Is active individual prevention against Covid-19 possible?

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Introduction

The Covid-19 pandemic is posing a major worldwide problem, although at various levels in the different States. Although Covid-19 in most cases develops benevolently and fearfully or asymptomatically, however it can present different percentages of serious complications, especially in elderly, defed or chronically ill subjects, with need of hospitalization and intensive care. Since Sars-CoV-2 is characterized by marked infectivity and a high percentage of serious complications (on average 3.6%), there has been a rapid spread, with logarithmic growth also of cases with serious complications, so that the Healthcare Systems have been subjected to high pressure, not always well sustainable. Therefore, in an attempt to contain the exponential growth of the virosis, various degrees of isolation and/or social distancing measures have been implemented in almost all States, with the closure of educational, economic, commercial and social activities (*lockdown*), albeit with different timing and different intensity and duration.This has, however, led to a particularly remarkable, almost deflagrating social and economic impact.For example in Italy from 20.02.2020 in about a month the following were detected: - stock market losses of 30%; - drop in the price of the barrel of crude oil by about 50%; - 6% decrease in GDP and subsequent reduction of 0.75% for each week of additive lock-down; - loss of about 2 million jobs, with unemployment rising to 11% of the potentially active population.[1] Considering that similar, albeit different, data are found in all the other affected States and that they depend on the *lockdown*strategies applied, it is understandable, that this viral spread containment strategy, although useful in an initial initial phase, cannot be sustained for too long.[1] Therefore, it follows the need to propose infection containment strategies, which are reconcilable with a reduction of the*lockdown* , pending the development of a decisive vaccination campaign. In this perspective, we must be open to new perspectives in the preventive field, just as new perspectives are being evaluated in the therapeutic field.

Sustainable individual prevention

The evolution of Sars-CoV-2 virosis, like all the other aerial viroses, passes biologically, substantially through the following steps:

step 1 : interhuman contamination by droplets (" *Függe droplets* ")

step 2 : local multiplication at the contamination site

step 3 : active infection

step 4 : inflammatory response

step 5 : symptoms and clinical evolution

step 6 : complications.

The management of the Covid-19 pandemic can be summarized in the following stages

phase 0 : the local spread of the virus has not yet occurred and so occurs only observation of the events, that have developed in other countries.

phase 1 : beginning of the infection with rapid growth of cases; therefore application of social isolation measures (*lockdown*) for the prevention of *step 1* (interhuman contamination) and, at the same time, commitment to increase the treatment possibilities of*step 6* (serious complications)

phase 2 : flattening/descent of the virosis diffusion curve and reduction of cases of serious complication; therefore interruption of the and resumption of interhuman activities. In this phase specific therapy methods are developed to interact on *steps 4* and*5* . However remains the need for social distancing methods, associated with the recovery of interhuman contacts, to continue controlling *step 1* (interhuman contamination).

In practice, these are the following passive contamination prevention methods: - personalized social isolation, aimed at subjects with Sars-CoV-2, also if asymptomatic, with electronic monitoring, through personalized geolocation methods; - maintenance of a minimum interpersonal distance, variously determined in distances between 1 and 3 meters; - use of protective face masks; - use of disposable gloves; - avoid touching mouth, nose or eyes

- frequent hand washing. [2,3]

phase 3 : development of adequate vaccination and implementation of a vaccination campaign and therefore stop of the effects of the pandemic on populations.

