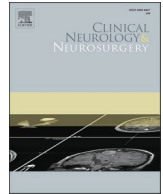




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# The impact of the reclusion on patients with blepharospasm during the COVID19 pandemic

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## ABSTRACT

**Background:** Blepharospasm (BS) is a focal dystonia that can be treated successfully with Botulinum toxin (BoNT). During the reclusion due to the Covid 19 pandemic many patients missed the scheduled treatment.

**Objectives:** Aim of the study is to evaluate Level of Disability (LoD) related to BS during the lockdown period.

**Methods:** LoD was assessed by an adapted version of Blepharospasm Disability Index (4iBSDI) during reclusion (T1), and three months after the first injection following the lock down phase (T2). 4iBSDI scores were compared between T1 and T2, a correlation between the change of LoD in the two periods (t-delta) and patients' clinical data was analyzed.

**Results:** LoD was not modified between the two periods in most of the patients and it was reduced at T1 in almost one third of the participants. No correlation between t-delta and clinical data was found.

**Conclusions:** LoD did not increase during the lock down period in most of BS patients although BoNT treatment was suspended. Environmental and psychosocial factors may contribute to determine the LoD due to BS.

## 1. Introduction

Blepharospasm (BS) is a focal dystonia characterized by the spasmodic bilateral contractions of the muscle orbicularis oculi and, sometimes, of other muscles around the eyes [1]. Usually, it manifests with involuntary eyelid closure, which is the most frequent clinical finding, and which is worsened by light exposure. Botulinum toxin (BoNT) is the most effective treatment for BS, and injections are usually repeated every 3 months, because of its self-limiting effect [2].

In 1976 Marsden first described BS principal clinical and epidemiological features, observing a higher prevalence in women aged 50–70 [3] with a peak at menopause period [4]. Moreover, several metanalysis and epidemiological studies determined the psychiatric characteristics of BS patients in order to find out how such features could influence the response to the treatment and the long-term prognosis [5]. Depression and obsessive/compulsive symptoms are reported to be associated to BS [6] and the onset of BS can indeed be preceded by stressful situation [7].

With the Covid-19 pandemic people were isolated for almost three months, from March to May 2020, they could only leave their home for primary necessities and any type of social aggregation was forbidden.

Also, BS patients had very limited social interactions, and, at the same time, they could not receive the scheduled BoNT injections, waiting more than the usual three months to be treated.

The aim of our study was to evaluate the impact of the forced reclusion due to the pandemic on the Level of Disability (LoD) caused by BS.

## 2. Materials and methods

Data were collected retrospectively from a pool of 39 BS patients periodically treated with BoNT injections at the Clinical Neurophysiology Unit of "Cardarelli" Hospital of Naples, from March 2020 to November 2020. All patients received abobotulinum toxin A that was the type of neurotoxin used in our department for the treatment of BS. All participants gave their written informed consent to participate in the study, which was approved by the local ethics committee. Patients responding to criteria of isolated and idiopathic BS were included [8–10], whereas the subjects with BS associated to other neurological disorders were excluded from the study. Clinical and demographic data, including age of patients, age at dystonia diagnosis and disease duration,

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were collected, and the LoD related to BS was rated by using a questionnaire, the Blepharospasm Disability Index (BSDI) adapted to the activities possibly conducted during the pandemic. BSDI measures disability related to BS analyzing 6 items: driving a vehicle, reading, watching TV, shopping, walking, doing everyday activities [11]. Shopping and driving were excluded, because of the impossibility to perform those activities during the Covid-reclusion period. Therefore, for this study the BSDI was limited to the other 4 items (4iBSDI) that we considered assessable although with a different size in comparison to activities performed before the reclusion. Each item is scored from 0, when there is no impairment, to 4, when it is not possible to do that activity. Total score ranges from 0 to 16.

BS patients' LoD was assessed at two different times: during the Covid period of reclusion at the time of the missed scheduled appointment for BoNT injection (T1), and 3 months after the first treatment performed during the unlocked period (T2). The questionnaire was administered by telephone at T1 and in person at T2. The study was limited to patients for whom T1 was at least two months after the onset of the lock down period so that the reclusion could similarly affect subjects of the study. For each patient the time elapsed between the treatments performed before and after the lock-down reclusion was about 6 months.

