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Alternatives to the therapeutic impasse due to bacterial resistance to antibiotics

S. Kouara, S. Filali, N. Garaali , M. Mahmoud, G. Yahyaoui
Microbiology Department, Central Medical Analysis Laboratory, Hassan II University Hospital, Fez, Morocco

Abstract :
The remarkable effectiveness of antibiotics has motivated their massive and repeated use in human and animal health. This created selection pressure on bacterial populations, leading to the emergence of resistant strains. This phenomenon, in constant increase, places the doctors in a therapeutic impasse. The objective of our work is to review the possible possibilities currently proposed. Old therapeutics are now being reevaluated such as honey and larvotherapy. Other therapies are being considered and developed, such as probiotics, odilorhabdines and phagotherapy, which is once again prompting the resumption of studies.
Key words : *antibiotic resistance, honey, larvotherapy, probiotics, odilorhabdines, phagotherapy.*

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I. Introduction :

The golden age of antibiotic therapy began in the second half of the 20th century. The remarkable efficacy of antibiotics motivated their massive and repeated use in human and animal health. This created a selection pressure on bacterial populations, leading to the appearance of resistant strains. This phenomenon, which is constantly increasing, places physicians in a therapeutic impasse.

Currently, the appearance of bacterial resistance to almost all antibiotics makes the treatment of certain bacterial infections impossible with sometimes unfortunate consequences, hence the interest in finding alternative or complementary solutions.

The objective of our work is to review the possible possibilities currently proposed, some of which are new and others older, dominated by phagotherapy, which is becoming the most successful means nowadays.

Antibiotic resistance problem :

Bacteria are microorganisms that evolve to adapt to various hostile conditions and fight against their rivals. Most antibiotics are designed to reproduce and improve this fight. However, the poorly controlled use of these antibiotics has allowed several bacterial resistances to emerge. On February 27, 2017, the World Health Organization (WHO) released a list of resistant bacteria that pose a global threat. Acinetobacter baumannii, Pseudomonas aeruginosa, and extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae thus represent a critical emergency because they are resistant to a large number of antibiotics. Six other bacteria, including Staphylococcus aureus, Helicobacter pylori, Salmonella, and Neisseria gonorrhoeae, represent a high emergency. Finally, Streptococcus pneumoniae, Haemophilus influenzae and Shigella spp are of moderate urgency [1].

The appearance of several antibiotic resistances, becoming more and more severe and impossible to manage, leads to the use of alternatives.

Alternatives to antibiotic therapy:

<u>The old alternatives:</u>

According to a review by Bourlioux, old therapeutics are now being re-evaluated, based essentially on honey and larvotherapy [2].

<u>Honey:</u>

Honey was recommended by Hippocrates in the treatment of wounds 2600 years ago. It has been shown that honey can be used not only as a source of energy, but also for its anti-inflammatory, antibacterial, antifungal and antioxidant effects. Indeed, it has an inhibiting effect on about 60 species of bacteria, gram-positive and gram-negative, aerobic and anaerobic, such as Bacillus anthracis, Corynebacterium diptheriae, Haemophilus influenzae, Klebsiella pneumoniae, Mycobacterium tuberculosis, Proteus, Escherichia coli, Pseudomonas aeruginosa, Salmonella, Shigella, methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus faecalis [3,4].

Numerous studies have shown that the activity of Helicobacter pylori in the human digestive system was reduced by 20% when honey was used [4, 5, 6]. The bactericidal activity of honey against Helicobacter pylori could be used in combination with antibiotics in triple therapy to help eradicate it. The main difference compared to antibiotics, honey will not develop antibiotic resistant bacteria, so it can be used continuously without this risk [7].

Honey can have bacteriostatic and bactericidal effects depending of course on the concentration. The mechanisms of its activity against bacteria are different from those observed in the case of antibiotics; antibiotics destroy the cell membrane of the bacterial cell or inhibit intracellular metabolic pathways, on the other hand, honey dehydrates the bacteria. The sugar content of honey and its acidic PH ranging from 3.2 to 5 decrease the growth of microbes. In addition, hydrogen peroxide produced by glucose oxidase is an important antibacterial component [6,7].

Currently, honey is also commercialized by a French company Melipharm in the form of sterile honey-based medical devices for the treatment of acute and chronic wounds [2].

Larvotherapy :

Maggots, or maggot therapy, has been used since ancient times by Napoleon's surgeon Dominique Larrey, who noticed that maggots ate the dead tissue of wounds with a curative effect on the wounded. In 2004, the Food and Drug Administration (FDA) approved this practice after a study conducted at the University Hospital of Caen in France showed that maggots could be used as an antibacterial drug [2].

The new alternatives:

Probiotics:

Probiotics are live microorganisms that, when administered in adequate doses, confer a health benefit to the host as defined by the Food and Agriculture Organization of the United Nations and the World Health Organization (FAO / WHO 2001) [8].

At the beginning of the 20th century, Metchnikoff suggested that the longevity of the Bulgarians was due to the consumption of fermented milk products. For this purpose, lactic acid bacteria in fermented milk products have been used for a very long time. Probiotic properties have been observed in many genera of bacteria and fungi, but the most commonly used probiotics belong to the Lactobacillus and Bifidobacterium species, which as commensals of the human microbiome are safe and non-pathogenic [8].