In this evolutionary context, thinking of the *phase 2* scenario, with the resumption of normal socio-economic activities, it makes sense to consider appropriate, to be able to add additional active prevention actions, pertaining to the second step of the infectious process (*step 2*), that is, the passing from contamination alone to clinically obvious infection, through local viral multiplication. Each virus exchanged contaminates the first arrival sites and will tend to multiply here. Only following consistent viral multiplication, does an infection take place, with all its pathophysiological consequences, linked to the inflammatory reaction. An important role is therefore represented by the size of the infectious load: if this is reduced, the clinical manifestations are equally reduced.[4,5] In the presence of a favoring pathophysiological pabulum (co-pathologies), the infection can sometimes evolve, even in a serious and sometimes lethal way, instead of passing benignly and going out, following the inflammatory and immune response.[5] Therefore, intervening at the level of contamination, we can think of reducing or preventing the passage to infection, reducing the possibility of viral multiplication and, therefore, the infectious load, and, with this, all further potentially related events. Personal prevention could, therefore, be pursued not only in a passive way, with the reduction of the risk of exchange of contaminating droplets (facial masks, glasses, gloves, prevention of interpersonal distancing, disinfection, hand washing, etc.), but also in an active way, with the prevention of the passage from contamination to active infection, intervening in reducing the multiplication of the contaminating viral particles. In this scenario, three active personal prevention practice methods could be applicable by each one individually:

- probiotic prevention, by using Streptococcus salivarius k12

- phytotherapeutic prevention, through phyto-extracts of the root of Echinacea angustifolia

- thermal prevention, using the Messini thermo-prevention method.

All these methods, if applied regularly, result in a direct and/or in an interferon-mediated antiviral effect. So they can act as limiters of the viral contaminant share and, with this, participate in reducing viral multiplication (*step 2*) and preventing infectious development*(steps 3-4-5*).

Prevention by oral probiosis (Streptococcus salivarius k12)

When evaluating a viral infection, we must not make the mistake of thinking that the pathogen arrives in a healthy territory, as it is free from microorganisms. In reality, it is necessary to think in terms of the relationships between microbial (bacterial, mycotic and / or viral) consortia.[6] In fact, if we evaluate the genome of each human subject, the specifically human eukaryotic one represents only 3.6%; the bacterial one is 9.5%; the viral one represents 67.7%.[6] Each of us, therefore, is, in reality, an integrated multi-being association, in which bacteria and viruses are present and essential to healthy human life. An infection, therefore, is not to be considered simply the afference of a pathogen and that's it, but it must be seen, as the interaction of

a new microbe on the balance of the pre-existing resident bacterial and viral consortium. Therefore the new microbial agent can more easily spread to the contamination site, if the microbial consortium residing therein is already per se altered or anomalous. This may be one of the explanations, why Sars-CoV-2 in many cases does not give symptoms, in others only mild symptoms and in some, instead, serious symptoms and complications. The eubiotic oral microbiota, as resulting from the Human Oral Microbiome Database/HOMD (*www.homd.org*) is a complex consortium, which includes 619 taxa in 13 phyla, namely: Actinobacteria, Bacteroidetes, Chlamydiae, Chloroflexi, Euryarchaeota, Firmicutes, Fusobacteria, Proteobacteria, Spirochaetes, Synergistetes, Tenericutes.[7,8] It is however characterized by a preponderant presence of Firmicutes of the genus Streptococcus, with the dominant species S. salivarius. The most documented Streptococcus salivarius in the world is the k12 strain. Through the release of bacteriocins (A2 and B), it antagonizes and counteracts the presence of a "pathogenic" oral bacterial consortium, characterized by the presence of species such as S. Pyogenes and Pneumococcus and by genera such as Moraxella and Haemophilus.[9] The oral microbiota in which the S. salivarius k12 strain is present is also characterized by the salivary presence of IFNγ higher than the average of the controls. This element strongly correlates with the ability of the k12 strain to reduce pharyngo-tonsillary recurrences and other viral respiratory diseases.[9] The lung microbiota both in healthy subjects and in pathology[5,9,10,11] is borrowed from the oral one. The stable and dominant presence of Streptococcus salivarius in the lung is an indication of eubiosis.[9,10] The stable presence of S. Salivarius k12 in the oral consortium would suggest its presence also in the lung and the creation, therefore, in the respiratory district of an eubiosis, potentially anti-pathogens and so also anti-viral.[9,10] Therefore the probiosis with Streptococcus salivarius strain k12 can be proposed as a useful means to support an oral and consequently optimal lung microbiota, which collaborates to prevent the engraftment and multiplication of exogenous virosis, especially through the increase of the presence of salivary γ-interferon (IFNγ).

