Stručni rad Acta Med Hist Adriat 2016; 14(2);373-386

Professional paper

ELECTROTHERAPY IN THE TREATMENT OF PATIENTS AFFECTED BY RABIES: EXPERIMENTS CONDUCTED AT THE "MAGGIORE" HOSPITAL OF MILAN IN 1865

ELEKTROTERAPIJA U LIJEČENJU PACIJENATA ZARAŽENIH BJESNOĆOM: POKUSI PROVOĐENI U BOLNICI MAGGIORE U MILANU TIJEKOM 1865. GODINE

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Summary

During the nineteenth century, the scientific context of rabies treatment was weak due to the lack of the literature on specific nosology of the rabies disease, and unspecific and ineffective therapy approaches. Electrotherapy already represented an important therapeutic approach for nervous system diseases, although not specifically for rabies.

In the present paper, the authors discuss the use of electrotherapy in the treatment of humans affected by rabies in an experimental study conducted at the Maggiore Hospital of Milan, with the aim of establishing the discovery of a possible specific therapy. By analyzing the printed scientific sources available in the Braidense Library of Milan, the authors describe

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four experiments conducted on patients of different ages. Symptoms and effects both during and after the electrotherapy are also highlighted. The experiments demonstrated that electricity is not an effective therapy in the treatment of rabies, being rather able to cause serious functional and organic alterations in all the patients.

Analyzing the Milanese experiments, the authors reported specific Italian history of a scientific and medical approach to rabies at the end of the 18th century, which led to the promotion of health education, reinforced prevention strategies and opened the way to the vaccination era.

Key words: *Rabies; Electricity; Rabies; Medical History; Medical Research.*

Introduction

Rabies is a dangerous viral disease – transmitted to humans from animals – that has been the subject of important studies in the past as well as the present [1]. The discussion regarding the aetiology and treatment of this disease falls within the field of zoonosis. In order to better understand the history of medical research on zoonotic diseases, we need to focus this analysis on some initial scientific discussions on animal diseases and the causes of their transmissibility to humans [2]. The first debates on animal diseases and their transmission to humans date back to the 18th Century, specifically in neo-Hippocratic medical nosology, where the primary goal was that of identifying and defining the precise cause of disease.

In fact, the need to define a clear correlation between cause and effect, led to the development of a primordial form of epidemiological studies aimed at demonstrating the specificity of diseases linked to certain factors, through categorization based on characteristics of places and areas (i.e. climate, soil, water, vegetation and certain phenomena such as earthquakes, etc.), or regarding patients, in relation to the different lifestyles, social and economic standing, as well as living, labour and cultural conditions. In the middle of 18th Century, medicine took on a new dimension as a social science. At that time, medicine began to see epidemic diseases as a result of inadequate economic, health and social policies, defining a close correlation between poverty, environmental degradation and poor housing, as well as unsanitary places and/or entire territories, and the occurrence and spread of endemic and epidemic diseases [3].

During what we could define at the "French Period", a great deal numerical data was recorded in order to evaluate the frequency and morbidity of certain diseases on a social and territorial level; clinical histories of patients were analyzed in order to define the nosology of each disease, and many studies

were done on preventive care and specific therapeutic approaches. Initially, zoonotic diseases were explained as the result of inhalation and absorption of organic particles exhaled from live animals (through the breath, perspiration and excreta) as well as from the manufacturing of meat and skins. From a physiopathological point of view, rabies was considered poisoning inflicted by insects and reptiles, rather than a real disease. Moreover, this interpretation is confirmed by literature published in the late of 18th Century (that is also called "vulgarization" of medicine), where the instructions to help and try to save people bitten by rabid dogs were found within chapters referring to the bites of poisonous animals [4-8]. Therapy consisted in cauterization and the application of topical caustic treatment on the wound, as well as the bloodletting in order to prevent the spread of the virus throughout the body.

However, while it was undeniable that rabies was transmitted through the bite of infected animals, several different theories were developed regarding how the poison spread, as well as the nature of the disease, prophylaxis systems and therapies to be taken and, above of all, the aetiology and the formation of pathogenic material in the bodies of animals, specifically in dogs [9].

