Neurological diseases

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NITROUS OXIDE CHRONIC ABUSE: LOOKING FOR DIAGNOSIS AND MONITORING BIOMARKER.


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BACKGROUND-AIM

Recently, recreational use of nitrous oxide (N2O), also known as whippits, has significantly increased. The chronic consumption leading to serious neurological sequelae such as subacute combined degeneration of the spinal cord which would be related to an action of N2O on vitamin B12 function. However, measurement of N2O in laboratory is not relevant for diagnosis related to his short half-life. Hence, different markers have been proposed in the literature such as vitamin B12 and homocysteine. But no clear recommendation for biological diagnosis is yet established. We therefore propose to determine the most specific biological marker of this chronic intoxication among these two markers.

METHODS

We prospectively collected plasma samples from patients with recreational nitrous oxide abuse in Lille University Hospital from 2020 to 2021. We prospectively measured plasma homocysteine by liquid chromatography coupled to mass spectrometry and plasma vitamin B12 by chemiluminescence.

RESULTS

Our preliminary results on 22 patients with chronic N2O intoxication showed high plasma homocysteine levels in any cases (mean 116 +/- 42.7 µmol/L). Absence of quantitative plasma vitamin B12 deficiency is found on 22.73% but vitamin B12 remains subnormal in these cases.

CONCLUSIONS

In case of N2O chronic intoxication, increase of plasma homocysteine is systematic but not the vitamin B12 deficiency. These results confirm that N2O has an action on the enzymatic targets of vitamin B12 and not on its levels. Indeed, vitamin B12 is the co-factor of methionine synthase which converts homocysteine into methionine. Homocysteine is therefore a marker of choice for the diagnosis and follow-up of this intoxication and decrease of vitamin B12 could only reflect an associated nutritional deficiency.
EVALUATION OF \( \kappa \) FREE LIGHT CHAINS INDEX AS BIOMARKER OF MULTIPLE SCLEROSIS

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BACKGROUND-AIM

The detection of oligoclonal bands (OCB) in the cerebrospinal fluid (CSF) is part of the diagnostic workup for Multiple Sclerosis (MS). However, it has some analytical drawbacks. Recently, kappa free light chains index (kFLCi) has emerged as a reliable indicator of intrathecal immunoglobulin G (IgG) synthesis. The aim of the present study was to assess the diagnostic accuracy of the kFLCi for diagnosing MS.

METHODS

We enrolled ninety patients with suspect of MS, who underwent lumbar puncture as part of their diagnostic work-up for OCB analysis, at the Palermo University Hospital "P Giaccone". Serum and CSF albumin levels were measured by a turbidimetric assay using the Optilite Analyser System (The Binding Site Group Ltd). OCBs were detected by isoelectric focusing, followed by immunofixation on the semi-automated agarose electrophoresis system Hydrasys (Sebia). CSF and serum FLC were analysed by turbidimetric assay (Freelite, The Binding Site Group Ltd) on the Optilite Analyser System (The Binding Site Group Ltd). We calculated the CSF/serum ratio of albumin, \( \kappa \) FLC, and determined the \( \kappa \) FLCi as follows: \( \frac{\text{CSF} \kappa \text{FLC}}{\text{Serum} \kappa \text{FLC}} / \frac{\text{CSF Alb}}{\text{Serum Alb}} \).

RESULTS

We included a total of 58 patients with MS and 32 patients with other neurological diseases (OND). MS patients showed significantly lower median serum kFLC (12.8 vs 17.0 mg/L, p=0.009) and higher CSF kFLC (2.60 vs 0.31 mg/L, p<0.001) levels and kFLCi (34.7 vs 2.8, p<0.001) than OND patients. A total of 90% of MS patients and 19% of OND patients tested positive for OCBs (p<0.001). The area under the curve (AUC) of kFLCi for MS diagnosing was 0.87 (95%CI 0.78-0.96). The best cut-off for kFLCi was 4.7, with a sensitivity, specificity, positive predictive value and negative predictive value of, respectively, 0.95, 0.72, 0.86 and 0.88. Lowering the kFLCi cut-off at 3.0, sensitivity increased up to 98%, but specificity decreased to 56%.

