Clinical interest of *Streptococcus bovis* isolates in urine

**Abstract**

**Introduction.** *Streptococcus bovis* includes variants related to colorectal cancer and non-urinary infections. Its role as urinary pathogen is unknown. Our objective was to assess the presence of urinary infection by *S. bovis*, analysing the patients and subsequent clinical course.

**Material and Methods.** Observational study, with longitudinal data collection, performed at our centre between all the cultures requested between February and April 2015. Clinical course of the patients and response to treatment were analysed.

**Results.** Two thousand five hundred and twenty urine cultures were analysed, of which 831 (33%) had a significant microbial count. *S. bovis* was isolated in 8 patients (0.96%). In 75% of these cases the urine culture was requested because of urinary tract infection symptoms; the remaining 25% because of fever of uncertain source; during the follow-up period no evidence of cancer or endocarditis was detected. *S. gallolyticus* subspecie *pasteurianus* was the only variant observed (100%). The clinical response to initial treatment was favourable in all cases.

**Conclusions.** *S. bovis* bacteriuria may have clinical significance, especially when *S. gallolyticus* subspecies *pasteurianus* is isolated in cases with underlying urinary tract disease.

**Keywords:** *Streptococcus bovis*, urinary tract infection, urine culture, *S. gallolyticus* subspecies *pasteurianus*.

**Significado clínico de los aislados de *Streptococcus bovis* en orina**

**Resumen**

**Introducción.** *Streptococcus bovis* comprende multitud de variantes de especie relacionados con infecciones no urinarias y cáncer colorrectal. Su papel como patógeno urinario es desconocido. Nuestro objetivo fue valorar la presencia de infección urinaria por *S. bovis*, analizando los pacientes y su evolución clínica posterior.

**Material y métodos.** Estudio observacional, con obtención de datos longitudinal, realizado en nuestro centro entre todos los urocultivos solicitados durante entre los meses de febrero y abril de 2015. Se analizó la evolución clínica y la respuesta al tratamiento.

**Resultados.** Se analizaron 2.520 urocultivos, de los que en 831 (33%) hubo un recuento microbiano significativo. Se aisló *S. bovis* en 8 (0.96%) pacientes. En el 75% de estos casos el urocultivo fue solicitado por clínica de infección del tracto urinario. El 25% restante por fiebre de origen no clínicamente evidente, durante el periodo seguimiento. La única variante presente fue *S. gallolyticus* subspecie *pasteurianus* (100%). La respuesta clínica al tratamiento inicial fue favorable en todos los casos.

**Conclusiones.** La bacteriuria por *S. bovis* puede tener significación clínica, sobre todo cuando se aísla *S. gallolyticus* subspecie *pasteurianus*, en pacientes con patología previa del aparato urinario.

**Palabras clave:** *Streptococcus bovis*, infección del tracto urinario, urocultivo, *S. gallolyticus* subspecie *pasteurianus*.
INTRODUCTION

Streptococcus bovis bacterial species is a group of bacteria that colonize the intestine of animals and humans. Nowadays, with the application of molecular techniques, this bacterial complex is composed of 3 subtypes (Streptococcus gallolyticus subspecies gallolyticus, Streptococcus gallolyticus subspecies pasteurianus and Streptococcus infantarius subspecies infantarius). This multitude of genetic variants are associated with human infection, causing bacteraemia, endocarditis, meningitis, or infection of the bile duct, and is most frequently associated with colorectal cancer.1

The findings of a systematic review showed that 69% of patients infected by S. bovis had concomitantly colorectal neoplasia, mostly those infected by the variant S. gallolyticus subspecies gallolyticus (biotype I). On the other hand, subgroup S. gallolyticus subspecies pasteurianus has been associated with other infections different from endocarditis and has not been associated with colorectal cancer.1-10 However, most studies to date do not differentiate between varieties or subspecies of S. bovis, which represents a significant limitation for the analysis of the results. Finally, until now, its role as a urinary tract infection (UTI) pathogen is not well known, mainly because it has not been properly studied11 and more research is needed.

Our objective was to analyse the clinical significance of the presence of significant S. bovis counts in urine, as well as the clinical response after receiving antibiotic treatment.

