СРПСКИ АРХИВ
ЗА ЦЕЛОКУПНО ЛЕКАРСТВО
SERBIAN ARCHIVES
OF MEDICINE

Address: 1 Kraljice Natalije Street, Belgrade 11000, Serbia
☏ +381 11 4092 776, Fax: +381 11 3348 653
E-mail: office@srpskiarhiv.rs, Web address: www.srpskiarhiv.rs

Paper Accepted* **ISSN Online 2406-0895**

Preliminary and Short Communication / Прелиминарно и кратко саопштење

Gordana Smieško[1,2], Vera Gusman[1,2], Pavle Banović[3,4,†]

Jack of all trades spotted in the Clinical Centre of Vojvodina – first detection of *Aeromonas hydrophila* from urinary tract infection samples

„Мајстор свих заната“ детектован у Клиничком центру Војводине – прва изолација *Aeromonas hydrophila* из узорака уринарних инфекција

[1]University of Novi Sad, Faculty of Medicine, Department of Microbiology with Parasitology and Immunology, Novi Sad, Serbia;
[2]Institute of Public Health of Vojvodina, Novi Sad, Serbia;
[3]Pasteur Institute Novi Sad, Novi Sad, Serbia;
[4]University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

Received: July 17, 2019
Revised: September 27, 2019
Accepted: September 29, 2019
Online First: October 9, 2019
DOI: https://doi.org/10.2298/SARH190717110S

†**Correspondence to:**
Pavle BANOVIĆ
Pasteur Institute Novi Sad, Hajduk Veljkova 1, 21000 Novi Sad, Serbia
E-mail: **pavle.banovic.mf@gmail.com**

Jack of all trades spotted in the Clinical Centre of Vojvodina – first detection of *Aeromonas hydrophila* from urinary tract infection samples

„Мајстор свих заната“ детектован у Клиничком центру Војводине – прва изолација *Aeromonas hydrophila* из узорака уринарних инфекција

SUMMARY

Aeromonas hydrophila is representative of group within the *Aeromonadaceae* family that mainly cause infections in humans. Aeromonads can induce meningitis, septicemia, respiratory and hemolytic uremic syndrome as well as gastroenteritis. Regarding diverse mechanisms involved in virulence and metabolic adaptation of *A. hydrophila* to various hosts and environments it is often introduced as "*Jack of all trades".* Here we report first isolation of *Aeromonas hydrophila* from urine samples of the three patients from Urology Department within Clinical Centre of Vojvodina. Epidemiological survey identified contact with surface water as only mutual risk parameter. Following that, novel antibacterial agents against *A. hydrophila* are discussed.

Keywords: *A. hydrophila;* urinary infection; resistance; antimicrobials

САЖЕТАК

Aeromonas hydrophila је представник групе унутар фамилије *Аеромонадаџеае*, која најчешће доводи до обољења људи, укључујући менингитис, септикемију, респираторни и хемолитички уремијски синдром, као и гастроентеририс, где се *A. hydrophila* сматра најчешћим узроковачем. Захваљујући различитим механизмима развоја вируленције и метаболичке адаптације наспрам различитих домаћина и утицаја спољашње средине, често се назива "мајстором свих заната". У овом раду извештавамо о првој изолацији *Aeromonas hydrophila* из узорака урина три пацијента Клинике за урологију Клиничког центра Војводине. Епидемиолошком анкетом је контакт са површинским водама идентификован као једини заједнички фактор ризика. Остатак текста је посвећен прегледу нових приступа антимикробне терапије против *Aeromonas hydrophila*

Кључне речи: *A. hydrophila*; уринарне инфекције, резистенција, антибиотици

Aeromonas hydrophila is detected in a broad variety of aquatic systems and it is regarded as an opportunistic pathogen. It is Gram negative bacterium and representative of group within *Aeromonadaceae* family that mainly cause infections in humans – motile aeromonads [1]. The presence of motile aeromonads was reported in a wide spectrum of food industry products (fish, meat, vegetables, milk, etc.), with predominance of *A. hydrophila* [2].

It is known that aeromonads have different virulence factors and can induce meningitis, septicemia, necrotizing fasciitis, respiratory and hemolytic uremic syndrome, and finally gastroenteritis in humans, where *A. hydrophila* was noted as most common causative agent [1, 3–7]. Zhou et al. [8] reported that *A. hydrophila* induce extra-intestinal infections more often in patients with malignancy.

