Administration (FDA) to expand the number and types of patients eligible for clinical trials.

OAB is primarily a neuromuscular problem in which the detrusor muscle contracts inappropriately during bladder filling. Detrusor overactivity can also occur in the absence of a neurogenic etiology. Idiopathic OAB is OAB in the absence of any underlying neurologic, metabolic, or other causes of OAB [1], or conditions that may mimic OAB, such as urinary tract infection, bladder cancer, bladder stones, bladder inflammation, or bladder outlet obstruction [4-7]. Overactive bladder is subclassified as *OAB wet* if associated with urinary incontinence and as *OAB dry* if it is not associated with incontinence [8].

OAB is the most common cause of incontinence, in both, men and women [8]. In general population was been reported a prevalence of OAB syndrome, more than 12.2% in women and 10% in men, that can be higher in patients aged more than 40 years [8]. Also, some researches have been estimated that the prevalence will increase in future to 21% according to the multiple risk factors that we are exposed to [9].

Overactive bladder is a clinical diagnosis that includes the presence of bothersome urinary symptoms. A preliminary diagnosis of OAB can be made on the basis of the history and physical examination, in conjunction with a few simple office and laboratory tests [10,11]. Treatment of OAB is aimed at reducing the debilitating symptoms in order to improve the overall quality of life in affected patients. Several treatment options are available for OAB including bladder and behavioural training, pharmacologic treatment and surgical therapies.

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The most common pharmacological option for treating OAB is anticholinergic drugs [12]. Mirabegron, a selective β_3 adrenoceptor agonist is an alternative of treatment which has been demonstrated its efficacy during the time [13]. The patient's persistence and adherence rates on those treatment options can be influenced by their multiple and bothersome side effects like dry mouth, constipation, headache, cognitive alterations, tachycardia, hypertension [13-15].

In those conditions the natural extract products can be a viable alternative of treatment in OAB syndrome [16]. Pumpkin (*Cucurbita pepo*) is a vegetable and the oil from its seeds have been used for many years for improvement of urinary symptoms of benign prostatic hyperplasia and for the treatment of irritable symptoms related to OAB [17,18]. The pumpkin seeds contain approximately 50% oil (linoleic, oleic acid and tocopherol), sterols, vitamins and microelements [19].

Through this study we intended to evaluate the efficacy and safety of using the combination between pumpkin seeds and soy germ extracts found in the product Uractiv Control in treatment of Overactive Bladder (OAB), wet and dry form.

Experimental part

Material and method

We performed a prospective study which started in May 2018 in Department of Urology from Târgu-Mureş, in collaboration with "George Emil Palade" University of Medicine, Pharmacy, Science and Technology of Târgu-Mureş. We included 165 patients diagnosed with Overactive Bladder wet (129 patients) and dry form (36 patients) evaluated over a period of 12 weeks.

The patients were treated with Uractiv Control 2x1 caps/day, 12 weeks. Uractiv Control tablets contain 152 mg extract of *Cucurbita maxima*, 50 mg of soy extract, 145 mg of Magnesium and 1.4 mg of vitamin B₆. The evaluation of the patients was performed using urine culture, ultrasound, bladder diaries, OAB questionnaire before and after the treatment and a personalized satisfaction questionnaire after 12 weeks of treatment. 48 of the patients were treated first during one month with placebo. These capsules were formulated in the same shape as the Uractiv control. These patients were randomised 2:1 and evaluated using the same strategy used for patients who received Uractiv Control.

Inclusion criteria:

- OAB symptoms (for more than 3 months)
- Increased urinary frequency
- Nocturia
- Urgency
- Urge incontinence
- Mixed urinary incontinence

Exclusion criteria:

- Urinary infections
- History of radiotherapy
- Neurogenic bladder
- Treatment for OAB or neurogenic bladder in less than 3 months
- History of surgery for stress urinary incontinence
- Severe liver, kidney or heart disease
- Pregnant women or breastfeeding

All the patients included in the study were in good health condition and respected the inclusion criteria.