CONCLUSIONS

In our study, kFLCi showed high sensitivity and moderate specificity. Thus, it could be used as a screening test for identifying patients at high probability of having MS, whose diagnosis should be confirmed by OCB detection. Such an approach would avoid unnecessary OCB analysis.
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CEREBROSPINAL FLUID ALPHA-SYNUCLEIN IN SEVERAL NEUROLOGICAL DISEASES

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BACKGROUND-AIM

Alpha-synuclein (α-syn) is a presynaptic neuronal protein, which regulates several neuronal functions. In the last decades, the role of α-syn as a biomarker of neurodegenerative diseases has been explored, especially in synucleinopathies, such as Parkinson’s Disease. However, only a few studies assessed its role as a biomarker in other neurological disorders. The aim of the study was to evaluate cerebrospinal fluid (CSF) α-syn levels in different neurological disorders.

METHODS

This retrospective observational study was performed at the Palermo University Hospital “P Giaccone”. We enrolled 158 patients with different neurological disorders who underwent lumbar puncture for CSF analysis as part of their diagnostic evaluation. Specifically, patients were sub-grouped as controls (n=35), including psychiatric disorders, Alzheimer’s Disease (AD) (n=25), cerebrovascular diseases (n=18), inflammatory central nervous system diseases (n=10), other neurological diseases (n=7), including epilepsy and brain cancer, PD (n=22), and peripheral neuropathy (n=41). We measured CSF α-syn levels by a commercial ELISA kit (Euroimmun, Lübeck, Germany) in all patients. Only in AD patients, we also measured CSF pTau and tTau levels by chemiluminescence enzyme immunoassay (CLEIA) (Lumipulse GpTau 181 and Lumipulse G Total Tau, Fujirebio Inc. Europe, Gent, Belgium) on a fully automated platform (Lumipulse G1200 analyzer, Fu-jirebio Inc. Europe, Gent, Belgium).

RESULTS

Patients with PD showed the lowest and patients with AD the highest levels of CSF α-syn (1372 pg/mL vs 2912 pg/mL, respectively, p<0.001). In AD patients, α-syn levels were found to be associated, at varying extents, with T-tau (rho=0.630, p=0.002), P-tau (rho=0.498, p=0.018), β42 (rho=0.485, p=0.022), and β40 (rho=0.488, p=0.021).

CONCLUSIONS

α-syn could represent a biomarker of neurodegenerative diseases. In clinical practice, it could be used as a specific biomarker of synucleinopathies, which are characterized by decreased α-syn levels, and as an unspecific biomarker of synaptic degeneration in non-synucleinopathy neurodegenerative diseases, which are characterized by increased levels.
PLASMA THIOL/DISULPHIDE HOMEOSTASIS CHANGES IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS

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BACKGROUND-AIM

Multiple sclerosis (MS) is a neuroinflammatory disease and inflammation and oxidative stress play important roles in its pathology. Thiol/disulphide homeostasis (TDH) is a special oxidative stress biomarker that has been found to be affected in several disorders including MS. There is no study demonstrating the effects of attack status of the relapsing-remitting multiple sclerosis (RRMS) patients on TDH levels. Our aim was to determine TDH levels in three different periods of RRMS patients and healthy individuals.

METHODS

The study was carried out in 29 patients with RRMS without a prior attack in the last twelve months (MS Control), 21 RRMS patients having a clinical acute attack within the last week (MS relapse), 12 of 21 MS relapse patients one month after the onset of attack and following 1000 mg methylprednisolone for 7 days (MS Remission) and 30 age- and sex-matched healthy individuals. TDH status was determined using an automated spectrophotometric analysis method. TDH levels in all patient groups and control subjects were compared with each other.