Contamination of food is mainly repercussion of using water contaminated with *Aeromonas spp*., as well as consequence of overall poor hygiene in working area during food processing or storage. It should be mentioned that milk is an exceptional medium for *A.*

hydrophila growth, as a result of its nutrient composition, pH and moisture content. Moreover, detection of *A. hydrophila* was reported in cheese, raw and pasteurized milk [2].

Since *A. hydrophila* has adopted diverse mechanisms involved in virulence and metabolic adaptation to various hosts and environments, it is often introduced as "Jack of all trades" [9]. Regarding wide presence and pathogenicity of *Aeromonas spp.* strains, extensive and protracted use of antibiotics in treatment and prevention finally resulted in evolution of antimicrobial resistant strains, mainly in aquatic microbial pathogen group [2, 5, 10, 11]. Furthermore, Daood reported a possible link between rising antibiotic resistance of aquatic strains and decreasing effect of antimicrobials in patients with *A. hydrophila* infections [12]. And indeed, carbapenem-resistant Aeromonas spp. were reported recently in humans [13]. Besides that, *A. hydrophila* resistance to chlorine, low temperature and ability to form biofilm is described [14].

Here we report the first isolation of *Aeromonas hydrophila* from urine samples of the three patients from the Urology Department within Clinical Centre of Vojvodina. Epidemiological survey was conducted in all three patients, where contact with surface water was identified as only mutual risk parameter. All three samples were inoculated on blood agar, endo agar and chromogenic agar and were examined after an incubation period of 18–24 hours. Due to the atypical growth over the plates, Matrix Assisted Laser Desorption Ionization - Time of Flight mass spectrometry was used (MALDI Biotyper, Bruker), where presence of *A. hydrophyla* was confirmed. Standard susceptibility to antimicrobials was determined via Kirby-Bauer disc diffusion method, therefore all three patients were treated with fluoroquinolones and reached remission.

Considering rising problem of multi-resistant *A. hydrophila*, several approaches have been recently suggested in order to outflank acquired bacterial resistance mechanisms.

Vijayakumar et al. have demonstrated remarkable effect of fucoidan, marine brown seaweed extract, coated with gold nanoparticles. The tested substance showed larger inhibition zone compared to chloramphenicol (23.2 mm vs 17.3 mm), as well as impressive biofilm inhibition activity against *A. hydrophila* [11]. Considering the treatment of aquatic organisms, as well as human patients, Rama Devi et al. conducted experiment with approach to target the quorum sensing system of *A. hydrophila* by introducing rosmarinic acid. They reported effect that includes significant inhibition of biofilm formation and production of

virulence factors in three *A. hydrophila* isolates (AH 1, AH 12 and MTCC 1739) [10]. Stanković et al. [15] introduced millipede *Pachyiuli hungaricus* defensive secretion compounds as potential antimicrobial agents. Even lowest concentrations of isolated compounds (0.20–0.25 mg/ml) were reported as effective in *A. hydrophila* growth inhibition. They identified a total of 44 compounds, within which 2-methyl-1,4,-benzoqinone and 2-metoxy-3-methyl-1,4-benzoquinone were most dominant. Antimicrobial activity of Serbian Propolis against *A. hydrophila* was demonstrated by Ristivojević et al. by a MIC assay, where zones of inhibition appeared at 0.05 mg/disc, while at a concentration of 0.20 mg/disc inhibition zone diameter was larger than 12 mm [16]. Ramena et al. [17] tested antimicrobial activity of various plant extracts against *A. hydrophila.* In most cases antimicrobial effect was insufficient compared to oxytetracycline, where only clove and cinnamon extracts showed inhibition zone diameter of 10.36 mm and 9.76 mm at concentration of 50 mg.

In conclusion, considering effect of reported compounds against *A. hydrophila*, wide range of question arises regarding compound isolation and stability, standardisation and effectiveness in animal models respecting pharmacokinetics and pharmacodynamics parameters that will finally influence potenial usefulness of novel agents. It should be noted that multi-resistant *A. hydrophila* strains are still not present in samples from Clinical Centre of Vojvodina, although the possibility for the emergence of resistant strains remains.

Ethical approval: All procedures described in this paper involving human participants were in accordance with the ethical standards and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest: None declared.

