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ΔΙΟΡΘΩΣΗ

Στον Τόμο 34, Τεύχος 5, στην έντυπη έκδοση, εκ παραδρομής παραλείφθηκε το όνομα ενός από τους συγγραφείς, του **Παναγιώτη Ιωαννίδη** στο άρθρο «*Νόσος του Hirayama*».
Το λάθος διορθώνεται με την παρούσα ανακοίνωση

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ERRATUM

In Volume 34, Issue 5, of the printed edition, the name of one of the authors, **Panagiotis Ioannidis,** was inadvertently omitted from the article entitled *"Hirayama Disease."*
This error is hereby corrected.

This issue presents three original contributions spanning acute cerebrovascular care, movement disorders, and headache medicine, each addressing clinically relevant questions with direct implications for everyday neurological practice.

Keramida et al. focus on **blood pressure management in acute intracerebral hemorrhage,** evaluating the use of intravenous clevidipine compared with standard antihypertensive regimens. In this prospective case–control cohort, clevidipine demonstrated high efficacy in rapid blood pressure control, achieving target systolic values within hours as monotherapy, without the need for additional agents. Importantly, treatment with clevidipine was associated with a significant reduction in hematoma volume at 24 hours, contrasting with stable/increased volumes in the control group. Hematoma retraction is rare in the acute phase and associated with intraventricular hematoma expansion; this finding may also be related to the small number of patients. Still, no serious adverse events were observed, underscoring the favorable safety profile of this ultrashort-acting calcium channel blocker in the hyperacute ICH setting. Although functional outcomes at three months were similar between groups, these findings support clevidipine as a safe and effective option for acute hypertension control despite its higher cost compared to standard calcium-channel blockers, with potential benefit in limiting early hematoma evolution, warranting confirmation from larger ongoing prospective studies (CLUTCH trial; NCT06402968).

Tsimpiktsioglou et al. present real-world data on **eptinezumab for migraine prevention.** In a cohort of patients with episodic and chronic migraine, most of whom had failed multiple prior preventive therapies, eptinezumab led to substantial reductions in monthly migraine days, pain intensity, and acute medication use, alongside marked improvements in disability and quality-of-life indices. Notably, the magnitude of benefit closely mirrors that reported in the PROMISE-1 and PROMISE-2 trials, confirming the reproducibility of efficacy in routine clinical practice. By confirming landmark trial results in a Greek patient population, this study supports the integration of eptinezumab into migraine care pathways, particularly for patients with high disease burden and unmet therapeutic needs.

Deligiorgi et al. address **voice and swallowing dysfunction in Parkinson's disease and atypical parkinsonian syndromes,** introducing a novel and clinically meaningful approach that integrates detailed voice assessment as a window into dysphagia risk in both groups of patients. Through combined perceptual, acoustic, and patient-reported measures, the authors demonstrate that specific voice parameters differ not only between patients and controls, but also between dysphagic and non-dysphagic individuals. The identification of fundamental frequency variability as a potential marker of swallowing impairment highlights the conceptual and practical link between phonation and deglutition, offering a non-invasive adjunct to clinical screening. This work strengthens the role of structured voice analysis in the multidisciplinary evaluation of parkinsonism and opens new avenues for early identification of patients at risk of aspiration.

Together, these three contributions from Greek centers exemplify how carefully conducted clinical research, ranging from acute stroke management to chronic neurological disease, can directly inform and refine patient-centred neurological care.

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Άρθρα...

PRELIMINARY DATA FROM CLEVIDIPINE ADMINISTRATION VERSUS OTHER ANTIHYPERTENSIVE TREATMENTS IN PATIENTS WITH ACUTE HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

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ABSTRACT

Background and Aims: Intracerebral haemorrhage (ICH) has been associated with worse functional outcome and increased mortality, related to hematoma volume and expansion. Blood pressure (BP) reduction may attenuate hematoma expansion. We sought to investigate whether clevidipine, an intravenous administered calcium-channel blocker, achieved better ICH volume reduction and better functional outcome in patients with hypertensive ICH compared to standard-of-care antihypertensive treatment. **Methods:** This is a prospective case-control study, assessing the clinical severity, the hematoma size differentiation and the clinical outcome in patients with hypertensive ICH, who received intravenous clevidipine in the acute phase versus standard-of-care antihypertensive treatment (clonidine and/or labetalol). **Results:** This study included forty-four ICH patients (clevidipine-group: 17 – controls: 27). There was no difference in demographic characteristics and admission National Institutes of Health Stroke Scale (NIHSS) score. A statistically significant ICH volume change on 24h follow-up brain computed tomography was observed in the clevidipine group (11.8% reduction vs 0.4% increase in the control-group; p-value: 0.04). Moreover, a non-significant trend towards NIHSS-score improvement at discharge was observed in clevidipine group [ΔNIHSS score 4 (1-7) in the clevidipine group vs 2 (0-4) in the control group], whereas functional outcomes and mortality at 3 months were similar. No serious adverse events were detected among patients treated with clevidipine. **Conclusions:** The present study highlights that clevidipine represents a safe and effective alternative in terms of hypertension control among ICH patients in the acute phase. However, these findings, indicating superiority of clevidipine, require confirmation in larger studies.

Key-words: intracerebral hemorrhage, clevidipine, antihypertensive agents, hematoma.

ΠΡΟΚΑΤΑΡΚΤΙΚΑ ΔΕΔΟΜΕΝΑ ΑΠΟ ΤΗ ΧΟΡΗΓΗΣΗ ΚΛΕΒΙΔΙΠΙΝΗΣ ΕΝΑΝΤΙ ΛΟΙΠΩΝ ΑΝΤΙΥΠΕΡΤΑΣΙΚΩΝ ΣΤΗΝ ΕΚΒΑΣΗ ΑΣΘΕΝΩΝ ΜΕ ΟΞΕΙΑ ΕΝΔΟΕΓΚΕΦΑΛΙΚΗ ΑΙΜΟΡΡΑΓΙΑ ΥΠΕΡΤΑΣΙΚΗΣ ΑΙΤΙΟΛΟΓΙΑΣ

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ΠΕΡΙΛΗΨΗ

Ιστορικό: Στην ενδοεγκεφαλική αιμορραγία (ΕΑ), ο όγκος και η επέκταση του αιματώματος σχετίζονται με αυξημένη θνησιμότητα και δυσμενέστερη λειτουργική έκβαση. Η μείωση της αρτηριακής πίεσης ενδέχεται να περιορίσει την επέκταση του αιματώματος. Σκοπός της παρούσας μελέτης είναι η διερεύνηση της αποτελεσματικότητας της κλεβιδιπίνης ως προς τη μείωση του όγκου της αιμορραγίας και τη βελτίωση της λειτουργικής έκβασης σε ασθενείς με ΕΑ υπερτασικής αιτιολογίας, σε σύγκριση με τη συνήθη αντιϋπερτασική αγωγή. **Μέθοδοι**: Πρόκειται για προοπτική μελέτη ασθενών-μαρτύρων με στόχο την αξιολόγηση της κλινικής βαρύτητας, της μεταβολής του όγκου του αιματώματος και της κλινικής έκβασης σε ασθενείς με υπερτασικής

αιτιολογίας ΕΑ, οι οποίοι έλαβαν ενδοφλέβια κλεβιδιπίνη κατά την οξεία φάση, συγκριτικά με ασθενείς που έλαβαν την καθιερωμένη αντιϋπερτασική αγωγή.
Αποτελέσματα: Συνολικά εντάχθηκαν στη μελέτη 44 ασθενείς (ομάδα κλεβιδιπίνης: 17– ομάδα ελέγχου: 27). Δεν παρατηρήθηκαν διαφορές όσον αφορά τα δημογραφικά χαρακτηριστικά και τη βαρύτητα της κλίμακας National Institutes of Health Stroke Scale (NIHSS) κατά την εισαγωγή. Στην ομάδα της κλεβιδιπίνης καταγράφηκε στατιστικώς σημαντική μείωση του όγκου αιματώματος στο 24ωρο (μείωση 11,8% έναντι αύξησης 0,4% στην ομάδα ελέγχου, p=0,04). Μη στατιστικά σημαντική τάση μεγαλύτερης βελτίωσης της κλίμακας NIHSS παρατηρήθηκε στην ομάδα της κλεβιδιπίνης κατά το εξιτήριο, [διάμεση μεταβολή NIHSS: 4 (1–7) έναντι 2 (0–4), αντίστοιχα], ενώ η λειτουργική έκβαση και τα ποσοστά θνησιμότητας στο τρίμηνο ήταν παρόμοια.
Συμπεράσματα: Η παρούσα μελέτη υποδεικνύει ότι η κλεβιδιπίνη αποτελεί μια ασφαλή και ενδεχομένως αποτελεσματική επιλογή στην οξεία φάση της ΕΑ. Ωστόσο, η πιθανή υπεροχή της ως προς τις άλλες θεραπείες χρήζει επιβεβαίωσης σε μεγαλύτερες μελέτες.

