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Original article

Behavior of MV140 vaccine to prevent recurrent urinary tract infections in patients with metabolic syndrome and smoking

Comportamiento de la vacuna MV140 para prevenir infecciones urinarias recurrentes en pacientes con síndrome metabólico y tabaquismo

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Abstract

Introduction: This study analyzed patients with metabolic syndrome and smokers treated with MV140 vaccine to prevent recurrent UTI.

Material and methods: 342 patients with recurrent UTI received MV140 vaccine between 2017 and 2020 in Barcelona, Spain. Variables analyzed: number of UTI at 3 and 6 months after MV140, age, gender, diabetes mellitus, body mass index, hypertension, total cholesterol, HDL-cholesterol, triglycerides and smoking. Patients were divided in Group 1: metabolic syndrome (2 or more variables), Group 2: no metabolic syndrome (less than 2 variables). On the other hand, patients were classified into smokers and non-smokers.

Results: Mean age was 74, 82% were women. At the beginning, 88,9% had 3-5 UTI. Overall effectiveness with MV140 was 72.5% at 3 months and 56.2% at 6 months.

Group 1 (36%) presented 0-1 UTI in 78.9% and 62.6% at 3 and 6 months. In Group 2 (64%) the results were 69% and 52.5%. Comparing both groups, no statistically significant differences were observed (p=0,25, p=0,26). Smokers had 77.4% and 61.3% at 3 and 6 months, and non-smokers had 69.3% and 52.7%. There were also no statistically significant differences (p = 0.5, p = 0.36).

Group 1 and smoking (28,7%) had 82% at 3 months and 66.3% at 6 months. Group 2 and no smoking (71,3%) reached 60.3% and 52% at 3 and 6 months. There were no statistically significant differences between both groups.

Conclusions: The overall efficacy of MV140 was high and safe, without side effects.

Patients with metabolic syndrome and smokers may benefit from this treatment

Keywords:
Recurrent urinary tract infections, inmunoprophylaxis, MV140 vaccine, metabolic syndrome, smoking

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Resumen

Introducción: Este estudio analizó pacientes con síndrome metabólico y fumadores tratados con la vacuna MV140 para prevenir ITU recurrente.

Material y métodos: 342 pacientes con ITU recurrente recibieron la vacuna MV140 entre 2017 y 2020 en Barcelona, España. Variables analizadas: número de ITU a los 3 y 6 meses de la MV140, edad, sexo, diabetes *mellitus*, índice de masa corporal, hipertensión arterial, colesterol total, HDL-colesterol, triglicéridos y tabaquismo. Los pacientes se dividieron en Grupo 1: síndrome metabólico (2 o más variables), Grupo 2: sin síndrome metabólico (menos de 2 variables). Por otro lado, los pacientes se clasificaron en fumadores y no fumadores.

Resultados: La edad media fue de 74 años, el 82% eran mujeres. Al inicio, el 88.9% presentaba 3-5 ITU. La eficacia global con MV140 fue del 72.5 % a los 3 meses y del 56.2 % a los 6 meses. El grupo 1 (36%) presentó 0-1 ITU en 78.9% y 62.6% a los 3 y 6 meses. En el grupo 2 (64%) los resultados fueron 69% y 52.5%. Comparando ambos grupos no se observaron diferencias estadísticamente significativas (p=0.25, p=0.26). Los fumadores tenían el 77.4% y el 61.3% a los 3 y 6 meses, y los no fumadores el 69.3% y el 52.7%. Tampoco hubo diferencias estadísticamente significativas (p=0.5, p=0.36).

El grupo 1 y tabaquismo (28.7%) tuvo 82% a los 3 meses y 66.3% a los 6 meses. El grupo 2 y no fumador (71.3%) alcanza el 60.3% y el 52% a los 3 y 6 meses. No hubo diferencias estadísticamente significativas entre ambos grupos.

Conclusiones: La eficacia global de MV140 fue alta y segura, sin efectos secundarios.

Los pacientes con síndrome metabólico y fumadores pueden beneficiarse de este tratamiento.