Results and discussions

We evaluated 165 patients who accomplished the inclusion criteria, over a period 12 weeks. 129 patients were diagnosed with OAB wet form and 36 with dry form. All the patients were treated with Uractiv Control 2x1 caps/day. 48 patients received placebo tablets 2x1/day over a period of one month.

The average age of the patients was 57.95 years \pm 13.12 SD for Uractiv Control group and 55.25 \pm 14.17 years for Placebo group.

The frequency of daily micturition before the treatment was between 7 and 15 episodes per day with a median value of 10 micturition per day. After the treatment with Uractiv Control the median daily frequency was reduced to 8 per day, with limits between 5 and 12. In placebo group the median micturition frequency was reduced from 11, before the placebo treatment to 9 per day (table 1).

Table 1
COMPARED CLINICAL RESULTS BEFORE AND AFTER TREATMENT WITH URACTIV CONTROL AND PLACEBO

	Uractiv Control	Placebo	P value
Mean age ± Standard Deviation	57.95±13.12	55.25±14.12	0.24
Median daily micturition before treatment Minimum- Maximum	10 (7-15)	11 (7-14)	0.92
Median daily micturition after treatment Minimum- Maximum	8 5-12	9 6-14	0.0001
Median nocturnal micturition before treatment Minimum- Maximum	3 0-5	2 1-4	0.29
Median nocturnal micturition after treatment Minimum- Maximum	1 0-3	2 0-3	0.0001
Median loss of urine episodes before treatment Minimum- Maximum	5 1-11	4 0-6	0.03
Median loss of urine episodes after treatment Minimum- Maximum	3 0-6	4 0-5	0.03

The frequency of nocturnal micturition was between 2 and 5 per night, having a median value of 3 before the treatment with Uractiv Control. After 12 weeks the median was reduced to 1/night. The frequency of nocturnal micturition in placebo group was 2 with limits between 1 and 4, before the treatment and the number remained the same after the placebo treatment. (table 1). There was no statistical difference between the frequency of micturition during the day and night between the two investigated groups before the treatment, p=0.92 and p=0.29.

We observed a statistical difference between the group of patients that were treated with Uractiv Control and the group with Placebo, concerning the improvement of daily micturition (p=0.0001) and nocturnal micturition (p=0.0001). The urinary incontinence episodes were between 4 and 11 per day, having a median value of 5, before the treatment with Uractiv Control. The symptomatology improved to 3 episodes/day after the treatment compared to placebo where we didn't find any improvement of the symptoms. There was a significant difference concerning the loss of urine episodes between the groups before and after the treatment with Uractiv Control, p=0.001 and compared with placebo, p=0.003.

The OAB questionnaire (OABq) was completed by the patient before starting the treatment and after 3 months of treatment. All patients' OABq score before the treatment was higher than 8 points. On the beginning of the treatment the average value of OABq score was 23.73±3.93 SD. After the treatment the OABq score decreased to an average of 17.73±3.73 SD points. After placebo treatment the OABq score was 20.92±4.09 SD (table 2). There was a statistical difference concerning the OABq result after the treatment with Uractiv Control, p=0.0001 and after that treatment compared with Placebo group, p=0.0001 (fig. 1).

Table 2
COMPARED OABq RESULTS BEFORE AND AFTER TREATMENT
WITH URACTIV CONTROL AND PLACEBO

	Uractiv Control	Placebo	P value
Mean OABq score before the treatment ± Standard Deviation	23.73 ± 3.93	24.92 ± 4.21	0.08
Mean OABq score after the treatment ± Standard Deviation	17.74 ± 3.75	20.92 ± 4.09	0.0001