Λέξεις-κλειδιά: Ενδοεγκεφαλική αιμορραγία, αντιυπερτασική αγωγή, κλεβιδιπίνη, αιμάτωμα

INTRODUCTION

Intracerebral haemorrhage (ICH) is a significant cause of morbidity and mortality and has been associated with severe long-term disability.[1] It accounts for 10% to 15% of all strokes, with an incidence of 24.6 per 100,000 person-years and increasing frequency due to the use of anticoagulants, antiplatelet agents, and aging population.[1-3] The economic impact of haemorrhagic strokes stems partly from their high mortality rate, with up to half of the patients dying within the first 30 days, often despite prolonged stays in Intensive Care Units.[4]

Management of ICH ranges from conservative to surgical treatment, depending on the location and the size of the haemorrhage, as well as the severity of neurological symptoms.[2,5] The therapeutic approach to ICH focuses on managing arterial hypertension, preventing haematoma expansion (HE) and controlling intracranial pressure (ICP).[6] Elevated blood pressure (BP) has been associated with higher risk of HE, unfavourable functional outcomes and higher mortality rates.[7-10] HE is a common cause of secondary neurological deterioration and is directly associated with survival and functional independence in up to one-third of patients after ICH onset. Expansion typically occurs within 24 hours, although delayed expansion has also been reported.[11] Its strong prognostic significance stems mainly from its potential to cause midline shift and herniation. Even relatively minor hematoma expansion can lead to neurological deterioration.[12,13]

To prevent hematoma expansion, the European Stroke Organisation (ESO) recommends initiating antihypertensive therapy as early as possible, ideally within 2 hours of symptom onset.[14] The reduction in systolic BP (SBP) should not exceed 90 mmHg from baseline. In patients with hyperacute ICH (<6 hours), a target SBP of less than 140 mmHg is suggested to reduce HE.[14,15] Intensified BP management in acute ICH appears safe. According to a meta-analysis by Tsivgoulis et al., patients without strict BP control had worse outcomes during 3-month follow-up. Furthermore, aggressive BP reduction was associated with less HE at 24 hours.[16]

Available treatment options for BP control include oral and intravenous (iv) antihypertensive medications. In the acute setting with severe hypertension, iv administration is recommended.[14] Antihypertensive drugs, administered iv and available in Greece, include labetalol (a beta-blocker) and clonidine (an α2 agonist). Recently, clevidipine, a dihydropyridine calcium channel blocker, was introduced.[17] According to the Evaluation of Patients with Acute Hypertension and Intracerebral Hemorrhage with Intravenous Clevidipine Treatment (ACCELERATE) trial, clevidipine monotherapy proved effective and safe for rapid BP reduction in a cohort of 35 ICH patients, also showing a positive impact on HE.[18]

In this observational study we sought to prospectively investigate the clinical severity, treatment, haematoma size evolution – expansion or reduction – and clinical outcome of ICH patients admitted to the Stroke Unit of the Second Department of Neurology of the National and Kapodistrian University of Athens, who received intravenous clevidipine for BP management during the acute phase of ICH. These patients were compared to a control group of age- and sex-matched ICH patients from previous five years, who received labetalol and/or clonidine during the acute ICH phase.

MATERIALS AND METHODS

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

ETHICAL APPROVAL AND PATIENT CONSENT

This study is in accordance with the Declaration of Helsinki principles, and institutional review board approval was obtained from the Ethics Committee of ''Attikon'' University Hospital (decision number: EDB 302/25-04-2024). Written informed consent was obtained from all patients or their legal representatives before enrolment.

Participants

This study was performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational research.[19] Participants were recruited from a prospective cohort of patients who were diagnosed with spontaneous hypertensive ICH (SBP on admission ≥140mmHg), admitted to the Stroke Unit of the Second Department of Neurology of the National and Kapodistrian University in Athens, Greece and treated with iv clevidipine within the first 24 hours of symptom onset.[14] The recruitment of the participants took place from January 2024 until April 2025, since clevidipine administration became available in our hospital in January 2024. A retrospective chart review from January 2018 up to December 2023 was also conducted for age- and sex-matched hypertensive ICH patients previously treated with other antihypertensive medications (labetalol, clonidine). The underlying cause for the ICH in both the clevidipine and the control group was found to be uncontrolled hypertension, excluding other common causes of ICH such as anticoagulant use, trauma or aneurysm rupture.

The patients were included in the present study if they were older than 18 years old, had a diagnosis of acute ICH and signed the informed consent. The exclusion criterion was refusal to provide informed consent or death withing the first 24 hours post admission, a fact which rendered the repeat CT scan impossible. Moreover, anticoagulant-related ICH were also excluded.

For each patient, demographics and previous history of arterial hypertension were recorded. All patients underwent an initial brain CT scan at admission and a follow-up brain CT 24 hours following admission. Hematoma volume, based on the ABC/2 formula, was calculated on both scans, and the ICH score was determined.[20,21] Both measurements were performed by two independent neurologists with experience in stroke neurology and the mean values of these measurements were used. Evidence regarding the BP upon admission, the National Institutes of Health Stroke Scale (NIHSS) score at admission and discharge and modified Rankin Scale (mRS) score at 3 months were documented.[22]

Additionally, in the clevidipine group, the time from clevidipine administration initiation to BP control, the days of clevidipine therapy and the maximum required clevidipine dose were recorded. Clevidipine was initiated and titrated according to the prescribing information to achieve the target SBP range. The clevidipine infusion rate could be titrated to control the SBP within the target range.

The primary endpoint of the present study was the evolution of the hematoma volume. HE was defined as a relative increase of ≥ 33% or an absolute increase of ≥ 6 mL in hematoma volume from baseline to follow-up CT. Secondary outcomes included 3-month mRS score, 3-month good functional outcome (defined as an mRS-score 0-2), ΔNIHSS between admission and discharge and 3-month mortality. Adverse events observed in the clevidipine group were also documented.

Statistical Analysis

Continuous variables were presented as mean with standard deviation (SD), in case of normal distribution, and as median with interquartile ranges (IQR), in case of skewed deviation. Continuous variables were tested with the Student's ***t***-test (normally distributed data) or Mann–Whitney U-test (non-normally distributed data). Categorical variables were presented as the number of patients with the corresponding percentages. For dichotomised variables, the chi-square test was used. All statistical analyses were conducted using the R software version 2025.05.0+496.[23]

RESULTS

In this study fourty-four ICH patients (clevidipine-group: 17 – controls: 27) were included. The baseline characteristics are summarised in **Table 1**. There was no significant difference in demographic characteristics. More specifically, the mean age in the clevidipine group was 61.9±10.6 years and 70.6% of the participants were male, whereas in the control group the mean age was 66.3±8.5 years and the participants were male in 66.7%. Moreover, there was no difference regarding the coexistence of known arterial hypertension. There was a trend of higher SBP values upon admission in the clevidipine group, without it reaching statistical significance. The diastolic BP values difference upon admission was significantly higher in the clevidipine group (absolute value of 109.4±16.4 mmHg vs 94.0±13.6 mmHg in the control group; p-value=0.001), supporting the trend in the SBP values. Pre-stroke mRS score and admission NIHSS score did not differ between the two groups. Clevidipine group presented with a significantly higher hematoma volume (21.8 ± 20.3 ml vs. 10.2 ±13.3 ml; p-value: 0.028) and a significantly higher ICH score [1 (1-1) vs. 0 (0-1); p-value 0.017] when compared to the control group. In the clevidipine group, the target SBP was achieved in 153.5±106.0 min,

the medication was administered for approximately 4 (3-5) days and the maximum dose of clevidipine recorded was 16.4±7.1 ml.

With regards to follow up and outcomes, data on ICH volume in the follow up imaging, the percentage of ICH volume change, and 3-month mRS score, 3-month good functional outcome, the ΔNIHSS during hospitalisation and the 3-month mortality were collected and are summarised in **Table 2**. A statistically significant ICH volume change on 24h follow-up brain CT, was observed in the clevidipine group (11.8% reduction vs 9.4% increase in the control-group; p-value: 0.041). Nevertheless, similar incidence of hematoma expansion [0 (0.0%) vs. 3 (11.1%); p-value: 0.155] was detected across the two groups. Moreover, a non-significant trend towards NIHSS-score improvement at discharge was reported in the clevidipine-group [ΔNIHSS score 3 (1-7) in the clevidipine group vs. 2 (0-4) in the control group; p-value: 0.169], whereas 3-month mRS scores and 3-month mortality were similar between the two groups. No serious adverse events were detected among patients treated with clevidipine and the medication was well tolerated. Adverse events of specific interest such as acute renal failure and rebound hypertension were not recorded.

DISCUSSION

In the present study, we investigated the effect of iv administered clevidipine on the HE among patients presenting with acute ICH and associated elevated BP. We compared data from clevidipine-treated patients with retrospectively collected data from patients with ICH that were treated with other iv antihypertensive agents in the previous years. Patients receiving iv clevidipine showed significant hematoma volume reduction without however significant differences in 3-month mRS scores compared to patients treated with other antihypertensive agents.

When assessing the findings, we deducted that clevidipine was effective in managing the arterial hypertension. Clevidipine monotherapy achieved BP control in all our patients within 3 hours without the additional use of another antihypertensive agent. This observation could greatly assist in every day clinical practice reducing the polytherapy, implementing easier to adhere to medication schedule and administration, and reducing potential side effects from drug interactions. Additionally, it is also deducted that a mean dose of 16mg of clevidipine was used, a dose that can be safely titrated to higher values if required by a patient with more refractory hypertension. The results of the present study are in accordance with findings of previous studies, indicating that clevidipine is suitable for use as a novel therapeutic agent in the assessment of acute hypertension, thereby overcoming the challenges of providing rapid BP control in emergency situations.[24,25]

Additionally, the hematoma volume reduction when compared to the control group further highlights the effectiveness and the positive clinical correlation of clevidipine. Elevated BP during the first few hours from ICH onset is associated with an increased risk of rebleeding and HE, which leads to poor outcomes at 3 months in patients with ICH.[9,26,27] The Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage (INTERACT) trial has previously proposed the need for early intensive lowering of SBP on the basis of decreased HE, with a target SBP of 140 mmHg in ICH.[28] This recommendation was also implemented in the very recently published ESO guidelines for the management of spontaneous acute ICH.[15]

Given our original data and the findings highlighted above, it is safe to assume that clevidipine represents a safe and effective alternative in terms of hypertension control among ICH patients in the acute phase. The quick onset of action, easy administration and the dynamic titration which can suit the personalised needs of each patient render this medication ideal for this specific subgroup of patients. Moreover, the fact that no adverse effects were reported, especially acute kidney failure which is common in the setting of BP control in ICH patients, strongly suggest that this medication should be implemented as standard of care treatment. These conclusions are in accordance with what has been already reported in the existing literature in the ACCELERATE trial, the ongoing Clevidipine for the Antihypertensive Treatment of Acute Intracerebral Haemorrhage (CLUTCH) trial (NCT06402968) and the recent ESO guidelines.[15,18]

A key strength of our study lies in its matched-control design, combined with the absence of alternative antihypertensive agents during the acute phase of ICH. This ensures that the observed BP reduction can be attributed exclusively to clevidipine, minimising the risk of therapeutic confounding. Nevertheless, the suggestion of clevidipine's superiority is constrained by the relatively small sample size analysed to date. The pronounced reduction in ICH volume observed in the clevidipine group – in contrast to the volumetric increase documented in the control group at the 24-hour follow-up scan – may also, at least in part, reflect the limited number of participants. Furthermore, patients in the control cohort were treated in a standard ward setting rather than within a dedicated stroke unit. This represents a potential source of bias, given the well-established evidence that organised stroke unit care is associated with improved survival, greater functional independence, and an increased likelihood of home discharge within one year of the event.[15,29]

In conclusion, the present study supports the efficacy and safety of iv clevidipine for the rapid management of arterial hypertension in the acute phase of ICH. The significant reduction in hematoma volume observed in the clevidipine group suggests a potential benefit in limiting HE, although no significant differences in 3-month functional outcomes or mortality were detected. These findings highlight clevidipine as a promising therapeutic option in this clinical setting, but confirmation through larger prospective studies or randomised-controlled clinical trials is warranted.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Table 1. Baseline characteristics.

