

Ozone Therapy in the Treatment of Some Strictly Neurologic Pathologies

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SUMMARY - *In this work the Authors analyzed the benefits and the results of the Ozonate Autoemotherapy through two procedures: Major Auto-Emotherapy (MAHT) and Platelet Rich Plasma (PRP) in patients affected by some strictly neurologic pathologies. The patients observed, even if they were affected by very different pathologies (Parkinson Disease with the interest of Nucleus of the Base and Spine-Cerebellum Atassy with prevalent interest in Spinal Cord and Cerebellum), had in common an altered Redox Balance because of an evident Stress Oxidative verified by scientific test. In this work the Authors analyzed, therefore the action of Autoemotherapy headed for contrasting the so called 'Free Radicals', which are the products and the true responsible of the Oxidation and that marked the different mechanism of the two components of Autoemotherapy: MAHT and PRP.*

Introduction

It is now generally accepted that the Oxidative Action (that takes place in our body and is important to keep some vital processes when included in physiological parameters), when excessive, can be significantly detrimental to determine pathological processes including some special severe condition as the "Oxidative Stress".

We have to clarify that, nowadays, does not exist a real pharmacologic therapy that can effectively fight oxidative stress, except for the one that use the natural antioxidants ingested with foods like certain vitamins (E, C, etc. .) which, however, have not yet shown any real effects.

Against this deficiency a valuable help comes from autohemotherapy in both the two forms: MAHT (Major Auto-Hemo-Therapy) and PRP (Platelet Rich Plasma).

The more realistic and fascinating Hypothesis about the effectiveness of MAHT against the harmful effects of a high oxidative stress is certainly the one developed by Prof. Velio Bocci.

Simplifying the theory of prof. Bocci we can say that it is rooted in the observation that if free radicals (oxidative stress real responsible) exceed a certain alert level in a slow and gradual way, they are not perceived by the endogenous antioxidant system as "aggressive", so the body does not react to them, as it considers the condition created still within physiological limits, on the contrary to what

suddenly happens for the same abrupt increase in acute or traumatic events of any kind insurgents.

A striking example of the above statement is offered by the latest theory on the genesis of Parkinson's Disease which is based precisely on the fact that the onset of a chronic oxidative stress at the level of the Substantia Nigra of Sommering would lead to the destruction of mitochondria of cells nigral with subsequent cell death and reduced production of dopamine.

According to prof. Bocci the mechanism of MAHT is therefore based on the fact that, at least in chronic diseases and in diseases where there is no genetic damage that affects specifically the endogenous antioxidant system (See below a short explanatory note) a sudden increase of free radicals even if slight and subliminal, occurring with the entry into the circulation in a short span of time of blood ozonated around 30-40 γ /ml would determine a reaction by the endogenous antioxidant system. Consequentially there would be an increase of the production of various enzymes with antioxidant action involved in the process.

This mechanism would explain the long latency between the first treatment with MAHT and its beneficial effects that would not be visible before than 20-30 days.

At this point, however, attentions should also be paid when the etiopathogenesis of the disease is known.

An example is provided by the Amyotrophic Lateral Sclerosis.

In this disease, in fact, the MAHT might be contraindicated if not even considered detrimental in those forms in which it has been hypothesized, like pathogenetic mechanism, a genetic deficiency of the production or the enzyme superoxide dismutase (Cr 21) or, according to peroxidative hypotheses, a reduction of glutathione reductase activity.

Special attention deserves the Amyotrophic Lateral Sclerosis (ALS) where, precisely in at least one form of it, one of the most reliable and recent pathogenetic hypotheses would trace the primary cause of the disease in question in a lack of probable genetic nature, that is the production of glutathione reductase (an enzyme known to play a major role in controlling the redox balance as very important element in the so-called endogenous antioxidant system) and where, therefore, the MAT is ineffective or even contraindicated.

According to the authors of this work the hypothesis that supports the use of the PRP against Oxidative Stress lies because some essential and fundamental components of the blood (erythrocytes and platelets) contain a rich set of endogenous antioxidants, especially some catalase which, activated and suddenly inoculated after a simple injection intramuscularly, exert a direct action even more rapid against oxidative stress with a duration in time significantly lower than the MAHT.

In particular it is necessary here to recall that, as universally known, all the cells of an organism are capable of producing antioxidant enzymes and such action will occur each time a cell produces free radicals in excess.

In such conditions, with a mechanism that could be called “on-demand”, when free radicals exceed a certain threshold limit, there would be a response by the cell affected by the process characterized by a specific and targeted production of antioxidant enzymes sufficient to neutralize the momentary aggressive oxidative action so that the body can defend from the harmful effects of free radicals present in excess in the same cell.