RESULTS

The lowest native thiol, total thiol levels and native thiol/total thiol ratio were found in the MS relapse patients in comparison to the MS control, MS remission groups and healthy controls. In contrast, disulphide levels, disulphide/native thiol and disulphide/total thiol ratios were highest in the MS relapse group compared to the other patient groups and healthy subjects.

CONCLUSIONS

Our findings indicate that increased oxidative stress in RRMS patients is reflected with decreased native and total thiol and increased disulphide levels. Since the formation of disulphide bonds is reversible, the progression of RRMS involving abnormal TDH may be controlled, converting disulphides to thiols. So, we suggest determining the dynamic TDH status as a novel and special biomarker in the diagnosis and prognosis of the RRMS patients.
KAPPA FREE LIGHT CHAIN INDEX AS A SCREENING TEST FOR CSF ISOELECTRIC FOCUSING

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BACKGROUND-AIM
Multiple sclerosis (MS) is a disease of the central nervous system. MS diagnosis is based on McDonalds’ criteria, which include clinical manifestations, characteristic lesions demonstrated by magnetic resonance imaging and, as of 2017, the presence of oligoclonal bands (OCB) in cerebrospinal fluid (CSF). OCB testing is performed by CSF Isoelectric Focusing, a manual, labour intensive and time consuming technique. There are five pattern types of OCB in CSF, with types 2 and 3 considered positive for the presence of OCB. The kappa free light chain index (kFLCI) has been studied as an alternative to OCB testing. The aim of this study was to evaluate the performance of the kFLCI as a screening test for CSF Isoelectric Focusing.

METHODS
The kFLCI is determined on each CSF sample that is to be tested for the presence of OCB through Isoelectric Focusing. A receiver operating characteristic (ROC) curve was drawn, and the area-under-the-curve (AUC) determined. Using the ROC curve, the highest value for which the negative predictive value (NPV) was 100% was determined. Microsoft Excel® and the R® programming language were used for all statistical analysis.

RESULTS
In a total of 415 samples, 268 belonged to female and 147 to male patients, with an average age of 46,03 years. Of these, 124 were found to have negative and 291 positive OCB. kFLCI measurements were between 0,1 and 874, for an average of 37,74. The AUC was 0,962. The highest kFLCI value for which the NPV was 100% was 2,21. There were 138 patients tested for OCB with a kFLCI below this value.

CONCLUSIONS
kFLCI has been shown to possibly be a useful screening tool for CSF Isoelectric Focusing. Additional validation before use in a clinical setting is required but unnecessary testing and its costs could potentially be prevented by this screening test.
PLASMA THIOL/DISULPHIDE HOMEOSTASIS CHANGES IN PATIENTS WITH RESTLESS LEGS SYNDROME

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BACKGROUND-AIM

Restless legs syndrome (RLS) is a common neurological condition. Oxidative stress plays an important role in its pathogenesis. Thiol-disulphide homeostasis (TDH) is a new biomarker of oxidative stress. We studied plasma TDH to determine whether TDH could be used as a new biomarker for RLS and evaluated correlations between TDH and various disease severity rating scales.

METHODS

A total of 25 RLS patients and 25 healthy controls were included into the study. TDH status was determined using an automated spectrophotometric analysis method and correlations were analyzed between the TDH status and various disease rating scales in the RLS patients.

RESULTS

Plasma total (401±27 µmol/L) and native thiol (354±30 µmol/L) levels were significantly lower, but disulphide level (24±6 µmol/L) was significantly (<0.0001) higher in the RLS patients compared to the controls (455±36, 424±37, 15±5 µmol/L, respectively). The disulphide/native thiol and disulphide/total thiol ratios increased, in contrast, native thiol/total thiol ratio decreased significantly in the RLS patients compared to the healthy controls (<0.0001). The disulphide levels correlated positively with age and various rating scores of the RLS patients. International Restless Legs Syndrome Study Group (IRLSSG) rating score and age correlated negatively with the total and native thiol levels.