BASELINE CHARACTERISTICS			
	Clevidipine (n=17)	**Controls (n=27)**	**p-value**
Age; mean (sd)	61.9 (10.6)	66.3 (8.5)	0.136
Sex (male); n (%)	12 (70.6%)	18 (66.7%)	0.999
Known History of Hypertension; n (%)	16 (94.1%)	15 (57.7%)	0.999
Systolic Blood pressure$_{adm}$ (mmHg); mean (sd)	197.2 (23.4)	167.2 (20.4)	0.056
Diastolic Blood pressure$_{adm}$ (mmHg); mean (sd)	109.4 (16.4)	94.0 (13.6)	**0.001**
pre-stroke mRS; median (IQR)	0 (0 – 0)	0 (0 – 0)	0.739
NIHSS$_{adm}$; median (IQR)	8 (2 – 14)	5 (3 – 9)	0.282
ICH Volume$_{adm}$ (ml); mean (sd)	21.8 (20.3)	10.2 (13.3)	**0.028**
ICH – Score; n (%) 0 1 2	3 (17.6%) 13 (76.5%) 1 (5.9%)	16 (59.3%) 9 (33.3%) 2 (7.4%)	**0.017**
ICH score; median (IQR)	1 (1 – 1)	0 (0 – 1)	**0.019**
Time from clevidipine therapy begin to blood pressure control (min); mean (sd)	153.5 (106.0)	NA	NA
Days of Clevidipine Therapy; median (IQR)	4 (3 – 5)	NA	NA
Max dose (ml) of clevidipine required; mean (sd)	16.4 (7.1)	NA	NA
adm: Admission, ICH: Intracerebral Haemorrhage, IQR: Interquartile Range, mRS: modified Rankin Scale, NA: Not available, NIHSS: National Institutes of Health Stroke Scale, sd: standard deviation			

Table 2. Follow up and outcomes.

FOLLOW-UP AND OUTCOMES			
	Clevidipine (n=17)	**Controls (n=27)**	**p-value**
ICH Volume - follow-up (ml); mean (sd)	20.3 (19.1)	14.7 (29.9)	0.493
ICH-Volume change%; mean (sd)	**–11.8 (8.1)**	**+ 9.4 (98.9)**	**0.041**
Hematoma expansion; n (%)	0 (0.0)	3 (11.1)	0.155
$NIHSS_{discharge}$; median (IQR)	4 (1 – 10)	3 (0 – 5)	0.479
ΔNIHSS; median (IQR)	3 (1 – 7)	2 (0 – 4)	0.169
Good functional outcome at 3 months (mRS: 0-2); n (%)	12 (70.6)	18 (66.7)	0.999
3month mRS; median (IQR)	2 (0 – 3)	2 (0 – 3)	0.524
3month mortality; n (%)	1 (5.9)	1 (7.4)	0.999
ICH: Intracerebral Haemorrhage, IQR: Interquartile Range, mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, sd: standard deviation			

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EPTINEZUMAB FOR THE PREVENTIVE TREATMENT OF MIGRAINE: REAL-WORLD DATA FROM THE NEUROLOGY DEPARTMENT OF THE ATHENS NAVAL HOSPITAL IN GREECE

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ABSTRACT

Background: Eptinezumab is the first anti-CGRP monoclonal antibody administered intravenously for migraine prevention. **Objective:** To evaluate the effectiveness and safety of eptinezumab in patients with episodic and chronic migraine during the first trimester of treatment in a real-world clinical setting. **Methods:** Seven patients received eptinezumab 100 mg intravenously. Baseline and 3-month assessments included monthly migraine days (MMDs), pain intensity, days of acute medication use and quality of life indices (HIT-6, MIDAS). **Results:** The cohort comprised six women and one man, mean age 40 years, mean migraine onset at 24 years. Five had episodic migraine without aura, one episodic migraine with aura, and one chronic migraine. All had failed at least two previous preventive treatments. At baseline, patients reported a mean of 10 MMDs, pain intensity 9/10, 15 days of acute medication use/month, mean MIDAS score 36 and HIT-6 score 70 (severe disability). After 3 months of treatment, MMDs decreased by 60% (mean 4 days), pain intensity to 4/10, and acute medication days by 75% (mean 4 days). MIDAS improved to 8 and HIT-6 to 44 (mild/none disability). No adverse events were observed. **Conclusions:** Eptinezumab was effective and well tolerated, substantially reducing migraine frequency, pain intensity, and acute medication use, while improving quality of life. Its intravenous administration and bioavailability may provide clinical advantages.

Keywords: migraine, eptinezumab, CGRP, prophylaxis, real-world evidence

Η ΕΠΤΙΝΕΖΟΥΜΑΜΠΗ ΣΤΗΝ ΠΡΟΛΗΠΤΙΚΗ ΘΕΡΑΠΕΙΑ ΤΗΣ ΗΜΙΚΡΑΝΙΑΣ: ΕΜΠΕΙΡΙΑ ΑΠΟ ΤΗΝ ΝΕΥΡΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ ΤΟΥ ΝΑΥΤΙΚΟΥ ΝΟΣΟΚΟΜΕΙΟΥ ΑΘΗΝΩΝ

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ΠΕΡΙΛΗΨΗ

Εισαγωγή: Η επτινεζουμάμπη είναι το πρώτο μονοκλωνικό αντίσωμα κατά του CGRP που χορηγείται ενδοφλεβίως για την πρόληψη της ημικρανίας. **Σκοπός:** Η αξιολόγηση της αποτελεσματικότητας και της ασφάλειας της επτινεζουμάμπης κατά το πρώτο τρίμηνο θεραπείας σε ασθενείς με επεισοδιακή και χρόνια ημικρανία σε πραγματικές κλινικές συνθήκες. **Μέθοδοι:** Επτά ασθενείς έλαβαν 100 mg επτινεζουμάμπης ενδοφλεβίως και αξιολογήθηκαν πριν και μετά το τέλος του πρώτου τριμήνου αγωγής ως προς τις ημέρες ημικρανίας ανά μήνα (MMDs), την ένταση πόνου, τις ημέρες χρήσεις φαρμάκων οξείας φάσης/μήνα και με βάση δείκτες ποιότητας ζωής (HIT-6, MIDAS). **Αποτελέσματα:** Το δείγμα περιλάμβανε έξι γυναίκες και έναν άνδρα (μέση ηλικία: 40 έτη· μέση ηλικία έναρξης ημικρανίας: 24 έτη). Πέντε είχαν επεισοδιακή ημικρανία χωρίς αύρα, ένας επεισοδιακή ημικρανία με αύρα και ένας χρόνια ημικρανία. Όλοι είχαν αποτύχει σε ≥2 προηγούμενες προφυλακτικές θεραπείες. Προ της χορήγησης του φαρμάκου, οι ασθενείς ανέφεραν κατά μέσο όρο 10 MMDs, ένταση πόνου 9/10, 15 ημέρες χρήσης οξέων φαρμάκων/μήνα, μέση βαθμολογία MIDAS 36 και HIT-6 70 (σοβαρή αναπηρία). Μετά από 3 μήνες, οι MMDs μειώθηκαν κατά 60% (μέσος όρος 4 ημέρες), η ένταση του πόνου σε 4/10 και οι ημέρες χρήσης οξέων φαρμάκων κατά 75% (μέσος όρος 4 ημέρες). Η βαθμολογία MIDAS βελτιώθηκε σε 8 και η HIT-6 σε 44 (ήπια/καμία αναπηρία). Δεν παρατηρήθηκαν ανεπιθύμητες ενέργειες. **Συμπεράσματα:** Σε αυτό το πραγματικό κλινικό δείγμα, η επτινεζουμάμπη ήταν

ΕΛΛΗΝΙΚΗ ΝΕΥΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ

αποτελεσματική και καλά ανεκτή, μειώνοντας σημαντικά τη συχνότητα των κρίσεων, την ένταση του πόνου και τη χρήση φαρμάκων οξείας φάσης, ενώ βελτίωσε την ποιότητα ζωής. Η ενδοφλέβια χορήγησή του και η πλήρης βιοδιαθεσιμότητα ενδέχεται να προσφέρουν κλινικά πλεονεκτήματα.

Λέξεις-κλειδιά: ημικρανία, επτινεζουμάμπη, CGRP, προφύλαξη, δεδομένα πραγματικού κόσμου

INTRODUCTION

Migraine is a debilitating and prevalent neurological disorder worldwide and remains inadequately controlled in many patients due to limited efficacy or poor tolerability of conventional preventive medications.[4]

Monoclonal antibodies targeting the calcitonin gene–related peptide (CGRP) pathway have transformed migraine prophylaxis.[4] Among these, eptinezumab is the first administered intravenously, offering immediate and complete bioavailability, and has demonstrated rapid onset and sustained efficacy in phase-III trials, including PROMISE-1 and PROMISE-2.[2-3] A recent meta-analysis confirmed its effectiveness and safety across episodic and chronic migraine.[2] Real-world evidence, including multi-site observational studies, has begun to reflect these benefits in broader patient populations.[1,7,9,11]

In this study, we present real-world clinical experience from Greece with eptinezumab in patients with episodic and chronic migraine treated at the Athens Naval Hospital, assessing its clinical impact and tolerability.

