Treatment of Recurrent Urinary Tract Infections with Uro-Vaxom®

Open Multicenter Study with 521 Patients

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Summary. 521 patients suffering from frequent urinary tract infections were included in this study. Patients were treated for 3 months with one capsule daily of Uro-Vaxom, together with any eventual antibiotic or chemotherapeutic, and observed for further 3 months. During this 6-month trial the number of recurrences was significantly reduced in comparison with the 6-month pretrial period (P<0.001). The high initial germ counts of both total and gram-negative germs were stabilized at a low level until the end of Uro-Vaxom therapy and remained low until the end of the trial (P<0.001 at both 3 and 6 months in comparison with initial values), as was also the case for the incidence of dysuria and pollakiuria (P<0.01). Total duration of antibiotic and chemotherapeutic administration followed this general improvement of the patients' condition. The product was well tolerated; side-effects were mentioned in 4.4% of the 521 patients, leading to treatment withdrawal in only two cases (0.4%). The overall efficacy of the test product was assessed by the physicians as positive in 80% of the cases both for its curative action beside the initial antibacterial treatment and for its consolidative long-term action until the end of the 6-month trial.

It is a widely recognized fact that urinary tract infections (UTI) are generally caused by gram-negative germs, mostly of the coliform class [5]. The main therapeutic approach involves the administration of antibiotics which usually bring about the expected positive results in the acute phase of urinary infections, but are not entirely devoid of side-effects [4, 7]. For the treatment of chronic or recurrent urinary tract infections, the repeated intake of antibiotics may lead to the appearance of resistant bacterial strains, which has also been demonstrated for E. coli [1], as well as to a possible weakening of the immune defence mechanisms [3].

For these reasons, immunostimulating drugs tend to take an increasing part in the treatment of infectious diseases [6]. The activation of the body's own defence mechanisms has been demonstrated for a new product of this therapeutic class, Uro-Vaxom, which contains as active principle immunostimulating fractions extracted from E. coli [8]. This activation leads to a significant decrease in the number of recurrences, bacteriuria, dysuria and the need for antibiotics and chemotherapeutics in patients suffering from recurrent urinary tract infections [2].

The aim of the present trial was to study this drug within a large patient collective under the conditions of current medical practice, giving a particular attention to its tolerance and therapeutic value. The binational study scheme seemed also of interest for testing the reproducibility of the results.

Patients and methods

521 patients with a past history of frequent recurrences of UTI were enlisted in 23 medical practices in the Federal Republic of Germany and in 67 in Switzerland. They were admitted into the trial at the time of an acute urinary infection after having given informed consent. The inclusion criterion was bacteriuria with at least 10⁶ germs/ml in midstream urine or eventually 10⁶ germs/ml in catheter urine, determined with the Uribak (Biotechnik Ltd., Hamburg, FRG) or the Bactrim-Urotube test (F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland) on CLED (total germs) or McConkey (gram-negative germs) medium. The exclusion criteria were dysuria without positive bacteriological results and confirmed urinary tract anomalies with stasis or lithiasis.

The patients were treated for 3 months with one capsule daily of Uro-Vaxom¹ (containing 6 mg of immunostimulating fractions extracted from E. coli in lyophilized form, OM Laboratories Ltd., Meyrin/Geneva, Switzerland), and observed for further 3 months. At the start and during the trial, the necessary antibiotics or chemotherapeutics could be prescribed concomitantly. Medical examinations were performed at trial onset, after 3 weeks, after 3 and 6 months, as well as at any recurrence. At each examination, the germ counts, the symptoms of dysuria and pollakiuria and any other relevant signs were determined and the duration of concomitant administration of antibiotics or chemotherapeutics was recorded. The physicians assessed the tolerance of Uro-Vaxom, as well as its curative action beside that of the antibiotic or chemotherapeutic in the initial infection and the consolidative long-term action during the 6 months of the trial. The data were analyzed statistically with the paired Student's t-test for normally distributed parameters, the Wilcoxon's test for comparison of ordinal or non-normally distributed parameters and the McNemar's test for dichotomic parameters.

¹ In Germany also marketed under the brand name Coli-Vaxom®
Results

Out of the 521 completed case reports, 451 were assessable in the statistical analysis of the efficacy parameters. The mean age of these 451 patients (365 women and 86 men) was 51.8 ± 0.9 years; a pyelonephritis was present in 115 cases. The reasons for exclusion were poor compliance or a too short observation period in 48 cases and non-conformity with the inclusion or exclusion criteria in 22 cases. All the 521 case reports were nevertheless considered for the tolerance analysis.

