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Short Communication

Could treatment with botulinum toxin protect against subsequent infection with COVID-19?

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ABSTRACT

We report comparative results, over three months, of the impact of SARS-CoV2 in our patients injected with botulinum toxin for functional purposes, compared to the general population. Botulinum neurotoxin type A (BoNT/A) is known to block acetylcholine (ACh) as well as many other neuroreceptors and neuromodulators. The recent mention of a potential protective effect of nicotine in COVID 19, by blocking ACh, attracted our attention and guided the present study.

Our results show a significant difference between the number of infected individuals in the general population and the number of patients injected with BoNT/A who showed signs of COVID 19.

1. Introduction

The recent mention of a potential protective effect of nicotine against SARS CoV2- [1] and the knowledge of the role of the nicotinic acetylcholine receptor in its infestation mechanism have led us to wonder about a possible comparable effect of botulinum toxin in the patients we treated.

Our ambition is not to offer a treatment for COVID 19, but to look for a possible protective effect that would require further investigation on a larger scale.

All those used to working with botulinum toxin know that one of the effects of the toxin is the blocking of acetylcholine. From there, the authors wondered what the effect of the presence of therapeutic BoNT/A could be at the beginning of an infection with COVID-19.

A prospective survey was carried out among the patients injected in our establishment to compare the percentage of COVID cases with the percentage in the general population.

Both figures have the same bias: the high proportion of asymptomatic patients. This common bias nevertheless makes them comparable.

2. Material and method

In our department, most of the pathologies treated concern the cephalic area, as well as the cervical area. Therefore, injections made in the face and skull area could diffuse to the cerebral level and block the target receptors of the coronavirus, as evoked by Melo-Carillo et al [2].

Indications such as migraine, Arnold's neuralgia (especially bilateral), trigeminal neuralgia or bruxism involve injecting large doses of BoNT/A in the scalp and face area.

2.1. Study design

This was a single center prospective study of patients treated with BoNT/A for the following pathologies: *Arnold's neuralgia, migraine, trigeminal neuralgia, cluster headache, Meige's syndrome, blepharospasm, bruxism, post-operative pain after cervical spine surgery, facial palsy, hypertrophic and keloid scars, glands in cerebral palsy (drooling) and spasmodic torticollis.*

Inclusion criteria were as follows: to have been injected regularly since at least January 2020, at the rate of one injection every 3 months, so that the synaptic blockage was always effective, for one of the pathologies mentioned above, and that the injection was not done outside the cephalic area (e.g. palmoplantar hyperhidrosis).

For 3 months (since this is the rate at which we see our patients), patients were systematically checked for the presence of symptoms which could raise suspicion of a Sars-CoV2 infection.

2.2. Results

2.2.1. Demographic results

During the inclusion period, 193 patients were thus given a BoNT/A injection for one of the target pathologies between May and July 2020, providing the basis for this study. *The sex ratio was 146 women /47 men and the mean age was 53.5 years (from 18 to 89 years).*

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2.2.2. Pathologies treated and doses used

All dosages are given in Botox* units (Allergan Pharmaceuticals, Westport, Ireland).

Arnold's Neuralgia was treated in 46 patients, average dose: 300 U.

Migraines: 33 patients, average dose: 250 U.

Bruxism: 101 patients, average dose: 300 U.

Post-operative cervical pain: 14 patients, average dose: 300 U.

Blepharospasm: 5 patients, average dose: 40 U.

Meige's syndrome: 2 patients, average dose:150 U.

Facial palsy: 24 patients, average dose:80 U.

Scars: 6 patients, average dose: 200 U.

Glands: 3 patients, average dose: 250 U.

Spasmodic torticollis: 2 patients, average dose: 350 U.

Cluster headaches: 4 patients, average dose: 200 U.

The total number of cases is greater than the number of patients, some being treated for several pathologies (Arnold's neuralgia and migraine for example).

2.2.3. Proven infectious signs

Only 2 patients developed a clinical presentation consistent with COVID-19 infection: One was a 53-year-old woman treated for Meige syndrome with 120 U, the other was a 70-year-old woman treated for Arnold's neuralgia with 150 U.

It should be noted that the 53-year-old patient had just come back from Las Vegas (Nevada, USA) when she showed signs of COVID 19. Her test was negative.

The other patient was not tested.

Neither was hospitalized.

These two patients have since been seen again and there was no Cytokine storm or autoimmune type reaction, more frequent in women for this pathology, even in the 70-year-old woman.

It might be interesting to verify whether the anti-inflammatory and anti-TNF alpha effects of BoNT/A could have protected them from these complications.

Several interesting facts are worth noting (apart from these 2 patients): One of our patients lives in a small hamlet in Lozere (a sparsely populated French mountainous region) where a cluster was declared and she was the only person not to be affected, even though she is 64 years old and has associated morbid conditions.

Another patient's daughter was infected, whilst she herself didn't have the slightest problem, although she has many comorbidities, even if she is only 46 years old.

3. Discussion

After our attention was drawn to acetylcholine receptors, bibliographical research highlighted the publication of Mahesh Kandasamy emphasizing the rationality for the possible use of BoNT to prevent SARS-CoV-2 infection and manage COVID-19 [3].

Angiotensin-Converting Enzyme 2 is a transmembrane metallocarboxypeptidase bound to the external surface of plasma membranes of the cells of many viscera and arteries.

It represents the point of entry of certain coronaviruses into cells, in particular Sars CoV2 [4].