Palabras clave:
Infecciones urinarias recurrentes, Inmunoprofilaxis, vacuna MV140, síndrome metabólico, tabaquismo

Background

Urinary tract infections (UTIs) are the most common bacterial infections in humans and appear in more than 80% of patients that use medical devices such as urinary catheters.[1,2] Diagnosis requires the presence of urinary symptoms such as dysuria, pollakiuria and urinary urgency, positive urine culture (presence of 100,000 or more colony-forming units) and absence of vaginal irritation in women.[1]

In 2010 Chipa-Paucar analyzed 114 patients with UTI due to Escherichia coli, 57 ESBL-positive and 57 ESBL-negative. The variables analyzed were age, gender, race, urinary obstruction, urinary incontinence, hypertension, obesity, rUTI, body mass index and diabetes mellitus. Diabetic patients had 2.53 times more likely to have ESBL-positive Escherichia coli UTI than non-diabetics, and patients with rUTI were 2.94 times more likely to develop ESBL-positive UTI than non-rUTI.[3]

Diabetic patients are more prone to develop infections. The incidence increases when hyperglycemia has an evolution of more than 10 years when the disease is advanced or poorly

controlled. Barutell Rubio in 2016 stated that diabetes mellitus was an independent risk factor for nosocomial urinary tract infection. In addition, serious complications such as emphysematous pyelonephritis, renal abscess and renal papillary necrosis, were more frequent in type 2 diabetes.[4–6]

In 2014, Toledo *et al.* prospectively analyzed 4840 patients with a body mass index over 25 Kg/m2 who attended an aesthetic clinic. They concluded that obese patients (BMI >30) had more UTI and vaginitis than overweight patients (BMI 25-30).[7]

Hypertension is one of the important long-term complications associated with post-UTI renal parenchymal damage. There is a 5 to 26% risk of hypertension in this setting. If renal damage is extensive or bilateral, the risk is higher.[8]

Lorenzo-Gómez *et al.* in 2020 published a retrospective multicenter study of 855 women with rUTI treated with continuous antibiotic treatment or bacterial vaccines to prevent rUTI. Patients were divided according to smokers and non-smokers. Non-smoker women, treated with antibiotics or vaccines, had less UTI recurrence and Escherichia coli resistance.[9]

Different studies show the association between obesity, dyslipidemia and diabetes mellitus with a higher incidence of UTI. On the other hand, smoking and hypertension may also be related to an increase in UTIs.

Metabolic syndrome is defined according to the WHO 1999 as the presence of insulin resistance or glucose >6.1 mmol/L (110 mg/dl), 2 h glucose > 7.8 mmol (140 mg/dl) and also any two or more of the next:[10]

1. HDL cholesterol < 0.9 mmol/L (35 mg/dl) in men, < 1.0 mmol/L (40 mg/dl) in women.
2. Triglycerides > 1.7 mmol/L (150 mg/dl).
3. Waist/hip ratio > 0.9 (men) or > 0.85 (women) or BMI > 30 kg/m2.
4. Blood pressure > 140/90 mmHg.

The recommendations of the 2022 EAU on prophylaxis of recurrent UTI are lifestyle modifications, probiotics, cranberry, D-mannose, intravesical instillations of hyaluronic acid and chondroitin sulfate, antibiotics and immunoprophylaxis with vaccines.

Immunoprophylaxis with oral OM-89 (Uro-Vaxom®) is sufficiently well documented and has been more effective than placebo in several randomized trials with a good safety profile. Therefore, it can be recommended for immunoprophylaxis in women with uncomplicated UTI1,[1–15] level of evidence 1a.

MV140 vaccine was marketed in Spain in October 2010 as immunoprophylaxis for rUTI, unlike OM-89 which is oral, and was administered sublingually with two pumps every day for 3 months.[16]

The objective of our study was to analyze the results of the MV140 vaccine to prevent recurrent UTI in patients with metabolic syndrome and smokers.