To this rule, of course, make exception corpuscular elements of blood, such as Platelets and Erythrocytes, which haven't any nucleus and therefore are not able to produce antioxidant enzymes independently, continuously or “on demand”.

However the corpuscular elements' progenitor cells provide them with antioxidant enzymes, produced in a larger quantity than what is needed, in order to let them survive even when already detached but still unable to produce independently antioxidant enzymes.

At this point the Platelets and Erythrocytes use

different antioxidant enzymes for different purposes:

- The Erythrocytes with their relatively long lifespan (approximately 120 days) will use the antioxidant enzymes substantially to defend the “EME” from very oxidative action because, as it is rich of iron, it has a strong tendency to oxidize if not able to bind the oxygen and therefore no longer able to carry out its mission.
- The Platelets, however, in their short life (4-5 days in all) basically and normally do not need that rich set of provided antioxidant enzymes, except for a small amount of them that will use them to defend their membrane from the attack of free radicals. Most of them, in fact, will be unusable and unused, unless they do not lose their membrane integrity and put at the disposal of the body their antioxidant enzymes together with all the other components of defense, as occurs, for example, in case of rupture of the endothelial barrier.

Starting from these brief considerations, the authors intended to use this innovative technique of autohemotherapy by MAHT and PRP in a rational and planned way and so, as specialists in Neurology, they found it appropriate to do the same test on some patients who were suffering from diseases of neurological interest that, in their opinion, could provide an altered redox balance.

The patients selected were in fact three men with Parkinson's disease and two subjects (one male and one female) affected by Spine-Cerebellar Atrophy both carriers of a sporadic form.

All patients affected by diseases of the nervous system had an altered redox balance, in the sense that in all was observed, using the specific test Caratelli, a discrete “Stress oxidation”.

At this point it is worth to point out that the present work, due both to the small number of cases treated, and to a lack of cross-checks, currently has no claim to scientific validity, but the authors, taking advantage from a careful observation of few clinical cases and good results obtained, consider it appropriate for the moment to make them objects of a simple scientific communication, hoping that it will arouse some interest and perhaps stimulate the desire to better investigate this fascinating field.

Materials and Methods

All the selected patients, once studied extensively and systematically classified clinically, after demonstrating at test Caratelli to present an altered redox balance, that is a discreet “Oxidative Stress”, were subjected to a single treatment protocol specifically defined as follows:

Treatment	Concentration Frequency	Duration
MAHT	25 γ / ml 2 times per week	From 1 st to 2 nd week
MAHT	35 γ / ml 2 times per week	From 3 rd to 4 th week
MAHT	40 γ / ml 2 times per week	From 5 th to 6 th week
MAHT	40 γ / ml 1 time a week	From 7 th to 10 th week
MAHT	40 γ / ml 1 day 15 days	From 11 th to 14 th week
PRP	5 cc a 70 γ / ml in m. Together with MAHT	Together with MAHT

Shown below only the date of two patients: a man with Parkinson's disease and a woman suffering from Sporadic Spine-Cerebellar Ataxia:

Patient. N° 1: B. N. , born 10/08/46

Family History

Ing neuropathological negate the noble

History Physiological

Pregnancy and Childbirth

The second of five siblings (brothers and sisters in abs) in full-term pregnancy by eutocia normo-condotta.

Psycho-Motor Development

- normal
- Suitable for lever.
- Married with healthy offspring.

Pathological History

Other Pathology

Common rashes's childhood.

Myocardial infarction in March 1999

In the month of June 1999 he had a surgeon of coronary angiography with implantation of two stents.

In 2005 he detected diabetes mellitus, the state-controlled oral hypoglycemic agents.

Specific Disease

Since August 2007, the patient started to present large tremor shook aside all left upper limb, which disappeared during the sleep, slow ideo-motor, micrograph, slightly Figés facies, bradykinesia species at left upper limb.