The term "probiotic" can refer to the following products: probiotic drugs, medical devices, and probiotic foods (foods, food ingredients, dietary supplements, or foods for special medical use). Generally, probiotic bacteria have a beneficial effect on the digestive system, but in some cases they can facilitate translocation or cause infections themselves. In addition, probiotic treatment of premature and newborn infants should be considered with caution, because at birth infants do not have a fully developed immune system and therefore, after administration of probiotics, the risk of fungemia or bacteremia increases considerably [8,9].

Odilorhabdines:

Odilorhabdins are a new class of antibacterial agents that could provide an answer to antibiotic resistance, discovered from an entomopathogenic bacterium of the genus Xenorhabdus from the family of enterobacteria. It has been shown to be active against the most worrisome multi-resistant gram-negative pathogens: Escherichia coli [10,11].

Odilorhabdines should be suitable for the treatment of complicated urinary and abdominal infections and multidrug-resistant nosocomial pneumonia with Gram-negative pathogens: ESBL enterobacteria, Pseudomonas aeruginosa, Acinetobacter baumannii [10, 11].

Phage therapy:

Bacteriophages are naturally occurring viruses, present anywhere in the environment: soil, water, skin or human digestive tract and which specifically and naturally infect bacteria. Their diversity is immeasurable since it is estimated that there are about 10^30 bacteriophages with 10^8 different genomes on the planet [12].

This diversity constitutes an almost unlimited reservoir of therapeutic antibacterial agents. The natural role of bacteriophages is essential since they are powerful regulators of bacterial populations. In aquatic ecosystems, bacteriophages are responsible for the lysis of 10 to 20% of the bacterioplankton biomass per day [13].

Only bacteriophages multiplying according to a lytic cycle are considered in therapeutics, the lytic cycle includes 4 steps: adsorption (attachment of the bacteriophage to the bacterium); injection of the genetic material of the bacteriophage into the bacterium; transcription of the genetic material; bacterial lysis with release of newly produced bacteriophages [14].

Their applications are numerous: biological treatment of human and animal bacterial infections (Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus...), antibiotic-resistant bacteria (Gram-negative resistance: ESBL; Gram-positive resistance: MRSA [15].

Today, experimental evidence of the efficacy of bacteriophages is growing. They are routinely used in the food industry, mainly targeting Listeria monocytogenes, enterohaemorrhagic Escherichia coli strains or various phytopathogens attacking plantations. There is also a large number of publications demonstrating the therapeutic efficacy of bacteriophages in animals, in different infection models and against different pathogens [14].

In humans, Dr Dublanchet, one of the world specialists in phage therapy, advocates the reintroduction of this technique based on bacteriophages to detect and/or destroy a wide range of antibiotic resistance, emerging bacteria and nosocomial infections, using a technology that aims to develop a phage bank with a targeted mission [15].

II. Conclusion :

In order to overcome the thorny problem of bacterial resistance to antibiotic molecules, several alternatives are being considered that are generating a sincere and important resumption of studies.

Phage therapy is not yet a universal therapeutic weapon. It needs to be thoroughly and rigorously evaluated, the only way to establish its most effective field of activity and the best benefit-risk ratio.

Conflicts of interest :
The authors declare no conflict of interest.

References :

[1]. OMS. List of bacteria for which new antibiotics are urgently needed. 2017. Accessible à l'URL : https://www.who.int/fr/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed.
[2]. Bourlioux P. De quelles alternatives notre arsenal thérapeutique anti-infectieux dispose-t-il face aux bactéries multi-résistantes ? . Annales Pharmaceutiques Françaises. 2013 ; 71(3), 150–158.
[3]. Kenjeric D, Mandic ML, Primorac L, Bubalo D, Perl A. Flavonoidprofile of Robinia honeys produced in Croatia. Food Chem2016;102:683—90.
[4]. Al-Jabri AA. Honey, milk and antibiotics. Afr J Biotechnol2005;4:1580—7.
[5]. Alvarez-Suarez JM, Tulipani S, Romandini S, Bertoli E, BattinoM. Contribution of honey in nutrition and human health: areview. Mediterr. J Nutr Metab 2010;3:15—23.
[6]. G. Ilia, V. Simulescu, P. Merghes, N. Varan. The health benefits of honey as an energysource with antioxidant, antibacterial andantiseptic effects.Scispo. 2020 ; 3519-10.
[7]. Asadi-Pooya A, Pnjehshahin MR, Beheshti S. The antimycobac-terial effect of honey: an in vitro study. Riv Biol 2003;96:491—6.
[8]. A. Zawistowska-Rojek et S. Tyski. Les probiotiques sont-ils vraiment sans danger pour les humains? . Pol J Microbiol. 2018 ; 67(3) : 251-258.
[9]. Boyle RJ, Robins-Browne RM, Tang ML. Utilisation des probiotiques en pratique clinique: quels sont les risques? . Am J Clin Nutr. 2006 ; 83 : 1256-1264.
[10]. Nosopharm. Accessible à l'URL : www.nosopharm.com/nosopharm-and-evotec-enter-into-collaboration-to-accelerate-development-of-novelantibiotics/.
[11]. Revue Francophone des Laboratoires. 2014 ; N°465 CAHIER 1.
[12]. Rohwer F. Global phage diversity. Cell. 2003;113:141.
[13]. Wommack KE, Colwell RR. Virioplankton: viruses in aquatic ecosystems. Micro-biol Mol Biol Rev 2000;64:69–114.
[14]. R. Prevel, N. Dufour.Potentialités des bactériophages pour l'infectiologie moderne. La Revue de médecine interne 37. 2016 ; 657–660.
[15]. Pherecydes Pharma. Accessible à l'URL : https:// www.pherecydes-pharma.com.

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