Material and methods

We present a prospective, descriptive, multicenter and comparative study of 342 patients with 3 or more UTIs over 12 months, who received immunoprophylaxis with MV140 between 2017 and 2020. Three hospitals in Barcelona, Spain, participated: *Hospital de Mataró* (57,3%), *Hospital Sant Joan Despí Moisés Broggi* (35,7%) and *Fundació Hospital Sant Joan de Déu de Martorell* (7%).

MV140 is an authorized treatment in Spain since October 2010 by Spanish Agency for Medicines and Health Products (AEMPS), and is manufactured by Inmunotek S.L. (Alcalá de Henares, Madrid, Spain) and is marketed by Q Pharma S.L. (Alicante, Spain). Each pump of MV140 was equivalent to a suspension of 10 to 9 head inactivated whole bacteria/ml, with an equal percentage for the four strains of the four most common pathogens of UTI in Spain: Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris and Enterococcus faecalis. In the case of autovaccine, MV140 contained the whole inactivated bacteria isolated in urine culture from the patient.

Effectiveness was defined as the presence of 0-1 UTI at 3 and 6 months of follow-up.

Variables analyzed were the number of UTIs at baseline and at 3 and 6 months, age, gender, diabetes mellitus, body mass index, hypertension, total cholesterol, HDL-cholesterol, triglycerids and smoking. The definition of the variables follows the values of the WHO 1999, defined in the background.

Patients were divided into two groups according to metabolic syndrome. Group 1: metabolic syndrome (2 or more variables), Group 2: no metabolic syndrome (less than 2 variables). On the other hand, patients were classified into smokers and non-smokers.

Variables were recorded in an Excel database and exported to SPSS program version 15.0 (IBM, Chicago, Illinois). Metric data was obtained for the quantitative variables and non-metric data for categorical variables. To compare proportions, the Chi-square test was used with the Fisher modification when necessary. To compare quantitative variables, Student's t-test was used.

Results

The mean age was 74 years with a range of 20-95. 82% were women and 18% men. At baseline, 49.7% had 3 UTIs, 26.9% 4, 12.3% 5, 7% 6, 3.2% 7, and 0.9% 8.

Group 1 represented 36% and Group 2 64%. Group 1 and smokers were 28.7% and Group 2 and non-smokers were 71.3% (Table 1).

Table 1: Study design

Table 1 STUDY DESIGN
Prospective, descriptive, comparative and multicenter study
n=342
Patients: >=3 UTI / 12 months
Inclusion period: 2017-2020
Baseline: 49,7% (3 UTI), 26,9% (4), 12,3% (5), 7% (6), 3,2% (7), 0,9 (8)
Prophylaxis: MV140 vaccine
Follow up: 3 and 6 months
Group 1 (metabolic syndrome): 36%
Group 2 (non metabolic syndrome): 64%
Grooup 1 and smokers: 28,7%
Group 2 and non-smokers: 71,3%

MV140 had an overall effectiveness of 72.5% and 56.2% at 3 and 6 months respectively.

Group 1 presented 0-1 UTI in 78.9% and 62.6% at 3 and 6 months. Group 2 had 69% and 52.5%. Comparing both groups at 3 and 6 months, no statistically significant differences were observed, with p=0.25 at 3 months and p=0.26 at 6 months (Table 2).

Table 2: Results in Group 1 compared to Group 2

Table2 EFFECTIVENESS	Group 1	Group 2	p
3 months	78,9%	69%	0,25
6 months	62,6%	52,5%	0,26

Regarding tobacco, efficacy in smokers was 77.4% and 61.3% at 3 and 6 months, and non-smokers had 69.3% and 52.7% respectively. There were also no statistically significant differences, p=0.5 at 3 months and p=0.36 at 6 months (Table 3).

Table3 EFFECTIVENESS	Smokers	Non-smokers	p
3 months	77,4%	69,3%	0,5
6 months	61,3%	52,7%	0,36

Group 1 smokers had 0-1 UTI in 82% at 3 months and 66.3% at 6 months. On the other hand, Group 2 and non-smokers had 60.3% and 52% at 3 and 6 months respectively. There were no statistically significant differences between both groups (Table 4).

No side effects were detected with MV140.