Neurological Examination

- Patient awake, conscious and well oriented in three dimensions

- Signs of meningeal irritation: none
- Cranial Nerves: free
- Tone: fairly increased waxy type
- Trophism and Motility: the 4 limbs preserved
- ROT: normal and symmetrical elicited in all four limbs
- Abdominal reflexes: present
- Babinski: absent bilaterally
- cerebellar tests: performed correctly
- Romberg: negative
- Gait: normal ambulant with reduced pendular movements of the upper limbs species left

Psychological Examination

Normal

Tests Performed:

- MMSE:
Score: 30/30
- Q-EEG-Brain Mapping:
The 'Spectral Analysis of' Spontaneous Brain Electrical Activity argues for moderate aspects of cortical atrophy in fronto-parietal paramedian left.
- Redox Balance:
Fort: 361 U (see n.: 160 - 310)
Ford: 1.52 mmll / l (see n.: 1.07 - 1.53)

Drug Therapy in Act

- Concor cp: cp ½ in the morning
- Ticlopidine cp: 1 tablet after breakfast and 1 tablet after dinner
- Stalevo 100: 1 hour 7 +1 cp 1 11.30 + 15.30 + 1 cp 20 hours
- patch Neupro 4 mg: 1 patch every 24 hours
- Sirius cp 100 cp: 1 tablet in the morning
- Novoform cp: 1 tablet with meals
- Raliprost cp: 1 tablet per day

Following are presented the rating scales for Parkinson's UPDRS at different times of life of the patient and in particular those carried out before and after treatment with ozone.

Discussion on First Case

From these above mentioned data it's easy to observe the wavering course of the disease, that generally responded well to drug therapy with Levodopa.

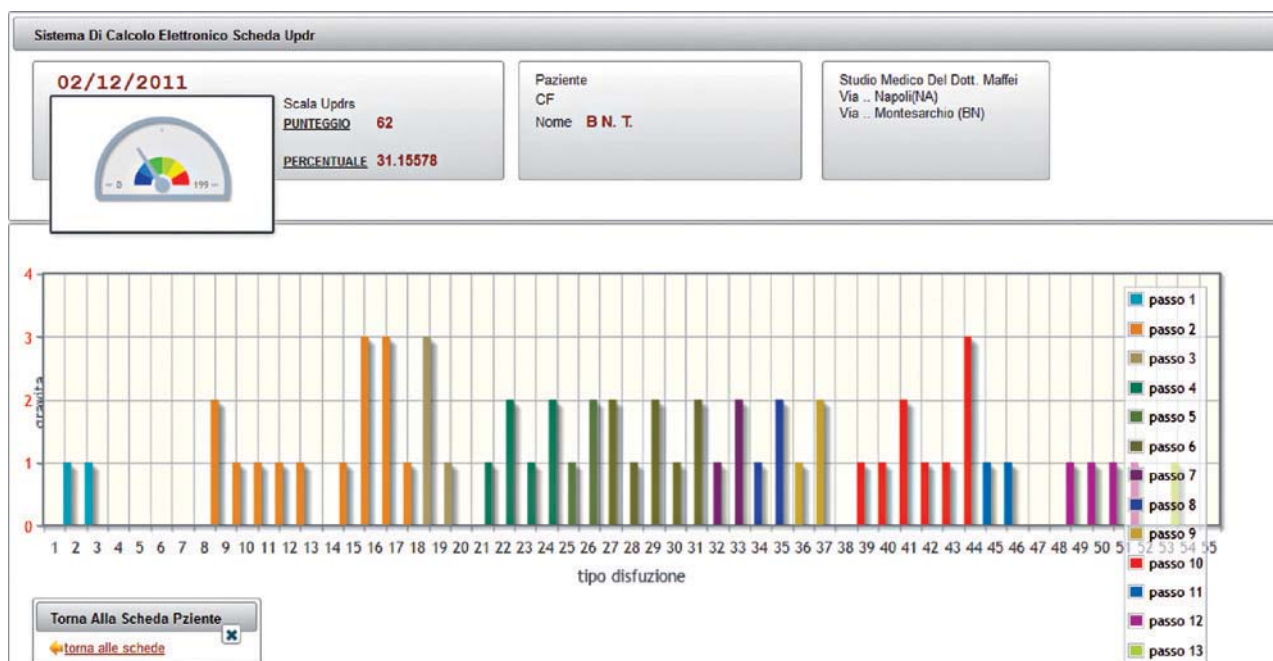


Figure 1 Second Rating UPDRS in pharmacological treatment with a discreet compliance by the patient.