Differences of 4iBSDI scores between the two periods (T-delta) were analyzed using a frequency graph. Positive values of T-delta correspond to a higher LoD in T2; negative values of T-delta mean a lower LoD in T2, a T-delta of 0 represents no LoD changes between the two periods.

A Correlation analysis between clinical and demographic features of BS patients and T-delta was assessed. A Linear Correlation was performed between the T-delta score of each patient and the following clinical and demographic data: current age, the age at BS onset and the disease duration.

Pearson's coefficient (R) and P values were calculated.

We studied the distribution of obtained continuous variables analyzing 4iBSDI scores at T1 and T2.

Mean values +/- standard deviation (SD) did not show a normal distribution hence Mann Withney U test was applied to variables. A  $P < 0.01$  was considered significant.

All statistical analysis was performed by using the SPSS statistics software vers. 27.0.

### 3. Results

The BSDI questionnaire was carried out on 38 patients, aged  $68.5 \text{ y} \pm 9$ . Age at BS onset was  $58 \text{ y} \pm 9$ , disease duration was  $10 \text{ y} \pm 5$ .

Analysis of frequency showed that the 4iBSDI score was not modified in 63.2% of cases, 28.9% presented increased 4iBSDI score at T2, and 7.9% of patients showed a 4iBSDI score reduction in T2. (Fig. 1).

Linear Correlation analysis between T-delta and clinical data showed no significant correlation for any investigated features. Pearson's Coefficient (R) and the P value for each correlation analysis are shown in Table 1.

Between T-delta and the age of the patients Pearson's coefficient R was  $-0.41$  while P was  $0.86$ .

Between T-delta and the age of BS onset R was  $0.13$  and P  $0.44$ . Finally, between T-delta and the duration of the disease R was  $0.30$  while P was  $0.07$ . Details in (Table 1).

Mean 4iBSDI values were the following:  $3.6 \pm 3.5$  at T1 and  $5.5 \pm 3.3$  at T2. The Shapiro-Wilk test was used to assess the normal distribution of parameters. Means distribution was not normal so the Mann-Whitney U test was performed to compare averages of 4iBSDI scores at T1 and T2, showing a significant difference of 4iBSDI scores between the two periods ( $P = 0.003$ ).

### 4. Discussion

This study is focused on LoD due to BS during the first lock down

## percentage of patients

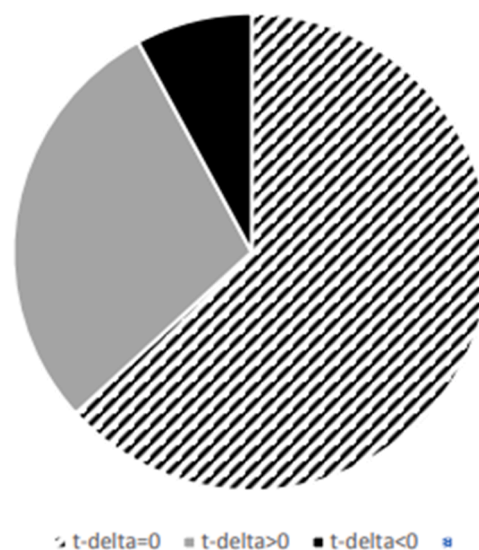


Fig. 1. Frequency analysis of patients with t-delta  $> 0$ ,  $< 0$  and  $= 0$ . T-delta is the difference between the mean 4iBSDI score at T1 and T2.

Table 1

Linear Correlation between T-delta and clinical and demographic variables. R: Pearson coefficient; level of significance  $P < 0.01$ .

| Correlations                      | Mean age at study<br>$\pm$ DS:<br>$68.5 \text{ y} \pm 9$ | Mean age at the BS<br>onset $\pm$ DS:<br>$58 \text{ y} \pm 9$ | Disease<br>duration $\pm$ DS:<br>$10 \text{ y} \pm 5$ |
|-----------------------------------|--|---|---|
| t-delta $\pm$ DS: $1.71 \pm 2.25$ | R = $-0.41$ ,<br>P = $0.86$                              | R = $0.13$ , P = $0.44$                                       | R = $0.30$ ,<br>P = $0.07$                            |

period of the Covid 19 pandemic.