According to Kandasamy [3] and others [5,6], the tropism of the coronavirus is much more significant for the brain than we had anticipated at first, when lung infections seemed to be preponderant, especially since at that time the Sars CoV2 infection seemed comparable to a kind of influenza (Fig. 1).

Fig. 2, also borrowed from Kandasamy [3], summarizes, in a non-exhaustive manner, the therapeutic action of BoNT/A in numerous indications.

It can be noted that a large number of the numerous indications cited in this diagram match pathognomonic symptoms of COVID-19. This, and the blocking effect of BoNT/A on Ach are the reasons for our study.

The percentage of our patients infected was less than 1%, whereas, according to the Pasteur Institute, 4.4% of French people have reportedly been infected [7].

It is true that our region (Occitanie) has not been one of the worst affected regions in France, quite the opposite, but it should also be pointed out that some of our patients come from very far away, and therefore, outside of the Occitanie region.

It should be noted that all these results date back to July 2020. The current increase in testing is changing the percentage of people who test positive relative to the general population, but the percentages compared above are concurrent.

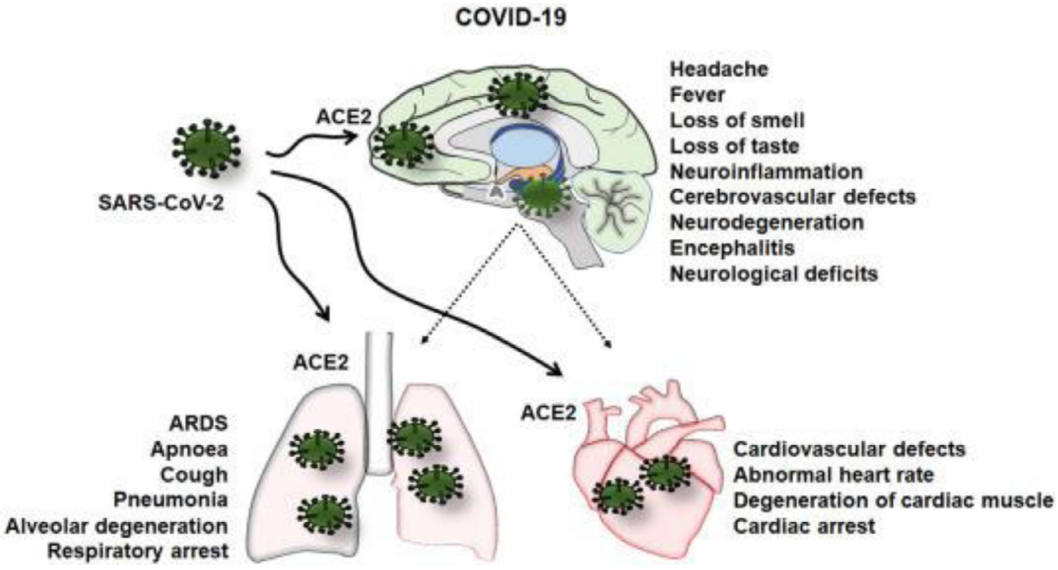

Fig. 1. Schematic representation of SARS-COVID-2 infection in the brain, lungs and heart that bears ACE2 expressing cells. The figure indicates the list of clinical symptoms of COVID-19 related to the brain, lungs and heart. Reproduced from Kandasamy M. [3], used with permission.

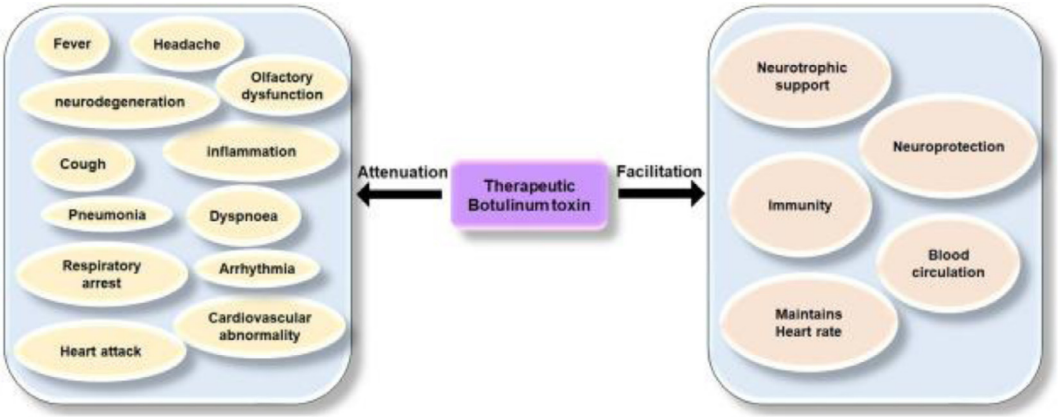

Fig. 2. An overview on the clinical use of therapeutic botulinum toxin to attenuate COVID-19. Reproduced from Kandasamy M. [3], used with permission.

4. Conclusion

To confirm our hypothesis, a microbiological study would be necessary to corroborate the blocking of virus binding through saturation of the receptors by BoNT/A. As we have already stated, this could under no circumstances be used as a treatment, even if its effectiveness is proven.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed and patients details

The authors declare that this report does not contain any personal information that could lead to the identification of the patients and/or volunteers.

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Authors' contribution

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Declaration of Competing Interest

The authors declare no financial or personal relationship that could be viewed as influencing the work reported in this paper.

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