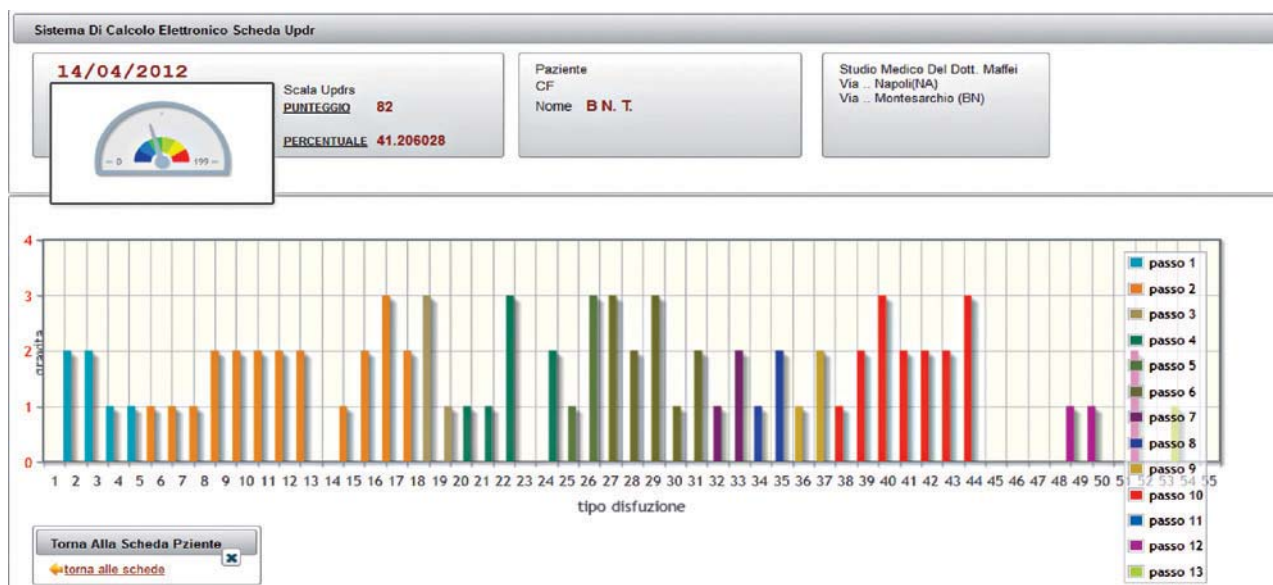


Figure 2 Third Rating UPDRS in which the patient has ceased to incorporate traditional therapy consistently and accurately (poor compliance).

The patient in fact passed suddenly from a UPDRS assessment of 62 points under the good compliance (see Figure 1) to an evaluation UPDRS of 82 points when the compliance was inadequate (see Figure 2) with a net worsening of symptoms up to over 32 % (see Figure 3). After a correct response of Levodopa therapy there was a new improvement in symptoms that descended to a UPDRS assessment of points 41 (see Figure

4) with a gain of 50 % (see Figure 5). At this point no more improvement was possible with an increase in the dosage of antiparkinsonian medicine while undesirable effects were made (example: in. Tardive dyskinesia and / or phenomena ON / OFF). That's why a cycle of autohemotherapy was recommend in both the two forms: MAHT and PRP.

The patient, after signing the informed consent,

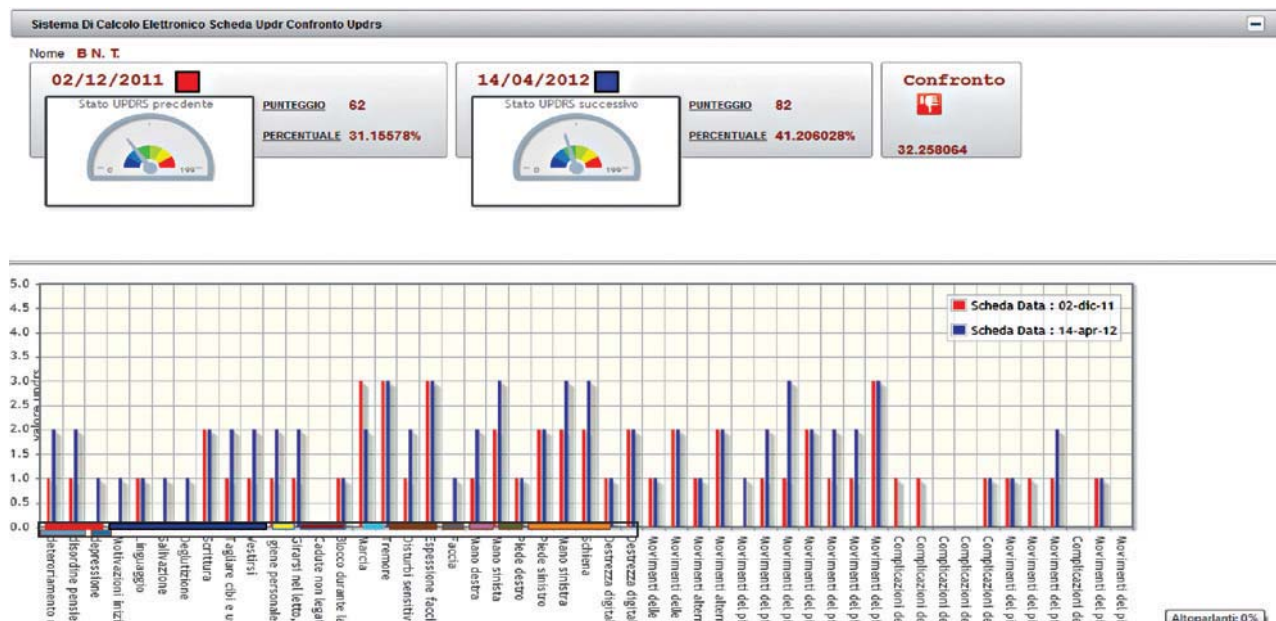


Figure 3 Comparison between second e third rating UPDRS.