CONCLUSIONS

Our findings indicate increased oxidative stress in the RLS patients reflected by decreased native and total thiol, and increased disulphide levels and positive correlations between the disulphide levels and various rating scores. We suggest dynamic TDH status to be used as a novel biomarker for the diagnosis and follow-up of the RLS patients.
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NEURON SPECIFIC ENOLASE (NSE) AS PREDICTOR OF DEATH OR VEGETATIVE STATE IN COMATOSE PATIENTS AFTER CARDIORESPIRATORY ARREST

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BACKGROUND-AIM

Neuron specific enolase (NSE) is an enzyme with a molecular weight of 78 kDa and a half-life in body fluids of approximately 24 hours. There is a neuronal tissue-specific \( \gamma \) isoform and an \( \alpha \) isoform present in neuroendocrine tissues, erythrocytes and platelets. When considered alongside established outcome predictors of coma, such as Glasgow coma scale, electroencephalogram, sensory evoked potentials and other clinical predictors, measurement of serum NSE concentrations provides additional information. Elevated levels are indicative of a poor outcome. Normal NSE blood range is <10 ng/mL. Values may vary by method. Increased serum levels of NSE have been observed in patients with traumatic brain injury, ischemic accidents, cerebral hemorrhage or hypoxic brain damage after cardiopulmonary resuscitation.

It has been described that NSE blood levels > 33 ng/mL at 72 h predict poor neurological outcome with a specificity of 100%. A lower value is also possible if the Glasgow Coma Scale score is low.

The purpose of this study was to assess the capability of NSE to predict irreversible brain damage in comatose patients with cardiorespiratory arrest and its usefulness in making decisions about limiting life-sustaining treatment (LLST). Another aim was to check the relationship with death of blood NSE values >33 ng/mL.

METHODS

Retrospective descriptive study, which included patients admitted to Intensive Care Unit (ICU) after cardiorespiratory arrest (CRA) and with blood NSE results (serial or not), between January 2018 and July 2021.

NSE was measured by electrochemical luminescence immunoassay on a Cobas autoanalyser (Roche®). The ICU clinical history and the neurophysiology reports were consulted to assess whether LLST was performed and to see if there was an absence of brain electrical activity (absence of bilateral N20) by evoked potentials and electroencephalogram tests.

RESULTS

30 ICU patients with CRA, either in the emergency department or after admission, were recruited. 12 patients were women (40%) and 18 men (60%). 23 patients were exits (76.66%), 18 of them with at least one NSE result > 33 ng/mL (73.91%)

6 deceased patients had blood NSE values < 33 ng/mL: 3 patients with absence of bilateral N20, 2 presented postive bilateral N20, in 1 patient no record of brain electrical activity was found.

7 non-deceased patients: 5 with presence of evoked potentials (71.42%), in 2 potentials were not performed.

NSE > 33 ng/mL as cutoff value predicted death with a sensitivity of 73.91%, specificity of 100%, positive predictive value of 68% and negative predictive value of 53.84%.

CONCLUSIONS

This study shows that blood NSE levels >33 ng/mL at any time of seriation are indicative of poor neurological outcome and mortality.

All non-deceased patients had blood NSE values <33 ng/mL and presence of evoked potentials.

NSE values were higher in patients with unfavorable neurological outcome, as well as the change in values between admission and 72 hours.

NSE seriation has a high predictive value for unfavorable neurologic outcome.

NSE can be considered a good predictor of poor outcome and mortality and it is useful in making decisions about limiting life-sustaining treatment (mortality specificity 100%).
THE EVALUATION OF ATYPICAL CHEMOKINE RECEPTOR (ACKR) LEVELS IN SERUM OF PATIENTS WITH TUMORS OF CENTRAL NERVES SYSTEM (CNS)

