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Research Article

Which antibiotics are active against Lactobacillus iners playing the prominent role in the female urobiome?

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Abstract

Urine is not sterile! Lactobacillus inners are the dominant agent in the human urobiome at least in women. These innocent bacteria attached firmly to the epithelium of the urinary bladder by strong interaction with the fibronectin on the surface of these cells. These colonizers inhibit uropathogenic bacteria to bind thus preventing the first step of an infection. Antibiotic therapy can interfere with the resident, protective flora. While ampicillin, pivmecillinam, cefotaxime,levofloxacin, nitroxoline and nitrofurantoin are active against L. iners. cotrimoxazole and fosfomycin are inactive.

Keywords: Urobiome; Lactobacillus inners; susceptible ampicillin; pivmecillinam; cefotaxime; levofloxacin; nitroxoline; and nitrofurantoin; resistant cotrimoxazole and fosfomycin.

Introduction

Urine is not sterile [1]! The female urinary bladder is generally colonized primarily by Lactobacillus infers [], [3]. These bacteria adhere firmly to the fibronectin on the surface of epithelial cells and hence these gatekeepers inhibit uropathogenic bacteria to bind. Thus, the first step of infection is prevented by L. infers.

In principle, antibiotic therapy can interfere with the resident flora of the urinary bladder [4]. The question is, which antibiotics used usually to treat urinary tract infection or to prevent recurrent infections are active against L. iners and which ones are not harmful.

Materials and Methods

Lactobacillus iners strain 1533 was bought from the German Leibniz collection of microorganisms and cell cultures DSMZ/Braunschweig. This strain was originally isolated from urine. The antibiotic susceptibility was determined by a disk diffusion test using Brucella-Agar [BectonDickinson, Heidelberg, Germany]. Incubation occurred at 36°C for 24 hours at a concentration of 5% CO2.

Authoritative breakpoints from EUCAST for Lactobacillus iners do not exist; the assessment of the laboratory results was adapted as far as available according to the interpretation of Guerin [5] or if applicable to EFSA [6]. For nitroxoline a breakpoint of 16 mm was taken as recommended by NAK [7].

Results

The antimicrobial activities of a selection of antibiotics, usually used for the therapy and/or the prevention of urinary tract infections [8], against L. iners was determined in a disk diffusion test (tab.1).

Table 1: In vitro activity of several antibiotics on Lactobacillus iners

antibiotic	inhibition zone	activity
ampicillin	29 mm	active
pivmecillinam	21 mm	active
cefotaxime	38 mm	active
nitrofurantoin	42 mm	active
nitroxoline	25 mm	active
levofloxacin	30 mm	active
cotrimoxazole	7 mm	inactive
fosfomycin	<7 mm	inactive

Some of the tested antibiotics could inhit the growth of L. iners, whereas some others dont (Table 1).
There may be, however, quantitative differences between some antibiotics, for example between nitroxoline and nitrofurantoin (fig. 1) as shown in the disk diffusion assay.

Figure 1: Comparative in vitro activity of nitroxoline (NIB 30) and nitrofurantoin F100) against Lactobacillus iners strain DMSZ 1533 on Brucella agar.

Discussion

More than 130 lactobacilli strains have been described so far [2]. L. iners is a peculiar member, since it has the shortest genome of all lactobacilli [9]. Consequently, this paltry species („iners ", i.e latin, means idle or iners) lacks some properties of other members such as Lactobacillus crispatus, Lactobacillus jensenii, and Lactobacillus gasseri, which are often associated with L. iners for example in the normal vaginal flora [2, 10] playing a decisive role for the homeostasis at this site. Lactobacilli in general produce a lot of bacteriocines sometimes even several ones [11]. These antimicrobial products have usually a narrow spectrum of activity namely against related bacteria but some exert even a broad antimicobial spectrum including even Candida, Gardnerella, and Escherichia coli. [12]. L. iners makes at least one, i.e. inecin L [13].
The prominent character of L. iners is, however, that this species attaches rather firmly to fibronectin on the surface of epithelial cells [14]. Indeed, it is the main agent of the local flora in the urinary bladder of women followed by Lactobacillus kitasatonis [2, 3] contributing to colonization resistance against uropathogenic bacteria.
This protective local standard flora can be altered by antibiotics given to treat urinary tract infections or to prevent recurrent infections [4].
Since lactobacilli are generally regarded as non-pathogenic except in few cases [5], their antibiotic suseptibility is not well studied [15, 16]. This holds especially true for L. iners, which has not yet been tested so far.
Although defined breackpoints Lactobacillus spp is not available, the laboratory results should be interpreted rather reluctantly. In general Lactobacillus spp. are hold to be susceptible to ampicillin [16, 17] as well as to nitrofurantoin [18, 19], but resistant to cotrimoxazole and fosfomycin [5, 15, 18, 20]. In addition, several Lactobacillus spp. have been reported to be resistant to nitroxoline [21, 22, 23]. The data about quinolones are rather controversial.
The spectrum of activities of certain antibiotics against L. iners – at least under the given test conditions (tab. 1) is divergent. Only fosfomycin and cotrimoxazole are inactive against this bacterium hence sparing possibly the protective local flora in the urinary badder in women whereas the betalactams, levofloxacin, nitrofurantoin as well as nitroxoline are more or less active in vitro and thus may harmful to the resident flora of the urinary bladder.

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