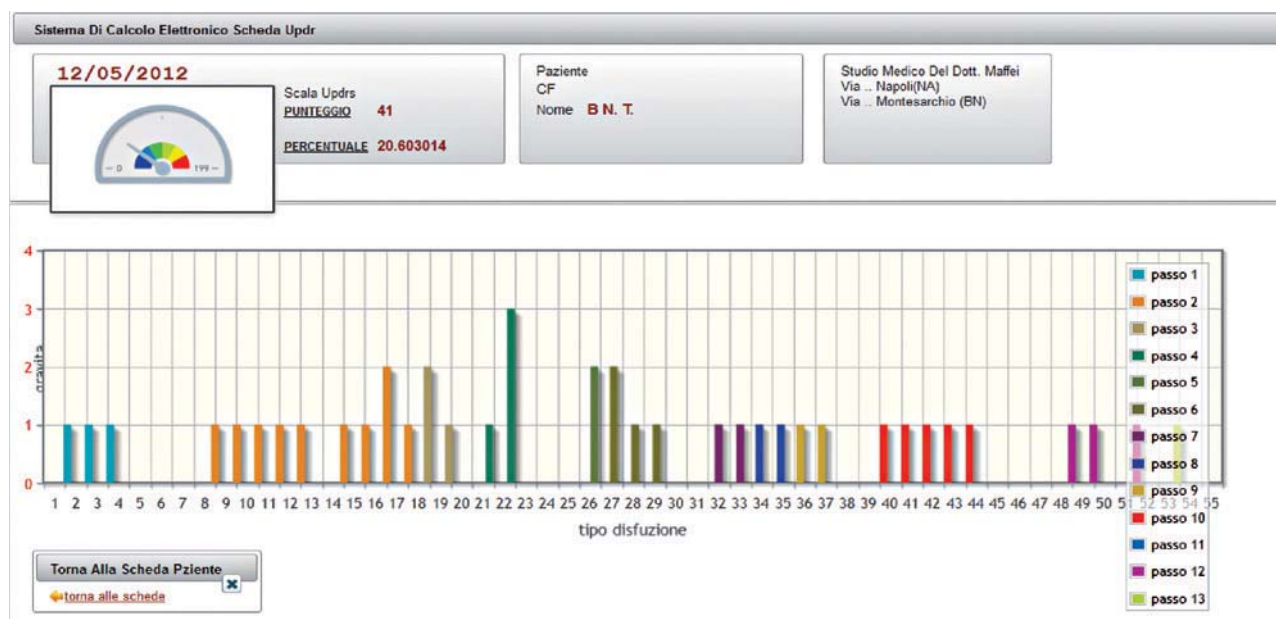


Figure 4 Fourth rating UPDRS in which the patient has taken the typical medication with careful and complete compliance.

decided to adhere to the recommendations and made a full cycle as required by our protocol as shown in the table.

At the end of the complete cycle required by our protocol, the patient underwent a new evaluation UPDRS with a score of 24 (see Figure 6), which led to an improvement of the clinical symptoms by over 41% (see Figure 7) while leaving unchanged both the quantity and the variety of antiparkinsonian drugs.

Patient N° 2: La M. T., born 08/06/66

Family History

Ing neuropathological negate the noble

History Physiological

Pregnancy And Childbirth

Eldest of three siblings (siblings abs) born at term pregnancy by eutocia normocondotta.