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BACKGROUND-AIM
Atypical chemokine receptor (ACKRs) is a transmembrane cell surface protein receptor expressed in immune cells, normal mesenchymal cells, and several tumor cells. It is suggested that the ACKRs are involved in the regulation of growth, survival, and metastatic processes in tumor cells, affecting multiple tumor growth pathways. However, the exact function and mechanism of the differential expression of ACKRs in many tumors are not well understood and require a deeper understanding of their role in carcinogenesis. The literature data indicate that the changes in ACKRs expression are already present in precancerous lesions and culminate in the adenomas with the highest potential for malignancy, which may indicate the prognostic value of this protein as a potential biomarker. The present study aimed to assess ACKR levels in the serum of patients with CNS tumors and healthy subjects. Moreover, it assessed the diagnostic utility of analyzed protein in CNS neoplasms.

METHODS
The study group consisted of 37 subjects, including 20 patients with CNS tumors and 17 healthy control individuals. The concentration of ACKR was measured in serum of patients using immunoenzyme assay kit (ELISA).

RESULTS
The concentration of ACKR was significantly higher in patients with CNS tumors in comparison with healthy control subjects. Serum ACKR revealed very high sensitivity (100%) and specificity (93%) in differentiation between patients with CNS tumors versus healthy control.

CONCLUSIONS
Presented findings suggest a potential role of ACKR in the pathology of CNS tumors and as a candidate biomarker, but these investigations need to be further clarified using a larger study group.
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COMPARAISON OF LUMIPULSE G1200 AND SIMOA TECHNOLOGY FOR THE QUANTIFICATION OF ALZHEIMER’S BIOMARKERS

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BACKGROUND-AIM

The exploration of Amyloid beta peptides and tau protein in cerebrospinal fluid (CSF) is a key element in the prognostic and diagnostic evaluation, particularly in Alzheimer’s disease.

METHODS

In this study, we compared LUMIPULSE® G1200 from Fujirebio and SR-X with SimoA technology from Quanterix for the determination of Aβ1–42, Aβ1–40, P-tau181, and T-tau. For the former, the Lumipulse G “β-Amyloid 1-42”, “β-Amyloid 1-40”, “Total Tau”, “Ptau 181” assays were used. For the second, the “Neurology 3-Plex A Advantage kit” and the “pTau-181 Advantage V2 kit” were used. In order to realize this comparison, 56 CSF for which these analysis were prescribed, were systematically measured on both devices.

RESULTS

For the Aβ1–40, the Passing-Bablok regression equation gave SIMOA = -756.6 (95% confidence interval (95%CI) is -1,723.6 to -8.97) + 0.97 (0.89 to 1.10) LUMIPULSE. For the Aβ1–42, the Passing-Bablok regression equation gave SIMOA = -59.9 (95%CI: -110.6 to -23.3) + 0.79 (0.73 to 0.86) LUMIPULSE. Therefore, a systematic bias for Aβ1-40 and a systematic and proportional bias for Aβ1-42 were observed. For T-tau and the P-tau181, the Passing-Bablock gave respectively SIMOA = 10.0 (95%CI: -5 to 26.8) + 0.23 (0.18 to 0.28) LUMIPULSE and SIMOA = -1.18 (95%CI: -4.96 to 1.45) + 0.59 LUMIPULSE (0.48 to 0.71). A proportional bias was observed for these two analyses. Interestingly, it was noticed that the ratio of median T-tau/P-tau181 concentrations of Simoa and Lumipulse was different (0.22, 0.13 respectively). Although the individual measurements may differ, the ratio should be similar. This suggests that both methods are measuring different isoforms or that SimoA technology may not measure all the T-tau.

CONCLUSIONS

In conclusion, the methods are not interchangeable and papers on SimoA technology should provide reference values. Caution should be particularly applied to the measurement of T-tau and P-tau181, due to the discrepancy observed between the two devices. In the future, a standardization will likely be needed.
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FREE KAPPA LIGHT CHAINS AND KAPPA INDEX: A NEW TOOL IN THE ANALYSIS OF CEREBROSPINAL FLUID.