Prevention by phyto-extracts of the root of Echinacea angustifolia

There are 9 species belonging to the genus Echinacea, but the most studied are three: Echinacea angustifolia, Echinacea purpurea and Echinacea pallida, all different from a botanical point of view, in composition and pharmacological activity, although similar in their clinical use. Echinacea has been better known to Europeans since the eighteenth century, while Native Americans have used it for much longer, for example, to heal wounds; in particular, the Cheyenne but also the Pawnee and Lakotah-Siux used it for sore throat, cough or as an analgesic.[13] Echinacea has several properties confirmed by research and these derive from the extremely eclectic composition of this family of plants in whose roots, but also in the aerial parts, there are several active ingredients that confer an immunostimulating, anti-inflammatory, antioxidant, antiviral[14] and antibacterial action . Echinacea purpurea root extracts are found to have immunomodulatory effects in experimental mouse models.[15] Specifically, the immunomostimulating action is determined by the polysaccharide fraction (*echinacein* , *echinacoside*), which leads to an increase in leukocytes, macrophages with their ability to engulf pathogens, and NK (*Natural Killer*) lymphocytes, capable of recognizing and destroying, for example, virus infected cells.[14] In particular, echinacein determines an anti-inflammatory action, while polyphenols and chicory acid an indirect free radicals activity, which protects the collagen, the main constituent of the human connective tissue.[16] The antiviral activity, on the other hand, is attributable to the generic ability of this plant to interact with the macrophage metabolic pathways of production of interferon α and β, capable of inhibiting the replication of viruses inside the infected cells and specifically to the chicoric acid and caffeic acid, as well as its derivative, echinacoside, substances that tend to hinder the aggression of viruses.[17] In fact, in virus infected cells, all Echinacea extracts increased the inducible amount of nitric oxide synthase (iNOS) and this effect varied, according to the type of extraction preparation. The results suggest that any potential antiviral activity of Echinacea spp. extracts are probably not mediated by direct induction of type I interferon, but rather involve iNOS.[18] Oral preparations containing hydro-alcoholic extracts of Echinaceae purpureae and Echinaceae pallidae root, administered 6 days before exposure to the influenza-A virus, expresses immunomodulatory activity and is a potent inhibitor of the pathology of the virus in vivo.[19] The documented antiviral immunomodulatory action of Echinacea extracts, could also be correlated with its prebiotic action on the human microbiota due to the presence in the Echinacea root extracts of inulin-type fructans (*ITFs*).[20] Therefore, the antiviral activity of Echinacea extracts is overall

documented. Consequently, the administration of Echinacea angustifolia preparations can be proposed as a preventive antiviral aid.