During the 6 months of the trial, the number of recurrences from urinary tract infections (bacteriuria ≥ 10^5 germs/ml at any examination after the beginning of the trial) was clearly lower than that recorded during the 6 months preceding the trial (on the average 0.85 as compared to 3.6 recurrences), which is also evident from the ventilation of the cases with regard to the number of recurrences before and during the study (P < 0.001, fig. 1). 237 patients did not suffer from any recurrence during the trial.

Total germ counts (CLED medium, expressed as mean power of ten per ml urine) was significantly reduced (P < 0.001) after 3 weeks and 3 months on Uro-Vaxom in comparison with the initial values (2.35 ± 0.11 respectively 2.32 ± 0.12 in comparison with 5.80 ± 0.05), with a still lower value after 6 months (1.86 ± 0.12, P < 0.001). The number of gram-negative germs (McConkey medium) decreased in a similar way (P < 0.001). The incidences of dysuria and pollakiuria were significantly reduced from 77.6 respectively 82.4 % to 17.1 respectively 20.2% after 3 weeks (P < 0.01) and to 13.6 respectively 16.1% after 3 months (P < 0.01), with a consolidation at a relatively low level by the end of the trial (10.3 respectively 12.1%, P < 0.01).

A parallel evolution between the cases investigated in Germany and those in Switzerland was observed for the reduction of bacteriuria, dysuria and pollakiuria.

The other various signs and symptoms such as pain, fever, leukocyturia, etc., which were present in a third of the patients at the start of the trial decreased also markedly by the end of the study, but were too heterogeneous to be analyzed statistically.

The total duration of concomitant treatment with antibiotics and chemotherapeutics, which was relatively high for the initial infection (1403 respectively
days) was strongly reduced after 3 months (587 respectively 903 days of treatment) and remained at that low level throughout the following 3 months (460 respectively 693 days of treatment).

The tolerance to Uro-Vaxom was good: side-effects were mentioned in 4.4% of the 521 patients, leading to treatment withdrawal in only 2 cases (0.4%). These effects were: gastrointestinal troubles (15 cases, one with treatment withdrawal), headache and/or vertigo (3 cases), pruritus (3 cases), nausea and erythema (1 case with treatment withdrawal), stop of hair growth (1 case).

The curative action of Uro-Vaxom, beside that of the initial antibiotic or chemotherapeutic treatment, was assessed as certain in 40% (173/431) of the cases and the long-term consolidative action in 58% (252/431) of the cases. The results were considered as positive ("certain" and "possible" assessments taken together) in 80% (343/431) of the cases for the initial curative action and in 81% (348/431) for the long-term consolidative action. The curative action was assessed as questionable in 12% (52/431) and the consolidative action in 10% (43/431) of the cases. The assessments were considered as nil for the remaining cases.

Discussion

521 patients suffering from recurrent urinary tract infections were included in this multicenter study performed in order to investigate the effect of a 3-month treatment with Uro-Vaxom. The total observation period was 6 months, which allowed for a founded judgement not only of the tolerance to this new medication but also of its clinical usefulness in this indication.

Tolerance to Uro-Vaxom was on the whole good, with side-effects mentioned in only 4.4% of the cases consisting mostly of gastrointestinal troubles. These effects were mild and transient, leading to treatment withdrawal in only 2 of the 521 cases (0.4%) considered for the tolerance analysis.

The overall efficacy of the bacterial extract Uro-Vaxom was considered as positive in 80% of the cases, which is clearly in accordance with the significant decrease in the objective signs of a urinary infection, such as bacteriuria and number of recurrences. Indeed, the comparison of the number of recurrences during the 6 months of the trial with respect to that of the previous 6 months shows a much lower occurrence. Furthermore, more than 50% of the patients did not suffer from any further recurrence after the beginning of Uro-Vaxom therapy until the end of the 6 months of the trial. The ventilation of the cases in function of the number of recurrences recorded before the study outset and their distribution during the trial shows a marked decrease in the number of recurrences per patient in the majority of the cases.

The initially high germ counts for both total and gram-negative germs show a stabilization at a low level by the end of the three-month therapy and remained as such until the end of the study, thus underlining the consolidative action of Uro-Vaxom. A comparable favourable evolution characterizes the incidence of dysuria and pollakiuria as well as the duration of concomitant intake of antibiotics and chemotherapeutics.

The results of this open multicenter trial confirm the conclusions of previous trials with Uro-Vaxom [2] and in particular its good tolerance as well as its therapeutic usefulness both in curing the urinary tract infection and in reducing the risk of further recurrences.

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References

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