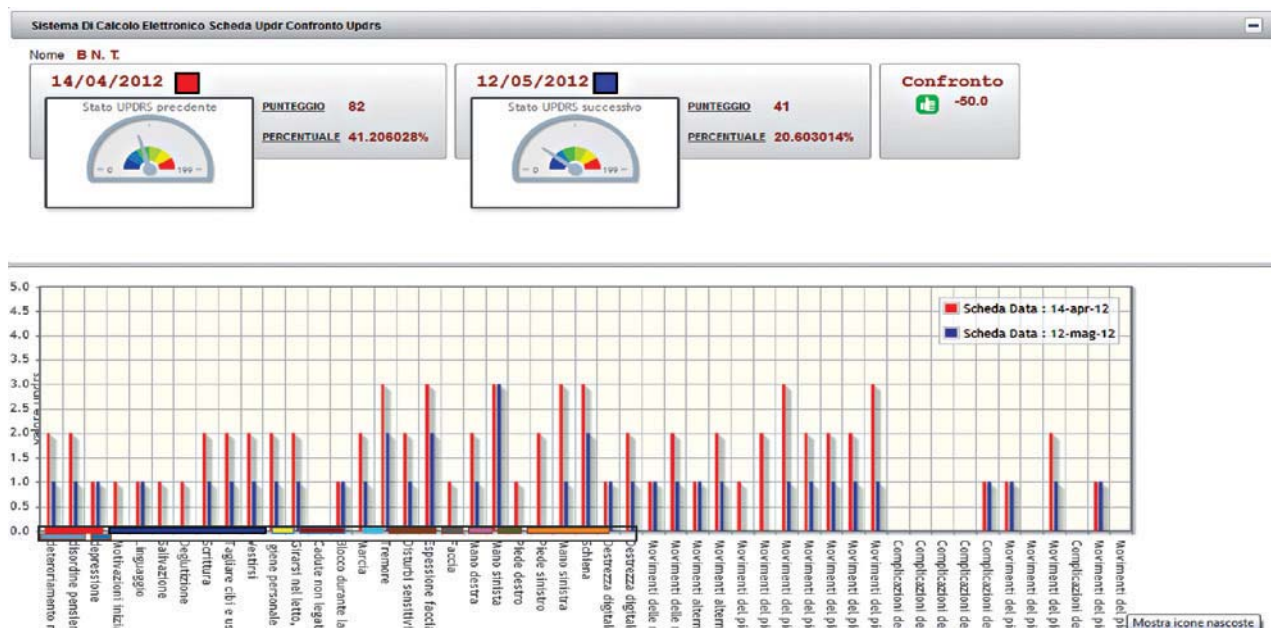


Figure 5 Comparison between third and fourth rating UPDRS.

Psycho-Motor Development

- normal
- Menarche at 13 years, rhythmic.
- Married with healthy offspring.

Pathological History

Other Pathology

Common rashes of children

Tonsillectomy and adenoidectomy in children.

Appendectomy at age 12.

Made of bone graft with insertion of metallic nail right knee for hypertrophy patellofemoral to the age of 32 years.

Cesarean section at 34.

At the age of 30 rose a migraine with aura characterized by violent headache that usually affects the fronto-zygomatic dx accompanied by photophobia, phonophobia, irritability and a sense of alienation.

These crises last for 2-3 days, and are completely insensitive to common analgesics.

At the age of 40 has been caused allergic sensitization so she is in a specifically treatment.

Specific Disease

At the age of 38, the patient started to show neurological disorders characterized by cerebellar series of language deficits with word scanned and explosive.

Subsequently, the symptoms became increasingly worsening with involvement of the soma with the

appearance of ataxic gait, impaired motor coordination, of balance and vision to the side and high.

For these symptoms, the patient was often admitted in neurological environments where she also made several genetic investigations of molecular type. However, they did not reveal any genetic abnormality.

In the last year the calligraphy is modified because of the difficulty in holding the pen and a form of ataxia affecting the writing (vowels often missing in the words).

In 2010 the patient presented symptoms framed in the "restless leg syndrome" using pramipexole. Since summer 2012, the patient has started to show urinary incontinence and memory loss of the recent events.

Neurological Examination

- Patient awake, conscious and well-oriented in three dimensions
- Speech: marked dysarthric nature of cerebellar with scarcely comprehensible speech
- Signs of meningeal irritation: none
- Cranial Nerves: free, however it should be noted marked difficulty in lateralization of the eye and vision towards the high
- Tone, Trophism and Motility: the 4 limbs preserved
- ROT: hyper-elicitable with slight predominance on the left
- Abdominal reflexes: present
- Babinski: dumb right big toe
- Tests cerebellar: frenage marked in the test index / nose species left