The Messini thermo-prevention

The SARS-CoV2, even if it is most aggressive, is still a Coronavirus, with capsid structure and lipid envelope.[6,12,21] Like other coronaviruses, SARS-CoV-2 has four structural proteins, known as: protein S (spike), E (envelope envelope), M (membrane) and N (nucleus); protein N contains the RNA genome while proteins S, E and M together create the viral envelope.[12] Coronaviruses, together with Rhinoviruses and Orthomyxoviruses, are often implicated in respiratory diseases of common cold, which, more often, appear mainly in cold seasons, or in periods of sudden thermal decrease. They mainly affect the upper respiratory tract, and, first of all, initially, the mucous membrane of the nasal and paranasal cavities in particular and/or of the larynx. Alphacoronavirus and betacoronavirus are distinguished; some cause mild diseases of the upper respiratory tract, including the common cold (229E, NL63, OC43, HKU1); others underlie far more serious respiratory diseases (Sars-CoV, Mers-CoV, Sars-Cov-2). Almost all these viruses, can be defined as "cryophilic" (*cold loving*), that is, they prefer and survive better at temperatures of around 33-35°C or lower; therefore they prefer the mucous membranes of the "colder" or "more easily cooled" bodily territories, that is, whose average temperature is lower than the average basal endocorporeal human standard (37°C). Coronavirus dried on smooth surfaces retains its vitality for over 5 days at temperatures of 22-25°C and relative humidity of 40-50%, that is the typical typology of air-conditioned rooms.[25] Conversely, the viability of the virus is rapidly lost ($>$ 3 log10) at higher temperatures and higher relative humidity (for example: 38°C and relative humidity$>$ 95%). The improved stability of the Sars-CoV at low temperature and low humidity environment can facilitate its transmission even in communities in the subtropical area (such as Hong Kong) in air-conditioned environments.[27] Moreover, innate immune defenses, however, have a temperature-dependent efficacy in limiting the replication of common cold viruses: it increases with hot temperature.[27] In fact, it is documented that hyperthermia induces endogenous production of γ-interferon (IFNγ), with a consequent antiviral effect.[29,30,31] Yamaya M.'s 2019 work on the effects of high temperatures on the replication of seasonal or pandemic human influenza virus[32] is particularly interesting, but, above all, the very recent February 2020 work published by Wang, reports, that the diffusion difference of the new coronavirus Sars-CoV-2 in different Chinese cities, correlate with its temperature. As a result, the minimum temperature increase of 1°C correlates with the reduction in the cumulative number of cases by a factor of 0.86 and at a temperature of 38°C the virus quickly loses its activity.[33] Even if the spread of viral pathologies of the airways, and in particular of the more serious ones, such as the recent pandemic from coronavirus Sars-CoV-2, cannot be influenced only by the ambient temperature, however the correlations existing between the spread of the virosis and environmental temperatures are documented.[34] These epidemiological evaluations are consistent with the potential of the use of hyperthermic treatment, not so much as therapy of acute pathologies already in place, but for prophylactic/preventive purposes. The Messini thermo-prevention method has been proposed for the prevention of seasonal common cold diseases,[35] but, considering the common structural bases with the other coronaviruses, it can be sensibly considered, to be also suitable for an active auxiliary personal prevention against Sars-Cov-2. The thermo-prevention, therefore, consists of individually heating the upper respiratory tract several times daily, so as to reduce the viral contaminating share, reducing or preventing its multiplication. This favors the interruption of the evolution from contamination to infection. This can be simply achieved by heating the nose, jaws, ear cavities and throat by means of a flow of hot air, generate, for example, by a simple hairdryer with at least 600 watts of power. The 70-80°C hot air-flow produced by hair dryers easily allows increasing the temperature of the affected areas to over 40-43°C. Such applications, repeated daily and regularly for two minutes, at least 4 times a day, allow effective active prophylaxis. The Messini method [35] suggests, therefore, the heating of the territories of the nasal cavities, of the areas of the frontal and maxillary sinuses, followed by the jaws with open mouth, subsequently of right and left ear, finally the right and left lateral cervical region with hot air flow at about 70-80°C, so that in these areas a temperature higher than 40-43°C is obtained. So is it possible to contrast the "vital" and replicative biological capacities of the "cryophilic" viruses, both directly, interfering with the viral capsidic structure,[22,23,24,26] and indirectly by increasing the local production of

IFNγ (γ-Interferon).[28,29,30,31] Obviously the result can only be obtained with a regular use of the method and, therefore, it is intrinsically subjective and dependent on individual diligence.

Conclusions

In the context of a *phase 2* of loosening the *lockdown* for the Covid-19 pandemic, it is reasonable to propose, to add to the expected strategy of social distancing, which seeks to reduce the inhuman spread of the virus (*step 1*), also active personal preventive strategies, which seek individually and daily to reduce the contaminating viral load, reducing the risk of passing from contamination to active infection (*step2*). This additional active individual prevention takes the form of three proposals: probiotic prevention, by means of Streptococcus salivarius k12; phytotherapeutic prevention, through phyto-extracts of the root of Echinacea angustifolia; thermal prevention, using the Messini thermo-prevention method.

Conflict of interest

The author declares no conflicts of interest

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