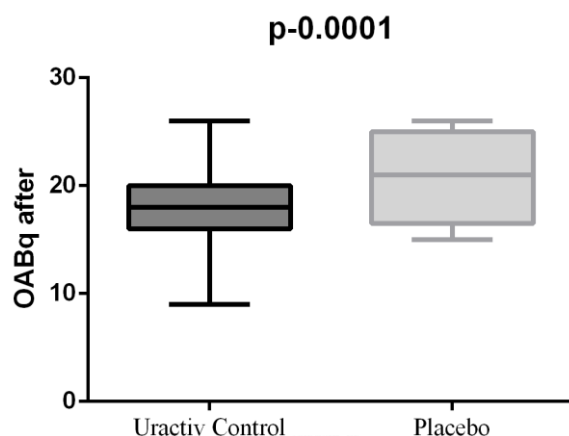


Fig. 1. Compared result of OABq score after treatment with Uractiv Control and Placebo

The evaluation of the patients after 12 weeks of treatment with Uractiv Control was assessed using a personalized satisfaction questionnaire. This questionnaire contain 4 questions concerning the patient's quality of life: improving the sleep, interacting with people, social and professional activity. The patient gave a rating to each question from 1 (not at all) to 5 (very good) concerning the quality of life improvement. The score limits could be minimum 4 and maximum 20 points. The average score, based on the patient's answers was 13.07 ± 2.87 SD points.

Patients did not report any significant side effects of the treatment.

Storage urinary tract symptoms are frequent in general population, both in men and women and their prevalence increase with age [19].

OAB syndrome is characterized by the presence of urgency accompanied by the sudden sensation of micturition that occur in the filling phase of the micturition process [20]. We included in this study 165 female patients with storage symptoms, diagnosed with Overactive Bladder wet and dry form. The mean age of the patients was related between the group who was treated with Uractiv Control and the group with placebo, $p=0.24$.

The pathogenesis of OAB is poorly understood. In the pathophysiology of OAB can be involved disorders of the urothelium, detrusor or brain, but those remain subjects of debate in literature [21]. OAB evolution can be related with multiple risk factors, including: age, body mass index, sex, educational level, parity, vaginal delivery, menopause, employment status, race, marital status, smoking or alcohol abuse [3,22-31].

Lower urinary tract symptoms in female with OAB syndrome have a negative impact on their social, professional and personal life [32]. The improvement of symptomatology in patients with OAB syndrome can increase their quality of life [33]. We included in the study, patients with the same symptoms and the same data were analyzed in the both groups. There were no statistical differences between the frequency of daily or nocturnal micturition, frequency of loss of urine episodes or OAB score between the groups, before the treatment with Uractiv Control or Placebo.

The purpose of OAB treatment is to improve the symptoms, using lifestyle, behavioral and conservative measures [34]. In most of the cases the patients magnify the gravity of the symptoms and we are tented to prescribe them medical treatment like antimuscarinics or $\beta 3$ adrenoreceptor agonists [13,24,28]. Those are effective treatments, with demonstrated persistence and adherence, but with multiple side effects like dry mouth, constipation, headache, cognitive alterations [13,25,30].

Phytotherapeutic treatment contain products like pumpkin seeds or soy germ extract that represent natural remedies known to improve the frequency of micturition in OAB syndrome or the loss of urine episodes [16]. In our study we used Uractiv Control product that contain 152 mg extract of Cucurbita maxima, 50 mg of soy extract, 145 mg of Magnesium and 1.4 mg of vitamin B6. The most important symptom related by the patients was the increased frequency of the micturition/day and the most bothersome was the loss of urine episodes and the necessity to use pads. In our study we observed a statistical improvement of the symptomatology, with the decrease of the number of micturition over the day and night (evaluated on the bladder diary conducted by the patients), decrease of loss of urine episodes and OAB score before and after the treatment with Uractiv Control. Also it was a statistical difference between the group treated with Uractiv Control and Placebo group concerning the same symptoms. In Placebo group were no statistical differences between the symptoms or OAB score before and after placebo.

The patients did not relate any side effects after the treatment with Uractiv Control or placebo. Our findings revealed that the combination between pumpkin seed and soy germ extracts which are found in Uractiv Control product may improve OAB urinary symptoms.

Conclusions

Uractiv Control represents a safe treatment option with no side effects and improvement of the storage symptoms and OAB score in patients with Overactive Bladder.

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