It results from the analysis of a brief questionnaire that could be administered also by telephone and allowed us to record a small clinical update of patients with BS during the lock down period. At that time was not possible to foresee when the reclusion would end, and a simple tool like the 4iBSDI has granted to collect data which could be analyzed later depending on how the pandemic would develop. Table 2.

A retrospective methodology was indeed the more suitable for scientific research as at the beginning.

of the lock-down phase it was not possible to plan prospective study. Finally, our data showed that most of the patients with BS did not report any change of LoD and almost one third of them presented a lower LoD during the reclusion in comparison to the following unlocked phase.

This result may be unexpected, especially because of the lack of treatment with BoNT during the reclusion, and for this reason further conditions affecting BS severity besides medical therapy were considered.

Moreover, in our study the LoD did not correlate with demographic and clinical features which consequently, would also not affect BS severity during the lock down phase.

On these bases, the unchanged or lower LoD at the reclusion period does not seem to be associated with the BoNT effect neither with demographic nor clinical features. We could then speculate that other factors related to the reclusion may affect BS severity.

Actually, psychological aspects of patients with BS were investigated by only a few studies on non-motor features of dystonia including psychiatric disorders, cognition [12], and personality traits. Fabbrini et al. reported in a case-control study that BS patients presented depressive symptoms more frequently than healthy controls and patients with hemifacial spasm (HFS) [6]. Two other recent comparative studies

**Table 2**

Scores of 4iBSD in T1 and T2. Mean 4iBSDI values were the following: 3.6 +/- 3.5 at T1 and 5.5 +/- 3.3 at T2. Mann Whitney U test showed significant results (P = 0.003).

| score_lock (T1) | score_unlock (T2) | t-delta |
|-----------------|-------------------|---------|
| 4               | 4                 | 0       |
| 2               | 2                 | 0       |
| 0               | 4                 | 4       |
| 4               | 8                 | 4       |
| 1               | 0                 | -1      |
| 4               | 4                 | 0       |
| 2               | 2                 | 0       |
| 2               | 2                 | 0       |
| 6               | 6                 | 0       |
| 4               | 3                 | -1      |
| 4               | 4                 | 0       |
| 0               | 10                | 10      |
| 6               | 6                 | 0       |
| 0               | 10                | 10      |
| 6               | 6                 | 0       |
| 0               | 6                 | 6       |
| 4               | 4                 | 0       |
| 2               | 2                 | 0       |
| 2               | 0                 | -2      |
| 2               | 2                 | 0       |
| 4               | 4                 | 0       |
| 4               | 4                 | 0       |
| 0               | 8                 | 8       |
| 0               | 4                 | 4       |
| 0               | 10                | 10      |
| 0               | 4                 | 4       |
| 6               | 6                 | 0       |
| 4               | 4                 | 0       |
| 12              | 12                | 0       |
| 10              | 10                | 0       |
| 0               | 0                 | 0       |
| 6               | 6                 | 0       |
| 10              | 10                | 0       |
| 8               | 8                 | 0       |
| 0               | 8                 | 8       |
| 4               | 4                 | 0       |
| 0               | 8                 | 8       |
| 12              | 12                | 0       |

reported clinical signs of obsessive-compulsive disorders more frequently in BS patients and in subjects with HFS [13,14]. A recent study of Berardelli et al., showed that BS patients present higher level of anxiety and depression and may have suicidal ideations [15].

A study on the personalities of BS patients assessing the Temperament and Character Inventory showed a higher level of persistence and a tendency to present a higher level of harm avoidance in comparison to patients with HFS and hyperhidrosis [16].