METHODS

Study design and setting

Single-centre, observational, prospective cohort study at the Neurology Department of the Athens Naval Hospital.

Participants

Seven adults with migraine (episodic or chronic), fulfilling ICHD-3 criteria, were included. All patients had failed at least two previous preventive therapies. Prior to data collection, all participants were required to read and sign an informed consent form, confirming their agreement to confidentiality, anonymity, and their right to withdraw from the study at any time.

Intervention

Eptinezumab 100 mg was administered intravenously once every 3 months.

Outcomes

Patient-reported outcome measures were assessed at baseline and after 3 months:

- Monthly migraine days (MMDs)
- Pain intensity (0–10 scale)
- Days of acute medication use per month
- Headache Impact Test (HIT-6)
- Migraine Disability Assessment (MIDAS)
- Safety

Adverse events were monitored during infusion and throughout follow-up.

RESULTS

Seven patients were included in the study, six women and one man, with a mean age of 40 years. The mean age at migraine onset was 24 years. Five patients had episodic migraine without aura, one had episodic migraine with aura, and one had chronic migraine. All patients had previously failed at least two preventive treatment options.

At baseline, the clinical burden was substantial. Patients reported a mean of 10 monthly migraine days (MMDs), with a mean pain intensity of 9 on a 10-point scale. The mean number of days of acute medication use was 15 per month. Disability indices reflected a high level of impact, with a mean MIDAS score of 36 and a mean HIT-6 score of 70, both consistent with severe disability (**Table 1**).

After three months of treatment with eptinezumab 100 mg, significant clinical improvements were observed. The mean number of monthly migraine days was reduced by 60%, from 10 to 4 days. Pain intensity decreased from a mean of 9/10 to 4/10. The number of days of acute medication use per month was reduced by 75%, from 15 to 4. Quality-of-life indices showed marked improvement: the mean MIDAS score decreased from 36 to 8, and the mean HIT-6 score from 70 to 44, reflecting a shift from severe to mild or no disability. Importantly, no adverse events were reported during the infusion or the subsequent three-month follow-up period (**Table 2**).

These results echo findings from phase-III trials and confirm significant reductions in MMDs and disability scores.[2-3] They align with real-world evidence reporting effectiveness even in complex patients, including prior non-responders to other CGRP antibodies.[1,7,9]

Table 1. Baseline characteristics of the study cohort (n = 7).

Variable	Value
Sex, n (%)	Female: 6 (86%), Male: 1 (14%)
Mean age, years (range)	40 (32–49)
Mean age at migraine onset	24 years
Migraine type, n (%)	Episodic without aura: 5 (71%) Episodic with aura: 1 (14%) Chronic migraine: 1 (14%)
Previous preventive failures	≥ 2 in all patients (100%)
Baseline monthly migraine days (MMDs)	10 ± 2
Baseline pain intensity (0–10)	9 (severe)
Baseline acute medication days/month	15 ± 3
Baseline MIDAS score (mean)	36 (severe disability)
Baseline HIT-6 score (mean)	70 (severe disability)

Table 2. Clinical outcomes before and after 3 months of eptinezumab treatment (n = 7).

Outcome measure	Baseline (mean ± SD)	3 months (mean ± SD)	% Change / Absolute Change
Monthly migraine days (MMDs)	10 ± 2	4 ± 1	↓ 60% (–6 days)
Pain intensity (0–10 scale)	9 ± 1	4 ± 1	↓ 56% (–5 points)
Acute medication days/ month	15 ± 3	4 ± 1	↓ 75% (–11 days)
MIDAS score	36 ± 5	8 ± 3	↓ 78% (–28 points)
HIT-6 score	70 ± 4	44 ± 3	↓ 37% (–26 points)

DISCUSSION

This real-world case series provides real-world evidence from Greece on the use of eptinezumab for migraine prevention. The results demonstrate a clinically meaningful reduction in monthly migraine days, pain intensity, and acute medication use, accompanied by marked improvements in disability scores as measured by HIT-6 and MIDAS. Importantly, no adverse events were reported, confirming the favourable safety profile observed in pivotal clinical trials.[2-3]

Our findings are consistent with data from the PROMISE-1 and PROMISE-2 trials, which established the efficacy of eptinezumab in episodic and chronic migraine, respectively.[2-3] In those randomized controlled trials, reductions of 50–60% in monthly migraine days were observed, along with improvements in patient-reported outcomes. The degree of improvement in our patients—60% reduction in MMDs and 75% reduction in acute medication use—is in line with these results and highlights the reproducibility of efficacy in real-world settings.[8,9,11]

A notable strength of our series is that all included patients had previously failed at least two preventive therapies, yet eptinezumab produced substantial clinical benefits. This underscores the role of anti-CGRP therapies, and specifically eptinezumab, in populations with high unmet clinical need. Additionally, the improvement in both pain intensity and disability measures suggests that eptinezumab's benefit extends beyond reducing attack frequency, to alleviating the overall disease burden and improving quality of life. [1,4]

The intravenous administration of eptinezumab is a unique feature compared with other monoclonal antibodies targeting the CGRP pathway. Intravenous delivery ensures immediate systemic availability and 100% bioavailability, which may contribute to the rapid onset of effect observed as early as day one in clinical trials. This is particularly relevant for patients with high-frequency attacks or severe disability, in whom early benefit may improve adherence and satisfaction with treatment. Moreover, the lack of cytochrome P450 metabolism reduces the risk of

pharmacokinetic drug–drug interactions, making it an attractive option for patients with comorbidities and polypharmacy.[5,7]

Despite these encouraging results, several limitations must be acknowledged. The small sample size limits the generalisability of our findings, and the short follow-up period precludes conclusions regarding long-term efficacy and safety. In addition, the open-label, uncontrolled nature of the study may introduce bias. Larger prospective studies and registry data will be essential to further define the real-world role of eptinezumab in different migraine subpopulations, including those with medication-overuse headache or comorbid psychiatric disorders. Larger, multicentre prospective registries and comparative studies—including onabotulinumtoxin A comparisons—are needed.[3,6,10]

Nevertheless, the magnitude of benefit observed in this initial experience is clinically significant and suggests that eptinezumab may represent an important addition to the preventive treatment options for migraine in Greece. Early real-world data such as ours are essential to complement randomised trial evidence, as they reflect patient populations and healthcare systems encountered in daily practice.

CONCLUSIONS

Eptinezumab is a safe, effective preventive therapy for episodic and chronic migraine, with robust improvements in clinical and patient-reported outcomes. Larger studies are needed to confirm these promising findings and to directly compare efficacy with other anti-CGRP monoclonal antibodies.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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PARKINSON'S DISEASE AND ATYPICAL PARKINSONIAN SYNDROMES: COMPARISON OF VOICE AND SWALLOWING PARAMETERS

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ABSTRACT

Introduction: Parkinson's Disease (PD) and Atypical Parkinsonian Syndromes (APS) are neurodegenerative disorders causing dysphonia and dysphagia. This study investigates auditory and perceptual voice parameters in PD and APS patients, with and without dysphagia, compared to a healthy Control Group (CG), and explores potential correlations between phonation and swallowing biomarkers.

Methods: Twenty patients with parkinsonism [10 PD (2 females, H&Y: 2.8 ±1, years of age (yoa): 68.5(58-76) and 10 APS (5 females, H&Y: 3.9±1, yoa: 71(59-74) and 20 healthy participants (12 females, yoa: 53.5 (48-71) were recruited during their routine appointment at the Movement Disorders Clinic. Participants underwent perceptual and objective assessments of voice (VHI, V-RQOL, GRBAS, acoustic and aerodynamic measures) and swallowing (EAT-10, SWAL-QoL, Water Swallow Test 90cc). Data were analyzed using non-parametric tests (SPSS, $p<0.05$).

Results: Both patient groups showed statistically significant differences in voice and swallowing parameters compared to CG, with APS patients being more affected compared to PD patients. The two experimental groups (PS and APS) were differed in variables: GRBAS (U=19, p=0.019), nonverbal oromotor abilities (U=21, p=0.029), F_0SD (U=22, p=0.035) amongst others. Patients with swallowing impairments within each of the PD and APS groups differed significantly compared to patients with no swallowing impairments, in parameters including non-verbal diadochokinetic tasks and GRBAS. The acoustic voice parameters were not significantly different in PD and APS with and without swallowing impairments.

Conclusions: Subjective and objective assessments are valuable for evaluating voice and swallowing in PD and APS. Specific voice parameters, reflecting pitch variability, can distinguish dysphagic from non-dysphagic patients, highlighting their potential predictive role in clinical evaluation of voice and swallowing function.

Key words: Parkinson's disease, Atypical Parkinsonian Syndromes, Dysphonia, Dysphagia

ΝΟΣΟΣ ΠΑΡΚΙΝΣΟΝ ΚΑΙ ΑΤΥΠΑ ΠΑΡΚΙΝΣΟΝΙΚΑ ΣΥΝΔΡΟΜΑ: ΣΥΓΚΡΙΣΗ ΠΑΡΑΜΕΤΡΩΝ ΦΩΝΗΣ ΚΑΙ ΚΑΤΑΠΟΣΗΣ

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ΠΕΡΙΛΗΨΗ

Εισαγωγή: Η νόσος του Πάρκινσον (ΝΠ) και τα άτυπα σύνδρομα Πάρκινσον (ΑΠΣ) είναι νευροεκφυλιστικές διαταραχές που προκαλούν δυσφωνία και δυσφαγία. Η παρούσα μελέτη διερευνά τις ακουστικές και αντιληπτικές παραμέτρους της φωνής σε ασθενείς με ΝΠ και ΑΠΣ, με και χωρίς δυσφαγία, σε σύγκριση με μια ομάδα υγιών ατόμων (ΟΕ), και διερευνά πιθανές συσχετίσεις μεταξύ των βιοδεικτών φώνησης και κατάποσης.
Μέθοδοι: Είκοσι ασθενείς με παρκινσονισμό [10 PD (2 γυναίκες, H&Y: 2,8 ±1, ηλικία (yoa): 68,5(58-76) και 10 APS (5 γυναίκες, H&Y: 3,9±1, yoa: 71(59-74) και 20 υγιείς συμμετέχοντες (12 γυναίκες, ηλικία: 53,5 (48-71) εντάχθηκαν στη μελέτη κατά τη διάρκεια της τακτικής τους επίσκεψης στην Κλινική Κινητικών Διαταραχών.