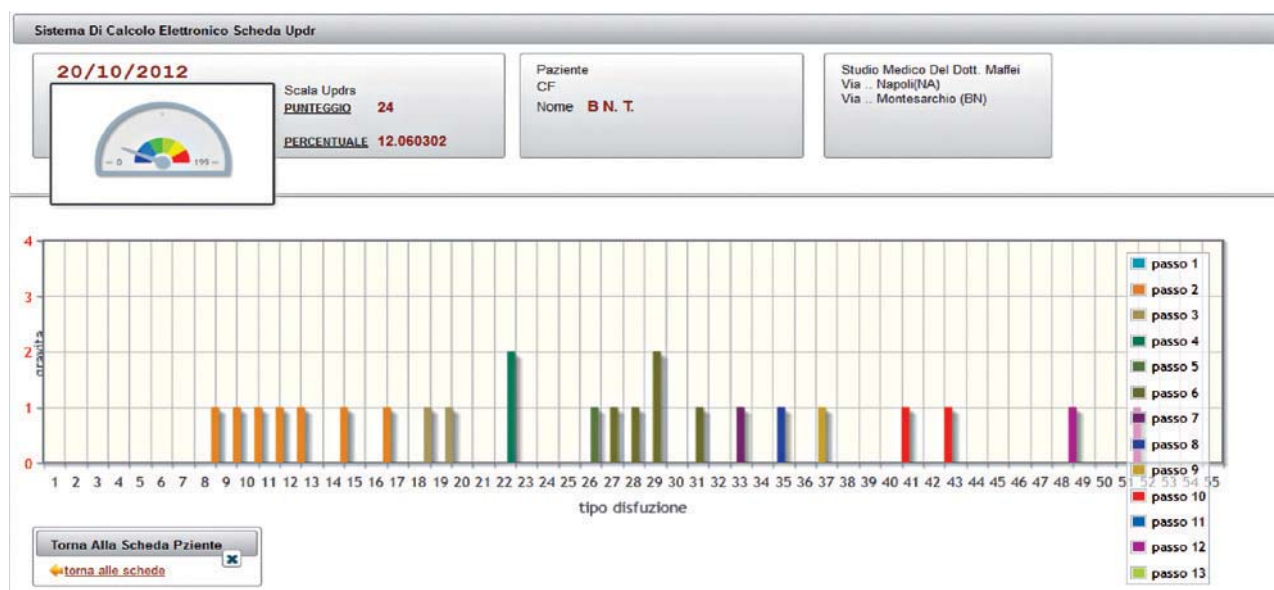


Figure 6 Fifth rating UPDRS in which the patient, in addition to maintaining a good compliance for the traditional therapy for over a month in more transposes a combined therapy of GAET e PAET.

- Romberg: multidirectional movements with open eyes and legs slightly apart; impossible to maintain the Romberg position with eyes closed to fall to 'back
- Gait: ataxic type practically impossible without support

Psychological Examination

Moderate memory impairment

Tests Performed

- MMSE (60):
Score. 28/30
- RM-Cervical Column Encephalon Angio-RM-intracranial (03/03/2005)

Atrophy of the vermis and both cerebellar hemispheres. Some rare little hyperintense foci in T2 FSE sequences and FSTIR, non-specific, out of the white matter biemisferica.

Regular width for the ventricular chambers.

Brain structures in the medial axis.

Regular size and morphology of the ventricular cavity and peri-cerebral CSF spaces.

Brain structures in the medial axis.

The MRA examination of the large arteries of the skull base, conducted with technical 3D TOP, was partly limited by motion artifacts of the patient. As far as possible to express, not observed gross abnormalities such major vascular structures which fall within the limits of resolution of the technique.

Disc protrusion at C2-C3 and C4-C5, with slight impression on the dural sac. Normal amplitude for the spinal canal.

- Bio-Humoral Investigation Practices normal
- Thyroid Function Tests normal
- EEG-Standard:
Brain electrical activity within normal limits
- Redox Balance
Fort: 336 U (see n.: 160 - 310)
FORD: 1.23 mmll / l (see n.: 1.07 - 1.53)

Therapy In Progress

- Mirapexin cp 0.26: 1 tablet / day

Now (Discussion about the Case N ° 2):

Considering that the general physical condition and the global mobility of the patient were filmed before and after treatment with autohemotherapy, here it is possible only to relate the current clinical status of the patient and relate the current neurological exam. The patient, after a cycle of ozonated autohemotherapy, both in the formulation MAHT and PRP as in our protocol already described, showed a marked improvement in clinical symptoms so, at present, the patient has almost taken a normal walk, returned to drive the car, achieved a good motor coordination, decreased until to disappear dysphagia and the word has become understandable. Overall, the patient has regained control of her daily activities and especially those involving her household and family.