REFERENCES

1. Albarral V, Sanglas A, Palau M, Miñana-Galbis D, Fusté MC. Potential pathogenicity of Aeromonas hydrophila complex strains isolated from clinical, food, and environmental sources. Can J Microbiol. 2016; 62(4):296–306.
2. Stratev D, Odeyemi OA. Antimicrobial resistance of Aeromonas hydrophila isolated from different food sources: A mini-review. J Infect Public Health. 2016; 9(5):535–44.
3. Kali A, Kalaivani R, Charles P, Seetha KS. Aeromonas hydrophila meningitis and fulminant sepsis in preterm newborn: A case report and review of literature. Indian J Med Microbiol. 2016; 34(4):544–7.
4. Bruscolini F, Barbieri F, Battistelli M, Betti M, Dominici S, Manti A, et al. A multi-approach study of influence of growth temperature and nutrient deprivation in a strain of Aeromonas hydrophila. Int J Food Microbiol. 2014; 188:1–10.
5. del Castillo CS, Hikima J, Jang H-B, Nho S-W, Jung T-S, Wongtavatchai J, et al. Comparative Sequence Analysis of a Multidrug-Resistant Plasmid from Aeromonas hydrophila. Antimicrob Agents Chemother. 2013; 57(1):120–9.
6. Tsai Y-H, Shen S-H, Yang T-Y, Chen P-H, Huang K-C, Lee MS. Monomicrobial Necrotizing Fasciitis Caused by Aeromonas hydrophila and Klebsiella pneumoniae. Med Princ Pract Int J Kuwait Univ Health Sci Cent. 2015; 24(5):416–23.
7. Soliani MI, Ocaña Carrizo AV, Gasparotto AM, Rocchi M, Monterisi A, Trucchia R, et al. Bacteremia by Aeromonas spp. in adult patients who go to a university hospital. Analysis of ten episodes. Rev Fac Cienc Medicas Cordoba Argent. 2019; 76(3):154–8.
8. Zhou Y, Yu L, Nan Z, Zhang P, Kan B, Yan D, et al. Taxonomy, virulence genes and antimicrobial resistance of Aeromonas isolated from extra-intestinal and intestinal infections. BMC Infect Dis. 2019; 19(1):158.
9. Nagar V, Bandekar JR, Shashidhar R. Expression of virulence and stress response genes in Aeromonas hydrophila under various stress conditions. J Basic Microbiol. 2016; 56(10):1132–7.
10. Rama Devi K, Srinivasan R, Kannappan A, Santhakumari S, Bhuvaneswari M, Rajasekar P, et al. In vitro and in vivo efficacy of rosmarinic acid on quorum sensing mediated biofilm formation and virulence factor production in Aeromonas hydrophila. Biofouling. 2016; 32(10):1171–83.
11. Vijayakumar S, Vaseeharan B, Malaikozhundan B, Gobi N, Ravichandran S, Karthi S, et al. A novel antimicrobial therapy for the control of Aeromonas hydrophila infection in aquaculture using marine polysaccharide coated gold nanoparticle. Microb Pathog. 2017; 110:140–51.
12. Daood N. Isolation and Antibiotic Susceptibility of Aeromonas spp. From Freshwater Fish Farm and Farmed Carp (Dam of 16 Tishreen, Lattakia). 2012; 28(1):13.
13. Rosso F, Cedano JA, Parra-Lara LG, Sanz AM, Toala A, Velez JF, et al. (in press). Emerging carbapenem-resistant Aeromonas spp. infections in Cali, Colombia. Braz J Infect Dis Off Publ Braz Soc Infect Dis. 2019.
14. Elhariry HM. Biofilm formation by Aeromonas hydrophila on green-leafy vegetables: cabbage and lettuce. Foodborne Pathog Dis. 2011; 8(1):125–31.
15. Stanković S, Dimkić I, Vujisić L, Pavković-Lučić S, Jovanović Z, Stević T, et al. Chemical Defence in a Millipede: Evaluation and Characterization of Antimicrobial Activity of the Defensive Secretion from Pachyiulus hungaricus (Karsch, 1881) (Diplopoda, Julida, Julidae). PLOS ONE. 2016; 11(12):e0167249.
16. Ristivojević P, Dimkić I, Trifković J, Berić T, Vovk I, Milojković-Opsenica D, et al. Antimicrobial Activity of Serbian Propolis Evaluated by Means of MIC, HPTLC, Bioautography and Chemometrics. PLOS ONE. 2016; 11(6):e0157097.
17. Ramena G, Ramena Y, Challa N. Identification and Determination of Minimum Inhibitory Concentrations of Plant Extracts having Antimicrobial Activity as Potential Alternative Therapeutics to Treat Aeromonas hydrophila Infections. J Microb Pathog. 2018; 2(1):1–9.