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BACKGROUND-AIM

The detection of oligoclonal bands (OCB) of Immunoglobulins G (IgG) in cerebrospinal fluid (CSF) is one of the Mac Donald criteria used for the diagnosis of multiple sclerosis (MS). The measurement of free Kappa light chains (κ), newly available in the CSF, allows the calculation of the Kappa quotient (Qκ) and Kappa index (Iκ). The determination of a cut-off value of the Iκ may increase sensitivity and specificity regarding the diagnosis of MS, compared to the detection of OCB in the CSF.

We present the results of our study on the determination of Iκ cut-offs through their sensitivities and specificities.

METHODS

We measured retrospectively on 397 serum and CSF samples: albumin, IgG and the free Kappa light chains using the Optilite (Binding Site®, Birmingham, UK) and dedicated reagents. The Qκ and Iκ were calculated. The detection of OCB had been previously realized by IEF on Hydrasis (Sébia®Lisses, France). Statistical analyses were performed with XLSTAT software.

RESULTS

The enrolment distributions were 235 female and 162 male, 152 patients presented OCB in CSF (OCB+) and 245 did not present OCB in CSF (OCB-).

In the OCB+ group, the median values were: 39.7 years age; 3.42 mg/L free κ in CSF; 0.26 Qκ and 49.8 Iκ. In the OCB- group, the median values were: 50.6 years age; 0.33 mg/L free κ in CSF; 0.03 Qκ and 3.60 Iκ. Significant differences were found for age, free κ in CSF, Qκ and Iκ index between OCB+ and OCB- groups.

The 100% sensitivity was obtained with a κ index cut-off = 1.44. The 100% specificity is obtained with a κ index cut-off = 41.68.

For us, the best κ index cut-off, allowing discrimination with 84.9% sensitivity and 89.2% specificity between OCB+ and OCB- patients, was established at 8.62. Compared with previously published κ index values from 2.9 to 12.3 in MS, our results are quite similar. The two strengths of our study are the large number of patients and the achievement of all the assays on Optilite.

CONCLUSIONS

The determination of the free κ light chain in CSF and the calculation of the κ quotient and the κ index is fairly new. We showed in this study, that κ index cut-off is a parameter that could substitute for the determination of OCB in the CSF, in many neurological pathologies diagnoses like MS.
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SERUM HOMOCITRULLINE LEVELS WERE POSITIVELY CORRELATED WITH EDSS SCORES IN PATIENTS WITH MULTIPLE SCLEROSIS


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BACKGROUND-AIM

Multiple sclerosis (MS) is a chronic, autoimmune disease. Myelin basic protein represents a candidate autoantigen in MS and its biological structure is modified by post-translational modifications (PTMs). Proteins undergo various PTMs during their in vivo life. These modifications cause important structural and functional changes in proteins. Increasing evidence shows that PTMs are involved in the pathogenesis of various diseases such as cancer, diabetes, neurodegenerative diseases. Carbamylation is one of the PTMs and it is showed that it contributes to molecular aging. Homocitrulline is the most common carbamylation product. So, this study was aimed to investigate serum homocitrulline levels in patients with MS.

METHODS

This study included 35 relapsing-remitting MS (RRMS), 45 secondary-progressive MS (SPMS) patients, and 60 healthy subjects. Briefly; 200 µl of samples were taken into ependorf tubes and 50 µl of d4-L-citrulline, 50 µl of d8-L-lysine and 850 µl of methanol were added. The mixture was vortexed for 30 seconds. The ependorfs were centrifuged at 13000 rpm for 5 minutes and the supernatants were taken into glass tubes then evaporated with nitrogen gas at 65 °C. 200 µl of 3N HCl / n-butanol mixture was added. The tubes were incubated for 30 minutes at 65 °C. Then, the solvents were evaporated with nitrogen gas. The residues were dissolved in 250 µL of acetonitrile: water including 0.1% formic acid mixture (20:80; v:v%) and 30 µL was injected. API 3200 triple quadrupole mass spectrometer was used (Applied Biosystems/MDS Sciex) as detector.