ΕΛΛΗΝΙΚΗ ΝΕΥΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ

Οι συμμετέχοντες υποβλήθηκαν σε αντιληπτικές και αντικειμενικές αξιολογήσεις της φωνής (VHI, V-RQOL, GRBAS, ακουστικές και αεροδυναμικές μετρήσεις) και της κατάποσης (EAT-10, SWAL-QoL, Water Swallow Test 90cc). Τα δεδομένα αναλύθηκαν χρησιμοποιώντας μη παραμετρικές δοκιμές (SPSS, p<0,05).
Αποτελέσματα: Και οι δύο ομάδες ασθενών παρουσίασαν στατιστικά σημαντικές διαφορές στις παραμέτρους της φωνής και της κατάποσης σε σύγκριση με την ΟΕ, με τους ασθενείς με ΑΠΣ να επηρεάζονται περισσότερο σε σύγκριση με τους ασθενείς με ΝΠ. Οι δύο πειραματικές ομάδες (ΝΠ και ΑΠΣ) διέφεραν σε μεταβλητές: GRBAS (U=19, p=0,019), μη λεκτικές στοματοκινητικές ικανότητες (U=21, p=0,029), F_0SD (U=22, p=0,035) μεταξύ άλλων. Οι ασθενείς με διαταραχές κατάποσης σε καθεμία από τις ομάδες PD και APS διέφεραν σημαντικά σε σύγκριση με ασθενείς χωρίς διαταραχές κατάποσης, σε παραμέτρους που περιλαμβάνουν μη λεκτικές διαδοχοκινητικές εργασίες και GRBAS. Οι παράμετροι της ακουστικής φωνής δεν διέφεραν σημαντικά σε και ΝΠ και ΑΠΣ με και χωρίς διαταραχές κατάποσης.
Συμπεράσματα: Οι υποκειμενικές και αντικειμενικές αξιολογήσεις είναι πολύτιμες για την αξιολόγηση της φωνής και της κατάποσης σε ΝΠ και ΑΠΣ. Συγκεκριμένες παράμετροι της φωνής, που αντανακλούν την μεταβλητότητα του τόνου, μπορούν να διακρίνουν τους ασθενείς με δυσφαγία από τους ασθενείς χωρίς δυσφαγία, υπογραμμίζοντας τον πιθανό προγνωστικό τους ρόλο στην κλινική αξιολόγηση της φωνής και της λειτουργίας της κατάποσης.

Λέξεις-κλειδιά: Νόσος του Πάρκινσον, Άτυπα Συνδρόματα Πάρκινσον, Δυσφωνία, Δυσφαγία

INTRODUCTION

Parkinson's Disease (PD) and Atypical Parkinsonian Syndromes (APS) are neurodegenerative disorders characterized by parkinsonism—bradykinesia, rigidity, and postural instability. AP syndromes include multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal syndrome (CBS), dementia with Lewy bodies (DLB), and vascular parkinsonism (VP). [1,2] These disorders may include a variety of neurological disorders similar to PD, but the clinical features are not only due to cell loss in the substantia nigra but also in other parts of nervous system that contain dopamine receptors, such as the striatum. Typically, the APS, commonly also known as 'PD-plus syndromes' are thought to be related to accumulations of alpha-synuclein (synucleinopathy) or tau (tauopathy) and these may affect multiple brain regions, including the pigmented nuclei in midbrain and brainstem, the olfactory tubercle, cerebral cortex, and parts of the peripheral nervous system.[2,3] Voice dysfunction is among the earliest clinical symptoms in people with PD (pwPD), affecting approximately 80-90% of patients.[4,5] Similar early voice changes are reported in PSP and MSA.[6-8] These conditions impair motor, behavioral, and sensory functions required for voice production,[9,10] disrupting respiratory support, vocal fold vibration, and resonance, which reduces voice quality, frequency, and intensity.[11-13]

Most pwPD develop hypokinetic dysarthria due to altered basal ganglia output consequent on dopamine denervation.[14,15] PD speech is characterized by monotonous pitch and loudness, weak and breathy voice from reduced vocal fold adduction, rough/hoarse voice from compensatory strategies or cricothyroid rigidity.[16-20] Patients with PSP and MSA often present with mixed dysarthria, exhibiting a combination of hypokinetic, spastic, and ataxic features. These clinical features likely arise as a result of more widespread multisystem neurodegenerative changes. Spasticity predominates in PSP, while motor and ataxic symptoms are more evident in MSA, affecting all speech subsystems.[21-23] CBS may also involve dysarthria reflecting cortical and motor dysfunction.[24]

Swallowing disorders are frequent in pwPD and a major cause of morbidity due to aspiration pneumonia.[25,26] Both oral and pharyngeal phases are affected, leading to abnormal bolus formation, multiple tongue elevations, delayed swallow reflex, prolonged pharyngeal transit time, and repeated swallows.[27] Pharyngeal motor nerve degeneration and dopaminergic deficits contribute to oropharyngeal dysphagia.[28] Dysphagia is also an early symptom in MSA, usually within three years after disease onset,[29] with oral and pharyngeal stages impaired in both MSA-P and MSA-C.[30] In PSP, swallowing dysfunction mainly affects the oral phase.[31] Dysphagia is also common in DLB and CBS, again reflecting broader motor and cortical impairments.[24]

Objective analysis of voice parameters in parkinsonism provides valuable information about voice disorders, respiratory/vocal insufficiency, and prognosis.[20,32] Perceptual assessments also help identify phonatory changes, while patient-reported outcomes reflect disease progression and quality of life.[33,34] Several studies report correlations between acoustic voice changes and swallowing difficulties in PD,[35,36] possibly due to a common pathophysiological mechanism.[12,37,38] However, voice measures alone show limited sensitivity for early dysphagia detection.

The aims of this study are 1) to compare the auditory and perceptual voice characteristics in pwPD and pwAPS, with and without dysphagia, against a

healthy control (HC) group and 2) to investigate the possible predictive value of specific voice parameters for detecting swallowing difficulties in pwPD and pwAPS.

MATERIALS AND METHODS

Participants

Patients with parkinsonism and age-matched healthy controls (HC) enrolled sequentially during routine visits at the Movement Disorders Clinic, Department of Neurology, General University Hospital of Patras between September 2023 and October 2024. Written informed consent was obtained from all participants before the experiments. All experiments were undertaken in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). The approval for the studies was granted by the Institutional Ethics Committee of the University Hospital of Patras (no. of approval 347/13-07-2023). Inclusion criteria were informed consent and age between 18–80 years. Exclusion criteria were speech, voice, or language disorders unrelated to PD/APS, orofacial anatomical disorders, and non-related respiratory conditions. Disease severity was assessed using the Hoehn and Yahr scale.[39] Patient evaluations were conducted at the hospital, usually lasting for 1 hour, while controls were assessed at their residence.

Procedures

Following consent, the patients' medical history was collected, followed by formal orofacial assessment (NOT-S),[40] informal nonverbal diadochokinetic tongue tasks, verbal diadochokinetic rate task (/pataka/ repetition) and perceptual and objective measures of voice and swallowing.

Swallowing tasks and recordings

Efficacy of swallowing was evaluated using the screening symptomatology list of EAT-10-GR [41] and Swallowing Quality-of-Life.[42] Swallowing efficiency was assessed with 90cc Water Swallowing Test.[43,44] Water swallowing procedures were performed with water at room temperature while the measurements of swallowing efficacy included time to complete swallowing of 90cc, measured with a stopwatch, remainder water quantity (mls), in the occasion when patients could not swallow full amount and any signs of dysphagia.

For the presence of dysphagia in the neurologically impaired population, the following parameters had to be present: 1) modified diet, 2) positive results on the screening tool EAT-10-GR [41] (score≥4), 3) swallowing speed in WST ≥10ml/s,[45] and 4) signs of penetration/aspiration (coughing, choking, wet voice quality, throat clearing, watering eyes, shortness of breath.[46]

Voice tasks and recordings

Voice assessment included the administration of the VHI,[47] V-RQOL scales,[48] GRBAS perceptual rating,[49] and acoustic/aerodynamic voice analyses.[46,50-54] Participants were asked to perform three repetitions of sustained vowel /a/, as long as possible at a comfortable pitch and loudness. Tasks were first demonstrated by the examiner. Voice was recorded and analyzed with Praat software (V6.1.16) During recordings in a quiet room without ambient noise, a sampling frequency of 44.1 kHz was used with a cardioid condenser microphone (Blue Snowball) placed 30 cm away from the level of the mouth. Acoustic and aerodynamic measures included maximum phonation time (MPT), mean fundamental frequency (mF0), F0 standard deviation (F0SD), maximum F0 (maxF0), minimum F0 (minF0), jitter (%), shimmer (%), noise-to-harmonic ratio (NHR), fraction of unvoiced frames (FUF), degree (%) (DVB) and number (NVB) of voice breaks, mean/maximum/minimum intensity.[46,50-54]

Inter-rater reliability of acoustic analysis

Inter-rater reliability analysis was conducted by 3 raters, one post-graduate speech-language therapist and two graduate students. All raters had received the same acoustic analysis training and used the same Praat version (V6.1.16). Cohen's weighted kappa was measured across the 3 raters (SPSS V.29), indicating good reliability (1 vs 2= k:0.726, 95%CI (0.597,0.856),1 vs 3= k:0.769, 95%CI (0.658, 0.880), 2 vs 3=k:0.85,95%CI (0.754,0.955)).