Neurological Examination of Play

- Patient awake, conscious and well-oriented in three dimensions

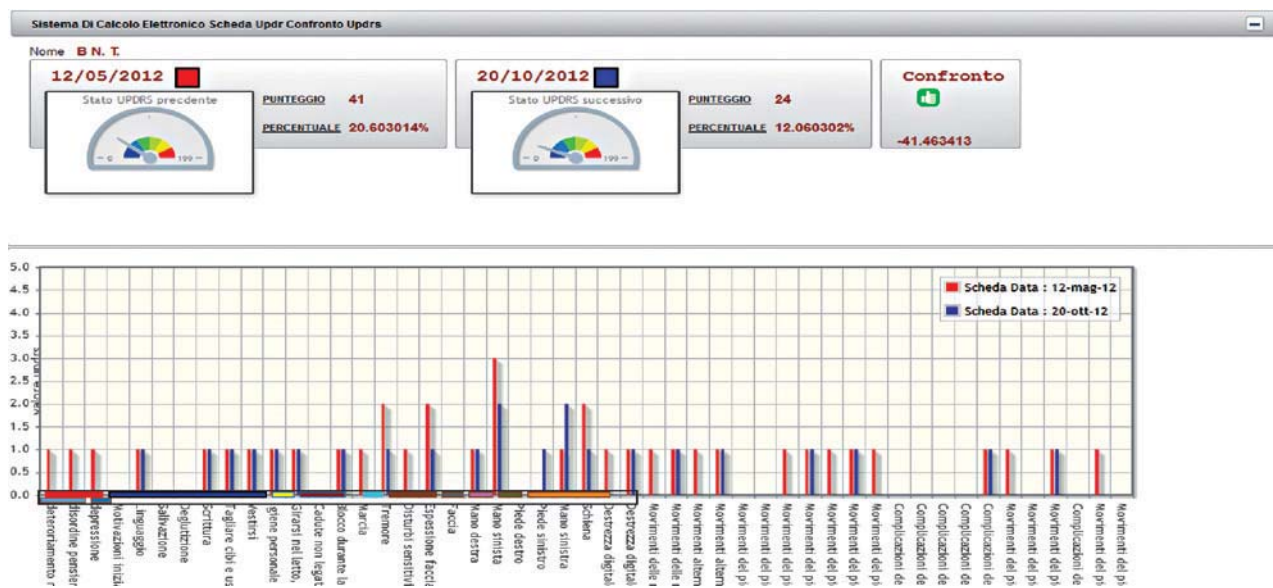


Figure 7 Comparison between fourth and fifth rating UPDRS.

- Favella: dysarthric but easily understandable
- Signs of meningeal irritation: none
- Cranial Nerves: free,
- Tone, Trophism and Motility: the 4 limbs preserved
- ROT: hyper-elicitable with slight predominance on the left
- Abdominal reflexes: present
- Babinski: dumb right big toe
- Cerebellar Tests: mild frenage in the test index / nose
- Romberg: multidirectional movements without falling
- Gait: normal

Conclusions

As can be seen now from the wide world’s scientific output on use of ozone in medicine, Ozone therapy has been used successfully in many diseases and in a number of more and more increasing cases with sometimes amazing data obtained. So we could say that it was found the cure for every ailment.

This statement, however, would be able to inflict a mortal blow to a therapeutic technique that every day it is detecting effective and reliable.

Even the present work, although consisting of a few cases, may be interpreted in a negative way and lead to a further denigration of the methodology in question.

However, in their attempt to explain the reason

for the success of the therapy, the authors believe that they can make a contribution to the question about the effect of medical therapy through the use of Ozone.

The authors consider the therapy with ozonated autohemotherapy, both in its formulation MAHT and PRP, as the only valid one:

The mechanism of autohemotherapy ozonated action resides in the fact that it would be acting in combat oxidative stress by neutralizing the free radicals that, for various reasons and in some specific situations, focus in excess of certain organs or cell groups apparatus, thus generating a “Specification of Pathology ‘Organ’ while what they would do with an Indirect Mechanism (MAHT) and a Direct Mechanism (PRP) as fully and specifically described in the work.

Therefore the action of the autohemotherapy ozonated would not be a universal good mechanism for every disease, but the oxidative stress in the pathogenic mechanism would be common to several diseases that would obviously be capable of effective contrast from the autohemotherapy ozonated.

In consequence of this reasoning, the fact that most diseases of the central nervous system respond well to autohemotherapy ozonated does not surprise because if it is true that the nervous system is the organ considered as the greatest consumer of oxygen, it must be equally true that properly in itself will be a greater chance that some part of it may occur more frequently a failure in the regulation of redox balance.

The natural consequence will be the appearance of a chronic oxidative stress and subsequent establishment in the long run of a neurological dis-

order whose pathophysiological substrate will be the aggression by an excess of free radicals in that particular section of the Central Nervous System.

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