

Primum non nocere (first do no harm). The SARS-CoV-2 pandemic course in oldest in Italy

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Summary. Dramatic outcomes of Covid-19 pandemia in Italy, in particular in the North, must be discussed. Maybe a bad strategy and lack of timely intervention together with concurrent social events, comorbidities of oldest persons, bed rest, inadequate nutritional support and drugs' side effects and infection of health professionals proved fatal for many. (www.actabiomedica.it)

Key words: COVID-19

Most people know the aphorism *Primum non nocere* taught to medical students, attributed to Hippocrates but timeless in its quiet sanity. “*First, do no harm*» remains a basic tenet of medical practice. Also in this period of global stress due to pandemia. But the complexity of modern medicine, as well as the great number of professionals taking care of a single problem and of a single patient, have resulted in bad strategy and a great confusion in policymakers, particularly concerning care of older people.

Different opinions among scientists, as occurred recently in COVID-19 pandemia in Italy, combined with the difficulties due to comorbidities and dependency of oldest persons have resulted in strategic errors, a significant part of which proved fatal for the patient and catastrophic for the society. Great interest was given to the apex of the pyramid (ICUs) instead of the base (prevention devices, lockdown of health facilities for old people).

Why so many problems in the approach to the pandemia, and in Lombardy and surroundings as well? Let us give a look at the story and related negative events.

a-first of all the delayed alarm coming from China, and maybe insufficient info on the virus. On January 5, WHO alerts about numerous cases of se-

vere pneumonia in China. On January 18 the Medical Literature Guide Amedeo (1) draws the attention to a study of the Imperial College of London on the real high number of cases in Wuhan and on 23 the Chinese government put millions of people in quarantine, with severe travel restriction starting from 25. On 30 WHO declares coronavirus a global emergency. On February 19 in Milan an international soccer match developed a coronavirus sociobiological bomb. On 20 the first patient in Italy was diagnosed, many days after his hospitalization, not so far from Milan. Bombs exploded one after the other within few days. At least 40 days were lost from when it was advisable to lockdown social and health wards of any type, and long term facilities as a priority.

b- as a consequence of the lack of a timely intervention with no appropriate prevention methodologies, virus entered into hospitals, nursing homes, day centers and doctor's offices. Health professionals were infected, contributing to diffusion of virus in their wards, offices and homes. It should have been necessary to provide timely and easy availability of masks, gloves and gowns for individual and social protection, just in January, at least in first part of February. And diagnostic instruments were not adequate for necessity of testing infected or supposed infected persons. Studies of sero-

logic response after COVID-19 are in their infancy, and we should expect larger more representative analyses as antibody testing rapidly becomes more available (2). Recent studies demonstrated that SARS-CoV-2 tends to persist longer in stool samples than in respiratory or serum samples (3). The median duration of viral RNA in stool samples was 22 days, compared with 18 days in respiratory and 16 days in serum samples. For patients with severe disease, the median duration of the virus in respiratory samples was 21 days, versus 14 days in those with mild disease.

c- the characteristics of residents in nursing homes were not considered. Most part is suffering from severe cognitive disorders, with a high level of functional dependence. The physical distancing rules affect people with dementia who find their normal routines disrupted, lack cognitive stimulation, feel lonely and anxious and at risk of delirium. All these highlights, coming from scientific societies, remained ignored. Similarly, all caregivers involved in the care of these subjects encountered challenges due to the disruption of normal routines and the loss of support and closure of services. Finally, health and social care professionals were striving to provide appropriate and timely treatment, support and care, despite fears for their own safety due to the lack of protective clothing and many became ill and many doctors died. The psychogeriatric patients living in skilled nursing homes had no adequate support in activities of daily living, in mobility, and nutrition. And when infected mortality was very high.

d- many medical treatments used in China without evidence do cause harm: learning how to navigate the risks of drug therapies, as well as their catastrophic consequences in older population was not taken into consideration. An inexpensive and old antiviral, amantadine, was never tested, in spite of use of drugs for HIV and similar. Recently (4) authors reviewed various treatment options for COVID-19 and lay out the evidence as it currently exists. No therapies have yet been proven effective. Using hydroxychloroquine and azithromycin to treat COVID-19 patients with preexisting cardiovascular disease is at risk of severe arrhythmia, polymorphic ventricular tachycardia, long QT syndrome, and increased risk for sudden death. Tocilizumab and colchicine are under controlled studies. People who have recovered from COVID-19 are en-

couraged to donate their plasma to help others who are severely ill. But this approach is for younger patients in ICUs. The National Institutes of Health panel (5) has released in last days guidelines on treating patients with COVID-19. The panel does not recommend any drug for pre- or post-exposure prophylaxis outside of clinical trials, does not make a recommendation for specific antiviral or immunomodulatory treatments, as no drug has been proven to be safe and effective.. It comes out against use of hydroxychloroquine plus azithromycin outside of clinical trials because of the toxicity risk, as well as against lopinavir/ritonavir or other HIV protease inhibitors because of negative clinical trial results and unfavorable pharmacodynamics. The panel also recommends against interferons and Janus kinase inhibitors and the use of systemic corticosteroids for mechanically ventilated adults with COVID-19 who don't have acute respiratory distress syndrome. Low-dose corticosteroids is better than no corticosteroids in patients with refractory shock.

e- last but not least both nursing homes and in-hospital patients with COVID-19 were frequently bedridden, and were at risk of *COMPLICATIONS OF BED REST*: Deep Venous Thrombosis, Pulmonary Embolism, Secondary pressure areas, Dehydration / Malnutrition, Contractures Deconditioning, Muscle weakness, Agitation and delirium, and **Multiple organ dysfunction syndrome**. The primary cause, Covid 19, triggers an uncontrolled inflammatory response with macro- and microvascular changes, endothelium damage, interstitial pneumonia, insufficient supply of oxygen and hypoxemia, cell death and organ dysfunction. Prophylactic use of low molecular weight heparin is now under study, with appropriate use considering high risk of thrombosis.

Are we today at the end of the story? Not at all. And what can we do to getting better outcomes?

First of all pay attention in all old persons to earliest clinical signs and symptoms, as altered taste and smell (6), delirium and hypoxemia. Recommend screening all healthcare workers for fever and respiratory symptoms at the beginning of their shifts, prioritizing them for testing, and ensuring options to discourage working while ill. The workers who developed COVID-19 had longer exposures to the patient and were more likely to be present for nebulizer treatments,

compared with workers who didn't become infected. Furthermore, high concentrations of live virus in the air in and around two hospitals in Wuhan, China was seen. The study showed viral particles were present in air samples from patients' toilet areas, in rooms where healthcare workers removed their protective equipment, and in two crowded public places near the hospitals. Certain hospital procedures, like intubating a patient, could generate infectious aerosols. The coronavirus could travel up to 13 feet (4 meters) as an aerosol in hospital settings (7). Could the same occur in nursing homes, day centers and in air conditioned wards? This should be studied ASAP. Wearing face masks, even when the evidence doesn't overwhelmingly support their use must be advisable. Masks are simple, cheap, and potentially effective and they could have a substantial impact on viral transmission with a relatively small impact on social and economic life.

Digital contact tracing: could it be useful? Not for residents of nursing homes, of course. And it is necessary to consider older person's digital divide in the use in the community (8).

Side effects of drug therapy in oldest people should be always considered: they are common because of comorbidities, multiple drug therapy and multi organ failure. Last but not least the necessity of providing activity and good nutrition in oldest population is mandatory, in any setting at any time. In conclusion: FIRST DO NO HARM.

Conflict of interest: The author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 26 April 2020

Accepted: 27 April 2020

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