Statistical analysis

Statistical analysis was performed using SPSS (v.29). Levene's test (p-value < 0.01) was initially used to test the homogeneity of variances. For values not following normal distribution, non-parametric tests (Kruskal-Wallis) were used to identify any differences in the distribution of the median between the three groups. Non-parametric comparisons (Mann-Whitney Test) per two groups were performed for the variables that showed a significant difference between the three groups. Correlations were made with non-parametric tests (Spearman's correlation coefficient). Analysis of the extent to which specific parameters can be indicative of swallowing disorders was performed with receiver operating characteristic (ROC) curves and area under the curve (AUC) values, treated with non-parametric statistics. A $p < 0.05$ was taken as a measure of statistical significance. All data are presented as group mean ± SEM, unless stated otherwise.

RESULTS

The study included 20 patients with parkinsonism [10 with PD (2 females, H&Y: 2.8 ± 1, years of age (yoa): 68.3 ± 6) and 10 with APS (4 females, H&Y: 3.9 ± 1, yoa: 70.1 ± 4.3)] and 20 HC (12 females, yoa: 57.3 ± 7).

Patients recruited completed the study with no adverse events. Table 1 shows the participants' demographics. The APS group included people diagnosed with MSA, PSP, DLB, and VP (**Table 1**).

Table 1. Participant demographics

Clinical feature	**PD (n= 10)**	**APS (n= 10)**	**HC (n= 20)**
Age *(median, range)*	68.5 (58-76)	71 (59-74)	53.5 (48-71)
Duration *(median, range)*	6 (2-20)	4 (1.5-6)	-
Gender *(m/f)*	8/2	6/4	8/12
MSA *PSP* *DLB* *VP*		2/1 1/3 1 1/1	
Hoehn & Yahr score	2.5 (2-5)	4 (2.5-5)	-
MSA *PSP* *DLB* *VP*		4 (3-5) 4.5 (2.5-5) 3 3,5 (3-4)	
Swallowing impairments *(SI, n)*	5	5	-

Table 1 shows the participants' demographics per group and disease profile (SI: swallowing impairment). MSA: multiple system atrophy, PSP: progressive supranuclear palsy, DLB: Dementia with Lewy bodies, VP: vascular parkinsonism, HC: healthy controls.

Table 2. Differences in voice and swallowing variables across groups

Median (Range min-max)		**PD**	**APS**	**HC**	**Sig. Level**
Age		68.5 (58-76)	71 (59-74)	53.5 (48-71)	H(2) = 22.4 p < 0.001
Self-reported SI					
EAT-10		1.5 (0-29)	9.5 (0-17)	0	H(2)= 18.6 p < 0.001
Swal-QoL Total		138.5 (52-149)	111 (81-150)	148 (132-150)	H(2) = 17.9 p < 0.001
Self-reported VI					
VHI Total		14 (0-102)	43 (1-71)	1 (0-39)	H(2) = 9.31 p = 0.010
VHI L		6 (0-39)	12.5 (0-25)	0 (0-14)	H(2)= 9.44 p = 0.009
VHI F		4 (0-29)	13 (0-27)	0,5(0-15)	H(2)= 11.60 p = 0.003
VHI S		3.5 (0-34)	12.5 (0-27)	0 (0-10)	H(2)= 9.311 p = 0.010
VR QoL	**Voice now**	1.5 (1-4)	2 (1-3)	1 (1-3)	H(2)= 6.63 p = 0.036
	VR QOL TS	12.5 (10-44)	15.5 (10-36)	10 (10-21)	H(2)= 12.5 p = 0.020
	VR QOL Voice Today	3 (2-4)	2 (1-4)	4 (2-5)	H(2)= 11.1 p = 0.004

Oromotor measures					
Informal nonverbal DDK (sec)	**Tongue inwards-outwards**	10.6 (7.4-19.1)	12 (7.9-25.2)	8 (4.2-10.1)	H(2) = 7.49 p = 0.024
	Tongue upwards -downwards	13.7 (10.7-26.9)	26.7 (11.7-39.8)	8.8 (6.7-13.2)	H(2)= 12.97 p =0.002
	Tongue Left-Right	15.4 (5.9-18.6)	16.8 (8.5-35.5)	6.8 (4.9-13.7)	H(2)= 9.25 p =0.010
NOT-S		11 (5-14)	9 (3-13)	0	H(2) = 22.9 p < 0.001
Speech measures					
/pataka/ repetitions (sec)		5.7 (4.1- 8.8)	6.8 (6.5-46.8)	4.4 (3.2-5.6)	H(2)= 12.41 p =0.002
Swallowing measures					
No of swallows for 90 cc		11 (5-14)	9 (3-13)	2 (1-3)	H(2) = 22.9 p < 0.001
Time to complete 90 cc (sec)		11.9 (7.2-16.7)	14.1 (7.1-34.4)	5 (4- 7)	H(2) = 21.8 p < 0.001
Voice Acoustic measures					
GRBAS		3 (0-8)	5.5 (3-11)	1 (0-3)	H(2)=22.69 p<0.001
Jitter (%)		0.7 (0.2-2.1)	0.8 (0.5 -1.8)	0,3 (0.1-0.6)	H(2)= 15.18 p < 0.001
Shimmer (%)		5.1 (2.7- 12.8)	8.3 (4.2-18.5)	4.1 (2.1-9.1)	H(2)= 10.33 p =0.006
MPT(sec)		11.23 (4.9-19.5)	10.5 (5.6-13.5)	8.11 (4.12-31.5)	ns
medF0		128.6 (84.2-222)	120.7 (82.6-270)	168.4 (95.4-299.7)	ns
minF0		154.2 (88.4-392)	183.9 (113.6-279)	172.4 (98-304.9)	ns
maxF0		154.2 (88-392.9)	183 (113-275)	172.41 (98.7-304)	ns
F0SD		2.15 (1-56.6)	15.9 (2.19-48.5)	1.87 (0.7-22.9)	H(2)= 10.36 p =0.006
Harmonics-to-noise ratio		16.7 (10.8-20.8)	14.3 (2.7-19.1)	18.9 (12.8-30)	ns
Fraction of unvoiced frames (%)		0 (0- 63.7)	1 (0-47.6)	0 (0-0.7)	H(2)= 17.31 p < 0.001
Number of voice breaks		0 (0-8)	0.5 (0-10)	0 (0-2)	H(2)= 9.13 p =0.010
Degree of voice breaks (%)		0 (0-25.3)	2,05 (0-47.1)	0 (0-1.64)	H(2)= 9.89 p =0.007
Mean Intensity		60.2 (54.9-69)	60.5 (44-69.5)	60.9 (50.5-75.5)	ns
Minimum Intensity		52.2 (49-66)	52.2 (41-66)	57.4 (46.8-71)	ns
Maximum intensity		62.7 (57-71)	65.6 (47-71)	63.9 (59-77.9)	ns

Table 2 shows the participants' demographics per group and disease profile (SI: swallowing impairments, VI: voice impairments, VHI: voice handicap index, VR QOL: voice related Quality of Life, NOT-S: Nordic orofacial screening test, MPT: mean phonation time, F_0: fundamental frequency, ns: non-significant)

Several parameters, including voice variables, differed significantly across the 3 groups (Kruskal-Wallis test), as shown in **Table 2**.

Regarding the different outcome measures, marked differences were observed across the 3 groups as shown in **Table 2**. Further analysis using the Mann-Whitney test showed that both experimental groups exhibited differences across specific parameter categories compared to the HC, with pwAPS being more affected compared to pwPD. Notably, age was significantly different across groups, both for pwPD vs HC (U=17, p<0.001) and pwAPS vs HC (U=9.5, p<0.001), which is further discussed below.

For pwPD vs HC, significant differences were found for SWAL-QOL-GR (U=28, p<0.001), NOT-S (U=29, p<0.001), DDK tongue movements (p<0.05), /pataka/ repetition (U=32.5, p=0.005), GRBAS (U=40.5, p=0.007), Jitter (%) (U=20, p<0.001) and VHI total score (U=52.5, p=0.013).

For pwAPS vs HC, significant differences were found for SWAL-QOL-GR (U= 18, p< 0.001), /pataka/ repetition (U=18, p=0.003), GRBAS scores (U=1, p< 0.001), VHI total score (U=18, p<0.001), VRQoL (U=33, p=0.002) and Jitter(%) (U=36, p=0.004). Results from NOT-S-GR exam also exhibited statistical differences for pwAPS patients (U=8, p<0.001) as in pwPD vs HC groups. Compared to the differences shown above for the PD group, for the pwAPS additional statistically significant differences were found concerning the following voice variables: F0SD (U=22, p<0.001), shimmer(%) (U=28, p< 0.001), fraction of unvoiced frames(%) (U= 24, p<0.001) and DVB(%) (U=52.5, p=0.035). These results suggest that voice parameters were more affected in the pwAPS compared to pwPD.

The two experimental groups (PD and APS) were directly compared to review the level and extent of differences and possible markers for differential diagnosis. Indeed, the two groups differed in variables: GRBAS (U=19, p=0.019), NOT-S (U=21, p=0.029), F0SD (U=22, p=0.035) and FUF (U=24, p<0.05).

Following the swallowing impairments profiling based on the aforementioned classification, we performed analysis for the 4 subgroups (pwPD with and without SI and pwAPS with and without SI). Patients with swallowing impairments within each of the PD and APS group differed significantly compared to patients with no swallowing impairments, specifically for NOT-S (U=22.5, p=0.038), VQOL (U=9.5, p=0.004), non-verbal DDK (U=9, p=0.019 for tongue inwards outwards, U=6, p=0.009 downwards-upwards) and GRBAS (U=19.5, p=0.02). None of the acoustic voice parameters could differentiate the 4 subgroups.