RESULTS

Serum homocitrulline levels [221.9 (69.3-875.5) vs 187.2 (53.3-450.5) µmol/mol lysine, p=0.007] were statistically significantly higher in patients with MS than the control. When MS subgroups were compared, serum homocitrulline levels were statistically significant higher in SPMS group [251.7 (105.4-875.5) vs 203.3 (69.3-678.3) µmol/mol lysine, p=0.031] than RRMS. Moreover, there was a positive correlation between Expanded Disability Status Scale (EDSS) and serum homocitrulline levels (r=0.261, p=0.019).

CONCLUSIONS

It was found that serum homocitrulline levels were increased in MS patients and there was a relationship between disease progression and homocitrulline levels.
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VITAMIN D RECEPTOR MUTATIONS INFLUENCE ON COURSE OF PARKINSON’S DISEASE IN PATIENTS TREATED WITH LEVODOPA

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BACKGROUND-AIM

Parkinson’s disease is second most often occurring neurodegenerative disease after Alzheimer’s disease. Vitamin D is a steroid hormone crucial for calcium homeostasis and bone metabolism. Several animal studies showed potential protective attributes of VD in dopamine cells. The aim of the study was to search for the connections between VDR gene mutations and course of PD development.

METHODS

Sequential analysis of VDR gene (Sanger sequencing) was performed on genomic DNA isolated from peripheral blood leukocytes of 100 patients with diagnosed Parkinson’s Disease treated with Levodopa. Tandem mass spectrometry (LC-MS / MS) of Vitamin D metabolites was also performed.

RESULTS

From analyzed VDR gene fragments splicing region of exon 1 turned out to be the most interesting one. Mutation of “start”(ATG) codon was detected in most cases. In examined patients C/C genotype was present 32 times, C/T 53 times and T/T 23 times. Patients in research group had statistically significant prevalence of SNP. We found that dominant C/C alleles showed statistically earlier average age of diagnosis. In addition, the presence of each subsequent T allele significantly delayed the onset of the disease (p = 0.014). We have also connected C/T genotype of rs2228570 variant with higher chance of levodopa-induced dyskinesias. Detected metabolites concentrations also further underline this connection

CONCLUSIONS

We conclude that VDR gene mutations may influence the course of Parkinson’s disease. Widely advised Vitamin D supplementation may not have expected impact on course of Patients with such changes.
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CREUTZFELDT-JAKOB DISEASE: ROLE OF THE LABORATORY IN THE DIAGNOSIS

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BACKGROUND-AIM

Transmissible spongiform encephalopathies (TSE) are a rare group of fatal neurodegenerative diseases caused by the deposition of misfolded prion protein particles in the brain. Precisely, the conversion of the monomeric cellular prion protein (PrPc) into abnormally folded multimers (prion scrapie (PrPSc)) is the hallmark event TSE on which one of the diagnostic techniques is based: The Real-Time Quaking-Induced Conversion (RT-QuIC). Also, a typical clinical presentation corroborating findings on electroencephalography (EEG), brain magnetic resonance imaging (MRI) and cerebrospinal fluid biomarkers (high concentration of 14-3-3 protein and elevated Total-Tau/Phospho-Tau ratio) provide an antemortem diagnosis.

Among human cases, Creutzfeldt-Jakob disease (CJD) is the most common TSE and 4 categories are recognized: sporadic (80-95%), genetic (10-15%), iatrogenic (<1%) and variant. One example of the latter is Heidenhain variant, characterized by isolated visual symptoms at disease onset with predominantly occipital lobe involvement.

METHODS

80-year-old female attended in the Ophthalmology department due to acute bilateral visual acuity loss of 3 weeks of evolution. No other symptoms. Since the ophthalmological exam did not show any alteration consistent with visual loss, she was referred to Neurology. No family history.

RESULTS

EEG: periodic synchronous triphasic sharp wave complexes (typical CJD).

MRI: hyperintense signal on occipito-parietal fluid attenuated inversion recovery (FLAIR) sequence (typical CJD).

