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Editorial

Lessons from COVID-19: How human behaviour may influence the science



The COVID-19 pandemic has affected and it is still affecting the entire world [1], which unfortunately, was not prepared to face such a new and dramatic situation [2]. It is time to admit too that healthcare organisations (national and international) and healthcare professionals were not prepared and that several mistakes, ‘identified’ as of today, have conditioned the destiny of those infected by the virus and of those around them.

1. Angiotensin-Converting-Enzyme-2 Receptor (ACE2)

1.1. Angiotensin-Converting-Enzyme inhibitors (ACEi) and Angiotensin-Receptor-Blockers (ARBs)

ACE2 has been identified as the receptor for the spike-protein of SARS-CoV-2 [3].

A serious concern about a possible induction of ACE2 was suggested related to the use of ACEi or ARBs [4]. At that time, many people with hypertension treated with ACEi or ARBs went into panic and suspended the therapy. This issue has been now solved with specific data against this concern [5], but we will never know the cost in terms of lost lives or cardiovascular events due to the interruption of the ACEi or ARBs treatment.

1.2. Diabetes and hyperglycemia

Mounting evidence suggests that diabetes is one the most relevant co-morbidities in affecting the prognosis of the COVID-19 [1]. However, it is not simply the presence of diabetes but the level of hyperglycemia during the disease that impacts on the prognosis [6]. This is true also for people without diabetes but with hyperglycemia during COVID-19 infection [6]. It is amazing that, excluding some recommendations published by experts in diabetes [7–9], in the available National and International professional guidelines and expert recommendations — 31 in PubMed accessed and examined on September 18th 2020 — the problem of diabetes and particularly of the need for a strict control of hyperglycemia is completely neglected.

1.3. Diabetes therapy

Inflammation plays a key role during SARS-CoV-2 infection. The Dipeptidyl Peptidase 4 receptor (DPP4) is expressed ubiquitously in many tissues, including those in the respiratory tract, thus representing a potential target to reduce the severity of COVID-19 [10]. At the same time, DPP4 is the target of incretin-based therapies, and this begs the question whether DPP4 inhibitors, currently used for the treatment of people with type 2 diabetes, may be effective against SARS-CoV-2 [10]. The scientific community is cautious about this hypothesis, since this assumption is based only on preclinical data. However the reporting of this hypothesis in the mainstream media led many people with diabetes to ask for this specific treatment.

On the other side, it has been hypothesized that the Sodium-Glucose-Transporter-2 inhibitors (SGLT-2i), the Glucagon-Like-Peptide-1 Receptor Agonists (GLP-1RAs) Pioglitazone and even Insulin might induce an over-expression of ACE2, therefore increasing the risk for more serious consequences for people with diabetes if infected [11]. The alarm has not been justified; on the contrary all the above-mentioned drugs for the treatment of diabetes also show very good anti-inflammatory action and, in the case of GLP-1RAs and SGLT-2i, proven cardiovascular protection [11]. Anyhow, this debate created a lot of confusion not only in people with diabetes but also in their attending physicians.

1.4. Corticosteroids

Corticosteroids are widely used in diseases with important inflammatory aspects. It is well known that COVID-19 is accompanied by a ‘cytokine storm’ which, of course means a very serious inflammatory condition [3]. However, in the beginning of the pandemic the recommendation was to avoid the use of corticosteroids [12]. The clinical evidence and a specific trial have demonstrated that this recommendation was completely wrong [13].

1.5. Hydroxychloroquine

No topic has been more hotly debated in the treatment of COVID-19 than the use of hydroxychloroquine.

Preliminary evidence suggested a potential benefit of using hydroxychloroquine in COVID-19, until two publications claimed to demonstrate the failure of such treatment [14]. These two papers were withdrawn for serious methodological issues revealed after their publication and the benefits of this treatment are still under research [14]. During this ‘debate’, hydroxychloroquine use was still promoted in the media and by some high-profile individuals. However, hydroxychloroquine may have serious side effects, particularly for the heart and in diabetes, where it is increasing the risk of hypoglycemia [14]. Again, the human cost of this confused situation is at present unknown.