DISCUSSION

This study examined subjective and objective voice parameters in PD and APS compared to a healthy control group and explored whether specific voice measures could be associated with swallowing impairments. Even though the groups were not age-matched, age-related differences for speech and voice swallowing problems were not observed (i.e. voice intensity etc), which allowed further direct comparison amongst the different groups. Statistically significant differences were observed between the patient groups and controls, as well as between the PD and APS cohorts, underscoring the clinical relevance and diagnostic potential of specific acoustic and perceptual voice markers that merit further discussion.

Voice and Swallowing Parameters in PD and APS

PD participants exhibited significant changes in both perceptual and acoustic measures, including increased GRBAS scores, elevated Voice Handicap Index (VHI) scores, higher jitter values, and reduced SWAL-QOL scores. These results align with previous findings by Bauer et al.[55]and Silva et al.[20] who reported higher perceptual scores and reduced maximum phonation time in PD. Jitter increases, commonly attributed to impaired neuromotor control of the vocal folds, are further corroborated by Abraham & Geetha (2023).[56]

In line with Silva et al.[20] our study confirms that PD patients exhibit measurable dysphonia, with increased jitter likely reflecting decreased laryngeal motor control. Furthermore, patient-reported outcomes in our cohort mirrored findings by Silbergleit et al.[57] and Van Hooren et al.[34], both of whom documented the progressive impact of PD on voice and swallowing-related quality-of-life. Notably, voice and swallowing complaints appeared to co-occur and intensify with disease duration and severity.

In the APS group, voice impairments were generally more severe and hetergoneous. Perceptual and acoustic measures, particularly jitter, shimmer, GRBAS grade, fraction of unvoiced frames (FUF), and degree of voice breaks—demonstrated significantly worse values compared to both PD patients and controls. These findings are consistent with Miller et al.[58], who showed that individuals with MSA-P and PSP experienced greater speech deterioration than those with idiopathic PD, although individual acoustic parameters were insufficient to distinguish APS subtypes reliably. The more extensive neurodegeneration observed in APS likely contributes to the broader disruption of laryngeal and articulatory control mechanisms.

Finger et al.[59] further support this interpretation, noting that patients with APS experience earlier and more pronounced voice and swallowing difficulties

than those with PD or essential tremor. This may reflect the faster disease progression and more extensive brainstem and cerebellar involvement typical of APS, particularly in MSA and PSP subtypes.

Concerning self-perception of swallowing difficulties, in our study there was a statistical significance concerning SWAL-QOL-GR questionnaire, where PD patients scored significantly lower than healthy controls. Plowman-Prine et al.[60] assessed 36 idiopathic PD patients (with and without dysphagia) using SWAL-QOL, PDQ-39, and Beck Depression Inventory (BDI), showing that dysphagia negatively impacted both swallowing-related and overall QoL. Similarly, Carneiro et al. (2014)[61] compared 62 idiopathic PD patients with 41 controls and found significantly lower SWAL-QOL scores across all domains in the patient group.

Regarding acoustic analysis, Holmes et al.[62] and Rahn III et al.[63] also found higher jitter (%) in PD than controls, attributed to irregular laryngeal contractions during phonation, impaired motor control of the vocal folds and aperiodicity in the acoustic signal.[53] Our study further revealed significant impairments in verbal diadochokinesis, reflecting fine motor speech deficits. Overall, these results confirm that PD patients experience measurable vocal impairments and reduced self-perceived voice/swallowing function, with consequences for QoL.

Based on our study's findings, along with those from other research, it is evident that specific acoustic voice parameters are significantly impacted in individuals with both pwPD and pwAPS. However, pwAPS demonstrated greater difficulties in certain voice parameters compared to pwPD. This includes more severe impairments in acoustic features like shimmer, F0SD, FUF and DVB indicating that vocal dysfunction in APS is more pronounced and widespread, reflecting the more rapid disease progression and greater motor involvement in APS compared to PD.

Voice parameters and their role in identifying swallowing impairments

The results showed that acoustic parameters could not be utilized currently to indicate the presence of swallowing impairments in pwPD and APS. This is in line with the above discussed literature, showing high heterogeneity in acoustic parameters, that were also used in our study. Nevertheless, across dysphagic patients within both PD and APS groups, there was a noticeable reduction in non-verbal diadochokinetic repetitions and overall reduced voice quality assessed by GRBAS, showing the degree of hoarseness, roughness, breathiness, asthenia (weakness), and strain. Some indications for differences in F_0SD were also observed with dysphagic patients exhibiting significantly altered F_0SD values, but further research is needed in order to evaluate the utility of the parameter as a potential marker.

Although as a marker the F0SD has not appeared in dysphagia literature, in a large-scale study, Skodda et al.[64] investigated how various prosodic speech parameters - including F0SD- change in pwPD and how these relate to motor symptoms. The researchers found that F0SD was significantly reduced in both male and female PD patients compared to age- and gender-matched healthy controls, supporting the clinical observation of monopitch speech in PD. Notably, the study revealed a strong inverse correlation between F0SD and disease severity, particularly in female PD patients, where F0SD significantly declined with higher scores on the UPDRS motor scale and Hoehn & Yahr stages. These findings suggest that reduced pitch variability (F0SD) is a robust and measurable marker of dysprosody in PD, potentially linked to akinesia and axial motor symptoms, and may reflect the effects of Parkinsonian hypokinesia on laryngeal control mechanisms.

The underlying rationale to investigate further the acoustic parameters in a larger cohort is that there is a shared physiological basis between voice and swallowing mechanisms, particularly involving the laryngeal musculature controlled by brainstem nuclei. Neuromuscular rigidity, bradykinesia, and coordination deficits may compromise both phonatory and deglutitive functions.[63,65]

Supporting Literature on Voice-Swallow Interactions

Subjective measures such as the VHI functional subscale and GRBAS perceptual scores were significantly worse in patients with swallowing impairments, suggesting that these perceptual indicators may provide early warnings for clinicians. Dumican & Watts reported a strong predictive relationship between voice complaints and perceived dysphagia severity in PD, particularly in non-tremor dominant phenotypes.[66]

Therapeutically, this overlap presents opportunities. For example, Park et al.[67] demonstrated that Lee Silverman Voice Treatment (LSVT) not only improved voice quality in MSA and PD but also enhanced swallowing function in both oral and pharyngeal phases. This cross-domain benefit underscores the interconnected nature of vocal and deglutitive subsystems. However, it is important to note that not all acoustic measures may be equally informative: Chang et al.[68] found no significant differences in shimmer, jitter, or NHR between aspirating and non-aspirating patients during VFSS, suggesting that voice analysis should be complemented with clinical assessments.

Some further insights have been added to the literature on shared connections of voice and swallowing from studies on Deep brain stimulation (DBS).

The modulation of bulbar motor output in PD with DBS has been associated with changes in swallowing timing parameters (e.g., pharyngeal transit time, latency of swallow initiation), while its effects on swallowing safety indices such as penetration–aspiration and pharyngeal residue remain inconsistent across studies. [69, 70] Changes in voice acoustics under DBS—particularly parameters reflecting phonatory stability, loudness regulation, and temporal control—are conceptually linked to the same basal ganglia–brainstem circuitry influencing oropharyngeal timing; however, current evidence suggests only partial correspondence, with stronger associations emerging for swallowing efficiency and timing metrics rather than safety outcomes.

Our study comes with limitations discussed further. While this study presents a sample that allows for comparisons with the existing literature, it is important to emphasize the need for further research with a larger sample size. The participants in the healthy control group were not age-matched, and this initially would not have allowed for further comparisons. However, parameters that would have differed due to aging such as voice intensity, showed similar values across the groups, which allowed further between-groups comparisons. Some parameters, which were treated with non-parametric tests based on the results of Levene's test, have been treated as parametric by other researchers, suggesting that a larger sample might offer more robust insights. Incorporating objective voice assessments, alongside subjective tools such as the VHI and GRBAS scales, allows for a comprehensive understanding of the patient's voice function. Moreover, self-reported questionnaires like the SWAL-QoL and EAT-10 provide insights into the patients' perception of their swallowing difficulties, which can guide tailored therapeutic approaches.

CONCLUSION

The findings from this study also reinforce the hypothesized link between voice and swallowing mechanisms in neurodegenerative conditions. Both voice production and swallowing rely heavily on laryngeal and pharyngeal muscle function, which are commonly affected by the motor deficits seen in PD and APS. This common pathophysiological basis further justifies the use of voice parameters as indicators of swallowing dysfunction. The results show that certain auditory and perceptual voice characteristics, alongside swallowing measures, can serve as valuable tools in differentiating between dysphagic and non-dysphagic patients.

Implications for Clinical Practice: The study highlights the importance of incorporating voice assessments into routine clinical evaluations of patients with PD and APS, particularly for the early detection of dysphagia. Given that swallowing disorders are a leading cause of mortality in these populations due to aspiration pneumonia, early identification through non-invasive voice measures could provide crucial preventive interventions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Ενημερωτικές Σελίδες...