According to those studies BS patients may present specific psychiatric and personality traits that could affect the severity dystonia. In our study we focused on the LoD due to BS, and it is reasonable to consider that it may be affected by daily difficulties of normal life and social interactions. During the lock down phase BS patients may have reported no change or a reduction of LoD because they were probably less exposed to stressful conditions related to social interactions and to problems due to their vision difficulties.

The assessment of LoD during the reclusion seems to be of special interest also because at that time most of the patients did not show an increased LoD, although they missed at least one of the scheduled treatments with BoNT. That result could suggest that the impact of psychosocial factors on BS could be very relevant.

## 5. Conclusions

The present study is limited by the lack of comparison with other groups of subjects and by a restricted number of BS patients. Therefore, our results should be confirmed by further investigations with a larger

number of patients and by prospective methodology. In conclusion, our findings on the change of LoD in BS patients related to the lock down/unlocked period might have interesting clinical implications. BoNT injections represent the most effective strategy to treat this type of dystonia, however a small number of patients have a weak response to the injections and would need further support for this movement disorder.

A recent article suggests having an “holistic” perspective in the management of dystonia [17] especially in the field of rehabilitation. We could likewise approach to patients with BS trying to identify aspects of daily life affecting dystonia in order to find a “customized” strategy of adaptation that may help people to improve their quality of life in their own social context. On this background the frequency of the treatment with BoNT could be planned depending on the possibility to manage also environmental aspects relevant for dystonia.

The Comprehension of psychosocial factors influencing BS finally may lead to a different management of dystonia including a new idea of rehabilitation in addition to neurotoxins.

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## CRediT authorship contribution statement

**Assunta Trinchillo:** Research project, Design, Execution, Manuscript. **Marcello Esposito:** Conception, Organization, Execution, Review and critique. **Filippo Iorillo, Gabriella Joanna:** Collection data. **Francesco Habetswallner:** Execution. **Assunta Trinchillo, Marcello Esposito:** Statistical analysis. **Marcello Esposito, Filippo Iorillo, Gabriella Joanna:** Writing of the first draft.

## Compliance Statement section

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Funding for the study

None.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- [1] G. Defazio, M. Hallett, H. Jinnah A., A. Conte, A. Berardelli, Blepharospasm 40 years later, *Mov. Disord.* Vol. 32 (No. 4) (2017) 2017, <https://doi.org/10.1002/mds.26934>.
- [2] M. Esposito, A. Fasano, C. Crisci, R. Dubbioso, R. Iodice, L. Santoro, The combined treatment with orbital and pretarsal botulinum toxin injections in the management of poorly responsive blepharospasm, *Neurol. Sci.* 35 (3) (2014) 397–400, <https://doi.org/10.1007/s10072-013-1526-2>.
- [3] C.D. Marsden, Blepharospasm-ommandibular dystonia syndrome (Brueghel's syndrome). A variant of adult-onset torsion dystonia? *J. Neurol., Neurosurg. Psychiatry* 39 (12) (1976) 1204–1209, <https://doi.org/10.1136/jnnp.39.12.1204>.
- [4] D. Martino, P. Livrea, M. Giorelli, G. Masi, M.S. Aniello, G. Defazio, Menopause and Menarche in Patients with Primary Blepharospasm: An Exploratory CaseControl Study, *Eur. Neurol.* Vol. 47 (2002). ([www.karger.com/journals/ene](http://www.karger.com/journals/ene)).
- [5] J. Yang, L. Zhang, Y. Hou, Q. Wei, R. Ou, J. Lin, W. Song, B. Cao, H. Shang, Sex related differences in nonmotor symptoms of patients with idiopathic blepharospasm, *Sci. Rep.* 11 (1) (2021), <https://doi.org/10.1038/s41598-021-97289-1>.
- [6] G. Fabbri, I. Berardelli, G. Moretti, M. Pasquini, M. Bloise, C. Colosimo, M. Biondi, A. Berardelli, Psychiatric disorders in adult-onset focal dystonia: A case-