1.6. Thrombosis

It is now well recognized that thrombosis is the most significant complication of COVID-19 and, consequently, the use of the anticoagulants is essential [7,8].

This important pathogenic aspect of COVID-19 emerged during autopsies of people who had died of the disease, which were performed against the recommendation of the health authorities [15].

1.7. Impact of human behaviour on science during COVID-19

As described above, several errors in COVID-19 treatment may have conditioned the outcome of the disease in many cases. Why has this occurred? Following are three possible explanations. First, the communication between different specialists has failed. As a consequence, at least hyperglycemia (in diabetes and non-diabetes) was not identified as an issue in COVID-19 treatment. Second, pure scientific hypotheses were considered equivalent to true evidence, without any substantial proof. This is the case of the ACEi, ARBs and of some

antidiabetes drugs. Similarly, the finding of the key pathogenic role of thrombosis has been discovered as some physicians decided not to respect the interdiction of the health authorities to perform the autopsy or to limit its execution. Third, some preliminary therapeutic data were interpreted without caution. This may be applied to the use of corticosteroids, which were banned for a period of time, and hydroxychloroquine, which was offering a hope for COVID-19 cure. Furthermore, these situations were driven by a global debate in the media, with excess information and ‘fake news’, causing widespread fear and confusion [16].

1.8. What should we learn from COVID-19 pandemic?

Effective communication, collaboration and trust in society are essential, including:

- Health-care professionals and patients;
- Different professional bodies, which release specific treatment guidelines;
- Professional health-care organisations and government;
- Mass media, general public and patients, avoiding infodemia (excess information) and consequently its negative effects;

There should be sharing both of best practices and unsuccessful ones at national and international levels in order to improve as quickly as possible the management of the pandemic. Last but not least we should aim for evidence-based medicine by combining validated scientific research with clinical expertise in the management of the disease in each and every patient.

Fig. 1 summarizes all these aspects.

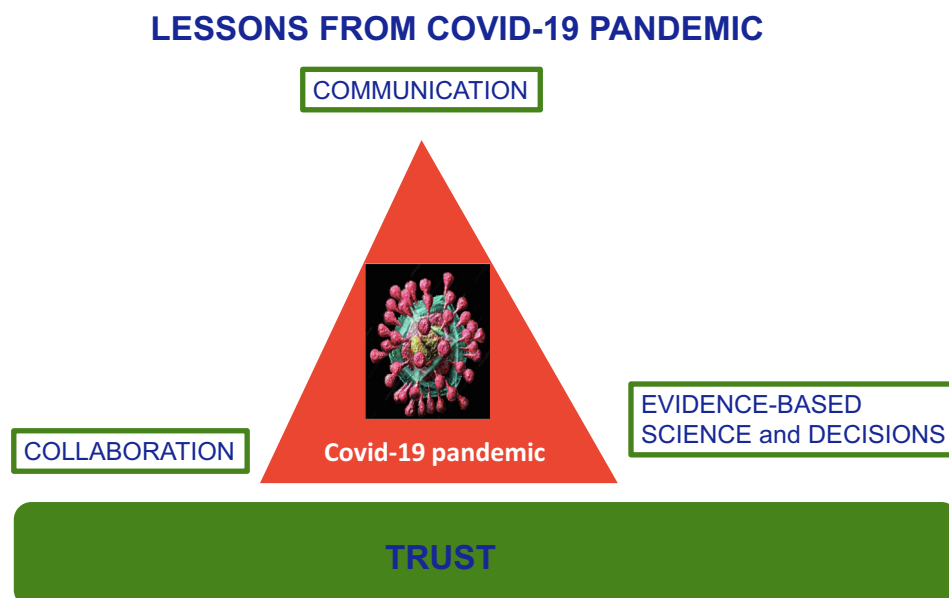


Fig. 1 – Effective communication, collaboration and trust leading to evidence-based science and decisions are essential between all the “players” involved in the pandemic of COVID-19.

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