Συνέδρια - Ημερίδες - Συμπόσια - Επιστημονικές εκδηλώσεις

2025 - 2026

- **6-8 Νοεμβρίου 2025: 28th CONFERENCE OF THE WORLD ORGANIZATION OF NEUROSONOLOGY (WON),** *Athens*
- **11-13 Νοεμβρίου 2025: The 2nd International Electronic Conference on Medicine,** *Online*
- **20-23 Νοεμβρίου 2025: 13ο Πανελλήνιο Συνέδριο Αγγειακών Εγκεφαλικών Νόσων,** *Θεσσαλονίκη*
- **11-14 Δεκεμβρίου 2025: 12ο Πανελλήνιο Συνέδριο Ελληνικής Ακαδημίας Νευροανοσολογίας,** *Θεσσαλονίκη*
- **6-8 Μαΐου 2026: European Stroke Organization Conference,** *Maastricht, the Netherlands*
- **15-17 Μαΐου 2026: 14ο ΔΙΕΘΝΕΣ ΣΥΜΠΟΣΙΟ ΤΗΣ ΕΤΑΙΡΕΙΑΣ ΓΙΑ ΤΗΝ ΕΡΕΥΝΑ ΤΗΣ ΠΑΡΕΓΚΕΦΑΛΙΔΑΣ ΚΑΙ ΤΩΝ ΑΤΑΞΙΩΝ,** *Λευκωσία*
- **4-7 Ιουνίου 2026: 37ο Πανελλήνιο Συνέδριο Νευρολογίας,** *Καλαμάτα*

Αρχεία Κλινικής Νευρολογίας

Για λόγους ενημέρωσης αρχείου, παρακαλούμε συμπληρώστε τα στοιχεία αλληλογραφίας σας και στείλτε το απόκομμα με fax στο: **210 7247556** ή αποστείλετε τα στοιχεία στο e-mail: **info@jneurology.gr**

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- *Εάν επιθυμείτε να λαμβάνετε το περιοδικό «Αρχεία Κλινικής Νευρολογίας» και σε ηλεκτρονική έκδοση συμπληρώστε την ηλεκτρονική σας διεύθυνση:*

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Σημειώσεις

Οδηγίες προς τους συγγραφείς

Το περιοδικό *ΑΡΧΕΙΑ ΚΛΙΝΙΚΗΣ ΝΕΥΡΟΛΟΓΙΑΣ* κυκλοφορεί κάθε δύο μήνες και αποτελεί το επίσημο όργανο της Ελληνικής Νευρολογικής Εταιρείας. Με την Υπουργική Απόφαση ΔΥ2α/Γ.Π.οικ. 66198/1/6/2006, που δημοσιεύθηκε στο Φ.Ε.Κ. 1034/Β/1-08-2006, προστέθηκε στον κατάλογο των περιοδικών με Εθνική Αναγνώριση.

Ύλη του Περιοδικού

1. Ανασκοπικά Άρθρα: Η έκτασή τους δεν πρέπει να υπερβαίνει τις 6.000 λέξεις.
2. Εργασίες: Κλινικές ή εργαστηριακές μελέτες. Δεν πρέπει να υπερβαίνουν τις 4.000 λέξεις (συμπεριλαμβανομένων έως 6 πινάκων και εικόνων). Δεν πρέπει να έχει προηγηθεί δημοσίευσή τους σε άλλο έντυπο. Περιλαμβάνουν σελίδα τίτλου, δομημένη περίληψη, εισαγωγή, μέθοδο, αποτελέσματα, συζήτηση και βιβλιογραφία.
3. Σύντομες ανακοινώσεις και Γράμματα προς τη σύνταξη: Σχόλια για εργασίες που έχουν δημοσιευθεί ή σύντομες αναφορές σε ένα θέμα. Δεν πρέπει να υπερβαίνουν τις 1.500 λέξεις και περιλαμβάνουν έως 2 πίνακες ή εικόνες.
4. Ενδιαφέροντα περιστατικά: Όριο λέξεων 1.500, με τη σελίδα τίτλου, περίληψη και τις βιβλιογραφικές αναφορές. Επιτρέπονται μέχρι 2 εικόνες ή πίνακες.
5. Νευρολογικές Εικόνες με εκπαιδευτικό ενδιαφέρον: Όριο 4 εικόνες για το ίδιο θέμα και 200 λέξεις.
6. Επιλογές και σχολιασμός της βιβλιογραφίας.
7. Νευρολογικά Νέα - Ειδήσεις - Ενημερωτικές Σελίδες, όπως νέα της Ελληνικής Νευρολογικής Εταιρείας και συγγενών εταιρειών, ανακοινώσει συνεδρίων και άλλων εκπαιδευτικών δραστηριοτήτων.

Δομή της ύλης

Γίνονται δεκτές εργασίες στα ελληνικά ή αγγλικά.
Υποβάλλεται πάντοτε ο τίτλος, τα ονόματα των συγγραφέων και η περίληψη και στα αγγλικά.
Τα κείμενα θα πρέπει να αποστέλλονται σε μορφή Microsoft Word document.
Σελίδα τίτλου: Περιέχει τον τίτλο, τα πλήρη ονόματα των συγγραφέων, το ίδρυμα προέλευσης, τη διεύθυνση και το τηλέφωνο του υπευθύνου για την αλληλογραφία και τον καταμετρημένο αριθμό λέξεων.
Περίληψη: Παρουσιάζει τα κυριότερα σημεία της εργασίας. Δεν πρέπει να υπερβαίνει τις 250 λέξεις. Στο τέλος της παρατίθενται 3-10 λέξεις ευρετηρίου.
Αγγλική περίληψη: Παρουσιάζει σε συντομία την εργασία. Η έκτασή της είναι ως 400 λέξεις. Στην αρχή της γράφονται τα ονόματα των συγγραφέων και ο τίτλος της εργασίας στα αγγλικά.
Λέξεις-κλειδιά: έως 6 λέξεις κλειδιά.
Βιβλιογραφία: Οι βιβλιογραφικές παραπομπές αριθμούνται με αύξοντα αριθμό ανάλογα με τη σειρά εμφάνισής τους στο κείμενο (Vancouver). Όλες οι βιβλιογραφικές παραπομπές να αναφέρονται μέσα σε αγκύλες. Π.χ. Ο Smith [1] ανέφερε ότι ... και τα ευρήματα αυτά επιβεβαιώθηκαν από τον Adams και συν [2]. Αναγράφονται έως και οι 6 πρώτοι συγγραφείς. Στον πίνακα της βιβλιογραφίας περιλαμβάνονται μόνο εκείνες οι βιβλιογραφικές παραπομπές που αναφέρονται στο κείμενο και ο πίνακας συντάσσεται με αύξοντα αριθμό που αντιστοιχεί στη σειρά εμφάνισης των βιβλιογραφικών παραπομπών στο κείμενο π.χ.
Πίνακες: Γράφονται σε ξεχωριστή σελίδα, μετά το τέλος των βιβλιογραφικών αναφορών. Αριθμούνται με τη σειρά εμφάνισής τους στο κείμενο και συνοδεύονται από σύντομη επεξήγηση.
Εικόνες: Αποστέλλονται τα πρωτότυπα σχέδια ή φωτογραφίες καλής ποιότητας. Να υποβάλλονται σαν αρχεία εικόνας ξεχωριστά από το κείμενο του MS Word. Αριθμούνται με τη σειρά εμφάνισης στο κείμενο. Στο κείμενο θα πρέπει να υπάρχει σαφής παραπομπή στον τίτλο των ηλεκτρονικών αρχείων. Σε ξεχωριστή σελίδα αναγράφονται οι τίτλοι των εικόνων και οι τυχόν επεξηγήσεις.
Ιατρική Δεοντολογία: Σε περιπτώσεις ερευνών που αφορούν ανθρώπους, η έρευνα πρέπει να έχει γίνει με βάση τη διακήρυξη του Ελσίνκι (1975). Σε περιπτώσεις φωτογραφιών ασθενών, θα πρέπει να υπάρχει έγγραφη συγκατάθεση.

Συνοδευτικό έντυπο υποβαλλόμενης εργασίας

Θα πρέπει να συμπληρωθούν ΟΛΑ τα σημεία του εντύπου. Άλλη συνοδευτική επιστολή δεν είναι απαραίτητη.

Είδος άρθρου (σημειώστε μόνο ένα)

❑ Ερευνητική εργασία ❑ Βραχεία εργασία - ενδιαφέρον περιστατικό ❑ Ανασκόπηση

❑ Βραχεία ανασκόπηση ❑ Ειδικό άρθρο ❑ Γράμμα στη σύνταξη ❑ Νευρο-εικόνες

Τίτλος:

Υπεύθυνος για την αλληλογραφία συγγραφέας:

Διεύθυνση:

Τηλέφωνο: FAX: e-mail:

Επιβεβαιώστε την πληρότητα της υποβολής του χειρογράφου σας, σημειώνοντας ΟΛΑ τα παρακάτω σημεία

- ❑ Τίτλος του άρθρου στα Ελληνικά και στα Αγγλικά με μικρά γράμματα
- ❑ Ονόματα συγγραφέων στα Ελληνικά και στα Αγγλικά *(πλήρη ονόματα π.χ. Νικόλαος Παπαδόπουλος)*
- ❑ Κέντρο προέλευσης της εργασίας στα Ελληνικά και στα Αγγλικά
- ❑ Δομημένη περίληψη στα Ελληνικά και στα Αγγλικά
- ❑ Έως πέντε λέξεις ευρετηριασμού *(κατά προτίμηση από το MeSH Hellas-Βιοϊατρική Ορολογία)* στα Ελληνικά και στα Αγγλικά
- ❑ Όλα τα ονόματα των συγγραφέων στις βιβλιογραφικές παραπομπές (*μέχρι 6 και στη συνέχεια* «*και συν.*» *ή* «*et al*»)
- ❑ Η βιβλιογραφία στις τελευταίες σελίδες των άρθρων

Δήλωση

Δηλώνω υπεύθυνα ότι:

1. Όλοι οι συγγραφείς της εργασίας συμφωνούν με το περιεχόμενό της και με την υποβολή της στο περιοδικό: *Αρχεία Κλινικής Νευρολογίας.*
2. Το ίδιο κείμενο ή τα αποτελέσματα της εργασίας δεν έχουν υποβληθεί για δημοσίευση σε άλλο Ελληνικό ή ξένο περιοδικό.
3. Δηλώνω υπεύθυνα ότι δεν υπάρχει θέμα υποκλοπής πνευματικής ιδιοκτησίας (σε περίπτωση εικόνων, πινάκων ή υλικού από άλλες δημοσιεύσει έχει ζητηθεί και ληφθεί η νόμιμη άδεια η οποία και συνυποβάλλεται).
4. Δεν υπάρχουν θέματα σύγκρουσης συμφερόντων – σε περίπτωση εξωτερικής χρηματοδότησης αυτό θα πρέπει να αναφέρεται στο τέλος της εργασίας.

Ο υπεύθυνος για την αλληλογραφία συγγραφέας

(υπογραφή)