Cerebrospinal fluid biomarkers (Roche Elecsys, Cobas e-801): Total-Tau/Phospho-Tau ratio = 76.8 (ratio >28 compatible with CJD).

RT-QuIC: Positive.

Finally, patient was diagnosed with the Heidenhain variant due to the visual symptoms and results obtained.

Evolution: Treatment for CJD remains symptomatic, as no cure is available to date. After rapidly progressive general worsening, one month later she died.

CONCLUSIONS

Despite the low prevalence of TSE, these diseases are a significant concern because of their etiological aspects, threat to public health, diagnostic difficulties and fatal outcomes. Therefore, the development of non-invasive diagnostic methods for early stages, such as biomarkers and RT-QuIC, is crucial to the implementation of strategies to delay disease progression.
Neurological diseases

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REVISION OF AN OLD STUDY OF KAPPA LIGHT CHAINS DETERMINATION IN CEREBROSPINAL FLUID FOR THE BIOCHEMICAL DIAGNOSIS OF MULTIPLE SCLEROSIS.

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BACKGROUND-AIM

The emergence of the determination of kappa chains in cerebrospinal fluid (CSF) entails a revolution for the differential diagnosis of multiple sclerosis (MS) with regards to other isolated neurological syndromes (both clinical and radiological). Although there is not a fully established consensus about its use yet, it seems to be one more tool helping in the biochemical diagnosis of this neurological disease, along with oligoclonal bands (BOCS) as well as imaging tests and patient symptomatology.

Objectives:

- To analyze the diagnostic value of CSF kappa chains with the established cut-off and their prognostic value at nine years for progression to MS in CSF kappa-positive patients.
- To assess the usefulness of CSF kappa with respect to BOCS in order to avoid BOCS determination when CSF kappa chain is below the cut-off.

METHODS

In 2013, 47 patients with suspected MS in whom BOCS and intrathecal IgG synthesis index study had been requested were targeted for study free kappa light chain was determined in CSF. Cut-off value was established at 0.53 mg/L according to the literature consulted.

In 2022 we reviewed the clinical history of this patients to study the progression to MS of those who were positive for kappa in CSF back in 2009, in contrast with the progression of those who were negative.

As statistical package we used PSPP for the descriptive study, frequency study and chi-square and McNemar test to analyze the cases.

RESULTS

Out of the 47 initial patients, 13 had to be discarded as no clinical history was available at that time due to loss of follow-up.

In 2009, 14/47 of the patients had a diagnosis of MS, 11 of them showing BOCS (p=0.0017) and 12 kappa positive (p=0.0008). 4 out of the 21 patients with positive kappa did not have positive BOCS either. Among them only 1 developed MS.

With the updated data, we found 13 patients (out of 34) with a diagnosis of MS. We have for BOCS an S=76.9% (LR+=4) and E=80.9% (LR-=0.28) and for Kappa S=76.9% (LR+=2.69) and E=71.4% (LR-=0.32).

2 out of the 26 kappa-negative patients in 2009 (7.69%) had CSF BOCS and only 1 (3.85%) had developed MS.

CONCLUSIONS

1. According to data in 2022, CSF kappa correctly classifies 73.5% of MS, with 17.6% false positives and 8.8% false negatives.
2. Sensitivity was initially higher for kappa, but in the long term it is equal. On the other hand BOCS has higher specificity.
3. We found more false positives with kappa in CSF than with BOCS. This does not lead to a loss of patients because all kappa positives would be confirmed with BOCS.
4. Of the kappa negatives in 2009, we would have misdiagnosed 7.7% of patients with positive BOCS, but of these we would only lose 3.85% with development of MS in this time.
5. As MS is slow-paced and the diagnosis is mainly clinical and radiological, the greater ease of technical determination for kappa and its lower price could allow us to screen patients with suspected MS initially with kappa in CSF.
6. The study should be extended to a higher number of patients to confirm these results.