MATERIAL AND METHODS

It was an observational study, with longitudinal data collection, between the months of February and April 2015, from Granada University Hospital Complex Microbiology Lab. (Hospital Virgen de las Nieves). This hospital is a reference centre in Andalusia, which serves a population of about 440,000 subjects. During this period of time urine specimens, from hospitalized patients and followed-up in the outpatient clinic were processed, following the previously described criteria.12 The sample was first inoculated on CHROMagar Orientation® medium (Becton Dickinson, Franklin Lakes, NJ, USA) in a quantitative manner using a 1-µl calibrated loop (COPAN, Brescia, Italy); in cases with underlying urinary tract disease, an additional 10 µl was inoculated on Columbia blood agar (Becton Dickinson). S. bovis suspicious colonies were identified using Gram stain, routine biochemical tests (MicroScan; Siemens Healthcare, Rockville, MD, USA) and mass spectrophotometry, using system Biotyper® (Bruker Daltonics, Coventry, UK). This allows the identification of subspecies. We investigated the sensitivity of isolates to penicillin, levofloxacin, fosfomycin and nitrofurantoin by microdilution (MicroScan). The isolates were classified as sensitive, intermediate or resistant to each antibiotic in accordance with the recommendations of the European Committee for Antimicrobial Susceptibility Testing.13

Clinical data. Once patients were identified with a S. bovis isolation in urine they were classified as symptomatic or asymptomatic. The presence of UTI was recorded as lower (defined by the existence of dysuria, urinary frequency and/or urinary urgency) or upper (if it was accompanied by fever and/or back or flank pain). Demographic and clinical data were collected and analysed: age, sex, race, underlying pathology (diabetes mellitus, hypertension, renal disease, cancer, etc.) and clinical condition (diabetes, diabetic nephropathy, uremia, etc.). We also obtained information about the treatment received (type of antibiotic and duration of treatment, and if this was effective) and hospital care (emergency vs. outpatients care). All data was entered into an electronic data collection system, which was validated after collection of all data. Statistical analysis was performed with SPSS 20.0. Results were expressed as mean ± standard deviation (SD). A p-value < 0.05 was considered statistically significant.

Table 1. Patient’s characteristics and strains of Streptococcus bovis

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age</th>
<th>Sex</th>
<th>Urine culture (microorganism)</th>
<th>Blood culture</th>
<th>Charlson' co-morbidity index</th>
<th>Underlying condition</th>
<th>Antibiotic treatment</th>
<th>Clinical course and outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Negative</td>
<td>6.3</td>
<td>High blood pressure (HBP), Stroke, AVB (auricular-ventricular blockade)</td>
<td>Amoxicillin clavulanic</td>
<td>ICU admission-Favourable</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>0.8</td>
<td>Unknown</td>
<td>Amoxicillin</td>
<td>Favourable</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>4.9</td>
<td>Amyloidosis, Still disease, CKD-Kidney transplant recipient, OSA.</td>
<td>Fosfomycin</td>
<td>Favourable</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>1.7</td>
<td>None</td>
<td>Ciprofloxacin</td>
<td>Favourable</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>3.8</td>
<td>Transplant Kidney recipient, Acute Pulmonary embolism (APE)</td>
<td>Ciprofloxacin</td>
<td>Favourable</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>M</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>2.5</td>
<td>BPH (Benign Prostatic Hyperplasia)</td>
<td>Unknown</td>
<td>Favourable</td>
</tr>
<tr>
<td>7</td>
<td>78</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>9.8</td>
<td>HBP, Hypertensive cardiomyopathy , Type II Diabetes, Diabetic nephropathy, Hydronephrosis</td>
<td>Cefuroxime</td>
<td>Favourable</td>
</tr>
<tr>
<td>8</td>
<td>85</td>
<td>F</td>
<td>S. gallolyticus spp. pasteurianus</td>
<td>Not performed</td>
<td>6.5</td>
<td>UTI, Metrorragy</td>
<td>Cefuroxime</td>
<td>Favourable</td>
</tr>
</tbody>
</table>
Clinical interest of Streptococcus bovis isolates in urine

RESULTS

During the study period a total of 2,520 samples of urine were analysed, of which 831 (33%) had a significant microbial count, with identification and antibiotic susceptibility study. S. bovis was isolated in 8 (0.96%) patients (table 1). Table 2 contains the antibiogram for each case. The median age of the patients was 56 years, being the majority of them women (87.5%). 50% had some underlying nephro-urologic condition: two patients had received a kidney transplant, one patient was carrying a percutaneous nephrostomy catheter and a double “J” for chronic hydronephrosis and another patient had benign prostatic hyperplasia.