Table4 EFFECTIVENESS	Group 1 & smokers	Group 2 & Non-smokers	p
3 months	82,7%	60,3%	0,19
6 months	66,3%	52%	0,1

Discussion

Bacterial resistance to antibiotics has increased over the last 20 years, thus many indolent urinary infections can be difficult to treat, and health cost has been increased.[17]

Pratley *et al.* in 2020 published a review of 1680 articles with 17 1970 patients treated with different vaccines to prevent UTI. MV140/Uromune® was used in 3 papers, OM-89/Uro-vaxom® in 9, Solco-Urovac® in 4 and EXPEC4 V® in 1. All vaccines except Solco-Urovac® had statistically significant efficacy.[16]

The 2022 EAU Guidelines advise, with the level of evidence 1 and grade of recommendation a, the use of vaccines to prevent uncomplicated recurrent UTIs. On the other hand, different studies show that UTI are more frequent in diabetics, dyslipidemia, hypertension, obesity and smokers. Our study analyzed the efficacy of the MV140 vaccine to reduce the number of UTIs in patients with these diseases. To date, this is the first study to analyze the benefit of MV140 in patients with metabolic syndrome and smokers.

Pedraza Avilés *et al.* analyzed 300 patients with type 2 diabetes and the incidence of UTI was 17%. They concluded that diabetics with urinary symptoms were 4 times more likely to present UTI than asymptomatic patients, regardless of the glycosylated hemoglobin value.[18] These results were probably due to the small sample analyzed with UTI, 51, against 342 in our study.

Nseir *et al.* in 2015 published a retrospective study of 244 premenopausal and obesity with UTI. They confirmed that obesity was associated with an increased likelihood of recurrent UTIs. The mean body mass index of women with UTI was significantly higher in obese than in controls.[19] In contrast, our study analyzed a sample of 280 women and found no differences in efficacy in relation to the presence of obesity, probably because more than 90% were menopausal in our study compared to 100% premenopausal in the Nseir study.

The study by La Vecchia *et al.* found that the resistance of the most frequent microorganisms in UTI, after prophylaxis with antibiotics or vaccines, was higher in smoker women. And also, smoking increased the risk of rUTI.[20] In contrast, in our work, the distribution of efficacy of the MV140 vaccine was homogeneous in smokers compared to non-smokers.

Despite the 2022 European Association Guidelines recommending the use of vaccines to prevent uncomplicated rUTI, our study shows that the MV140 vaccine can be used with high efficacy and safety in patients with complicated UTI, for example, with metabolic syndrome, and also in smokers. Therefore, these patients can benefit from immunoprophylaxis against UTI.

Lorenzo-Gómez *et al.* demonstrated in 2020 that 263 non-smoker patients had the best results to reduce the number of UTIs in front of 97 smokers. Our study didn't find statistical differences related to smoking in a cohort of 342 patients. The difference was probably due to the different sample size.[9]

The main limitation of our study was the sample size and the follow-up only at 6 months.

We recommend a minimum follow-up of 12 months, a larger sample size and a further extension of the study to other risk factors for developing UTI, such as ureteral catheters, urinary stones or urinary diversion so that the results can be representative of more population.

This study was carried out in accordance with The Declaration of Helsinki. The manuscript is in line with the Recommendation for the conduct, reporting, editing and publication of Scholarly Work in Medical journals. Ethics committee approval was not required because no human or animal experiments were performed. Written consent was obtained from all participants in this study.

Conclusions

The overall efficacy of MV140 was high, 72% at 3 months and 56% at 6 months. The treatment was safe and without side effects.

The efficacy of MV140 had a homogeneous distribution in patients with metabolic syndrome and also in smokers.

According to our work, patients with these comorbidities could safely benefit from immunoprophylaxis with MV140 to reduce the number of UTIs.

CRediT Taxonomy

Cristóbal Ramírez-Sevilla wrote the article and recorded the data collection. He was the major contribution for submitting this paper.

Esther Gómez-Lanza performed the statistical analysis with SPSS program version 15.0.

Josep Miquel Puyol-Pallàs contributed with the data collection.

All authors read and approved the final manuscript.

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Conflict of interest

The authors declare no conflicts of interest.

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