- control study, *Mov. Disord.* 25 (4) (2010) 459–465, <https://doi.org/10.1002/mds.22983>.
- [7] Johnson, L.N. , Lapour, R.W. , Johnson, G.M. , Johnson, P.J. , Madsen, R.W. , & Hackley, S.A., n.d., Closely Spaced Stressful Life Events Precede the Onset of Benign Essential Blepharospasm and Hemifacial Spasm.
- [8] Defazio, G., Hallett, M., Jinnah, H.A., & Berardelli, A. (2013). Development and validation of a clinical guideline for diagnosing blepharospasm. ([www.neurology.org](http://www.neurology.org)).
- [9] G. Defazio, H.A. Jinnah, A. Berardelli, J.S. Perlmutter, G.K. Berkmen, B.D. Berman, J. Jankovic, T. Bäumer, C. Comella, A.C. Cotton, T. Ercoli, G. Ferrazzano, S. Fox, H. J. Kim, E.S. Moukheiber, S.P. Richardson, A. Weissbach, L.J. Wrigth, M. Hallett, Diagnostic criteria for blepharospasm: A multicenter international study, *Park. Relat. Disord.* 91 (2021) 109–114, <https://doi.org/10.1016/j.parkrelendis.2021.09.004>.
- [10] H.A. Jinnah, A. Albanese, The New Classification System for the Dystonias: Why Was It Needed and How Was It Developed?, in: *In Movement Disorders Clinical Practice*, Vol. 1 Wiley-Blackwell,, 2014, pp. 280–284, <https://doi.org/10.1002/mdc3.12100>.
- [11] J. Jankovic, C. Kenney, S. Grafe, R. Goertelmeyer, G. Comes, Relationship between various clinical outcome assessments in patients with blepharospasm, *Mov. Disord.* 24 (3) (2009) 407–413, <https://doi.org/10.1002/mds.22368>.
- [12] G. Maggi, A. D'Iorio, G. Mautone, S. Peluso, F. Manganelli, R. Dubbioso, M. Esposito, G. Santangelo, Cognitive correlates of prospectivememory in dystonia, *ParkinsonismRelatDisord* 66 (2019) 51–55, <https://doi.org/10.1016/j.parkrelendis.2019.06.027> (Sep).
- [13] L.F. Fontenelle, P.G. Pacheco, P.M. Nascimento, A.R. de Freitas, A.L. Rosso, A. L. Teixeira, E.C. Lauterbach, Obsessive-compulsive symptoms among patients with blepharospasm and hemifacial spasm, *Gen. Hosp. Psychiatry* 33 (5) (2011) 476–481, <https://doi.org/10.1016/j.genhosppsych.2011.05.016>.
- [14] R. Munhoz, H.A.G. Teive, M.V. DellaColetti, F.M.V. Germiniani, F.M. Iwamoto, C.H. F. Camargo, L.C. Werneck, Frequency of obsessive and compulsive symptoms in patients with blepharospasm and hemifacial spasm, *ArqNeuropsiquiatr* 2005 63 (2–A) (2005) 213–216, <https://doi.org/10.1590/s0004-282x2005000200004>.
- [15] I. Berardelli, G. Ferrazzano, D. Belvisi, V. Baione, G. Fabbri, M. Innamorati, A. Berardelli, M. Pompili, Suicidal ideation, hopelessness, and affective temperament in patients with blepharospasm, *Int. J. Psychiatry Clin. Pract.* (2020) 1–6, <https://doi.org/10.1080/13651501.2020.1790613>.
- [16] G. Santangelo, A. D'Iorio, S. Peluso, G. Mautone, C. Vitale, F. Manganelli, L. Ruggiero, M. Esposito, Personality traits associated with blepharospasm: A comparison with healthy subjects, patients with facial hemispasm and patients with hyperhidrosis, *J. Clin. Neurosci.* 74 (2020) 130–134, <https://doi.org/10.1016/j.jocn.2020.02.018>.
- [17] V. Bradnam Lynley, M. Meiring Rebecca, Boyce Melani, Alana McCambridge, Neurorehabilitation in dystonia: a holistic perspective, *J. Neural Transm.* 128 (2020) 549–558, <https://doi.org/10.1007/s00702-020-02265-0>.