The mean value of CCI was 4.53. In 75% (6/8) cases the urine culture was requested by symptoms compatible with UTI; the remaining 25% by fever without evident clinically focus; no evidence of cancer or endocarditis history was detected during the follow-up period. Microhaematuria was present in 37.5% (3/8) of the cases and pyuria in 25% (2/8). Also 25% of the patients were deceased donor kidney transplant recipients with functioning graft and chronic immunosuppressive treatment. 25% had co-infections with Escherichia coli. The S. bovis variant isolated was S. gallolyticus subspecies pasteurianus (100% of the cases), being all susceptible to penicillin. The clinical course during the follow-up was favourable in 87% (7/8) of the patients, but one patient was admitted to the ICU for ischemic stroke. The survival rate was 100% during the study period.

DISCUSSION

To date the importance of S. bovis as producer of UTI is unknown, and its pathogenesis is not well known. So, we set ourselfs the objective of go further in this sense. Our research is useful to bring our experience, providing more data on this topic. Matesanz et al.11 have recently described the involvement of the S. bovis as genitourinary pathogen, mainly the subspecies S. pasteurianus, informing that the infection is most commonly acquired in the community and affects women more frequently. Given that our population corresponds to hospitalized patients and patients followed-up at our outpatient clinic we cannot compare this fact and only describe their presence on patients attending at the hospital. In addition, S. bovis colonies shared phenotypic microbiological characteristics with Enterococcus spp. and Streptococcus viridans group11,12, as well as in the macroscopic and microscopic morphology and biochemical tests, and may be confused with these in the laboratory. Due to the fact that Enterococcus spp. is frequently a causal pathogen of UTIs11,16 and sometimes we can be confused with S. viridans group this problem is especially important since the

<table>
<thead>
<tr>
<th>Patients</th>
<th>Susceptibility of Streptococcus bovis strains.</th>
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<tbody>
<tr>
<td></td>
<td>CFU/ml</td>
</tr>
<tr>
<td>1</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>2</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>3</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>4</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>5</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>6</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>7</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
<tr>
<td>8</td>
<td>Gallolyticus spp. pasteurianus</td>
</tr>
</tbody>
</table>

S= susceptible, I= intermedia, R= resistant
frequency of UTI by *S. bovis* could have been underestimated in epidemiological studies.

It has been published that bacteraemia caused by *S. bovis* and *Enterococcus* spp. could have a urinary origin. In our series blood culture was only taken in one patient, which was negative, so we cannot compare this fact and only refer that patients did not need it.

Different studies highlight the role as uropathogen of the variant of *S. bovis* called *S. gallolyticus* subspecies *pasteurianus*, and similarly all our isolates corresponded to this subspecies. Other subspecies of *S. bovis*, such as *S. infantarius* and *S. gallolyticus*, have been less isolated in urine. Therefore, our findings confirm the importance of *S. pasteurianus* as urinary pathogens, mainly by being present in symptomatic patients and for a meaningful count. In the literature episodes of renal failure in patients with endocarditis by *S. bovis* has been published, although they do not specify the subspecies, including cases of acute tubular necrosis associated with sepsis, immune complexes glomerulonephritis, crescentic glomerulonephritis and kidney failure associated with antibiotic treatment.

In conclusion, *S. bovis*, mainly the subspecies *S. pasteurianus*, can cause UTIs in cases with underlying urinary tract disease. However, it is advisable to continue studying the relationship of the UTI with this agent analysing populations.

**CONFLICTS OF INTEREST**

The authors declare no conflict of interest

**FUNDING**

None to declare

**REFERENCES**