In the first half of 19th Century, when the idea of the transmissibility of rabies as a result of a poison became more solid, rabies began to be considered as a virus that spreads from the point of inoculation through lymph, blood and tissue. Although quite distant from modern microbial conceptions, rabies was described as an active morbific, restless and intoxicating agent that could contaminate the entire body through inflammatory processes [10, 11].

Taking into consideration this historical and scientific context, the authors aim to describe and discuss specific events and theories that led to the use of electricity in the treatment of patients suffering from rabies in the 19th Century, focusing on the Maggiore Hospital in Milan, Italy, about thirty years before L. Pasteur discovered the vaccine. Historical evidence shows that on July, 6th, 1885, Louis Pasteur treated the first human patient, a child named Joseph Meister, with the new vaccine [12,13].

HISTORICAL AND SCIENTIFIC BACKGROUND

Starting in 1863, the idea to use electricity in the treatment of patients suffering from rabies was the subject of important discussions within the Commission of the Maggiore Hospital of Milan. In those years, the scientific information was quite poor due to the fact that literature lacked specific

nosology of this disease. Although several academics showed interest in rabies, therapies described in literature were ineffective. The majority of these therapies, in fact, was considered more as alternative remedies rather than medical treatments in the strict sense of the term.

With regard to rabies prevention, the painter and teacher Angelo Luigi Stella made a proposal, in 1854, to the physic medical and statistical Academy of Milan that included the removal of teeth for all dogs, at least for those that could be considered pets [14]. This thesis was criticized by Luigi Porta (1800-1875), professor of clinical surgery at the University of Pavia, who argued that the bite would have been pathogenic in any case, due to the fact that the mucous membranes of rabid animals come in contact with the tissues and blood of the victim through the tearing of skin. With this in mind, Porta reaffirms that it was necessary to make muzzles mandatory for all dogs, in addition to isolation of animals suspected of having contracted the infection and, if rabid, put them down [15].

As far as medical treatments were concerned, real and effective therapy were entirely lacking. The treatment consisted simply in prevention of the spread of the virus in the body, after patients had been bitten by rabid animals. The only therapy was the cauterization of wounds with hot iron or with caustics and possibly the surgical removal of infected and bordering tissues. As with all critical diseases, the correct way to proceed was the discharge of blood and lymph through bloodletting, diets and drugs that stimulate bowel movements.

Due to the fact that other types of rabies treatment, such as Hydrophobia treatments with Daturine, had negative outcomes, cauterization of wounds was considered the only tested and recognized medical treatment able to block the spread of the virus. The process of cauterization generally involved the removal of tissues near the wound, and the subsequent cauterization of damaged tissue using a hot tool. Other effective treatments did not exist at that time.

The process described above was also confirmed by health policies followed in those years by the Italian Government. In this regard, we should also mention the legal order issued by the Italian Minister for the Interior on May 26th 1854. This legal order provided a sort of detailed guideline to prevent the spread of rabies in animals as well as humans. According to these guidelines, the precautions were focused on three main steps: 1) prevent animal infection; 2) prevent the transmission of rabies to others animals and

humans when rabies developed; 3) protect humans from being bitten by rabid animals, and, if rabies had already developed, to cure humans as soon as possible. In order to prevent the spread of rabies among animals, the Italian Minister stated on one hand the need to reduce the number of domesticated animals and pets and on the other hand that all people owning a domesticated animals or pets had to follow a few recommendations to protect the health of dogs and cats (fresh food, warm environment during the winter, etc).

For people who had been bitten by animals suspected of having rabies, it should be noted how the Minister stated different recommendations with respect to patients, presenting evident rabid symptoms (such as dizziness, severe pain especially close to the wound, difficulty swallowing, spasmodic torticollis, agitation, anguish, etc.) or lack thereof.

Regarding patients with no evident symptoms, cleaning of the wound without delay is required, in addition to the assistance of a doctor. In particular, guidelines recommended washing the wound with salty water and vinegar or water with soap or lye solution or urine. The use of acid-based solutions in water, vitriol, lime and gun-powder were also strongly recommended.

On the other hand, when symptoms were clearly evident, the patient had to be admitted in an isolate place and notification to the security authority had to be sent. The fact that patient was hospitalized in an isolated place was not to prevent him from spreading the virus to others, but rather in order to procure themselves a peaceful place and also provide medical treatment and care without annoyances. Of course, this case also required the support of a doctor [16].

In the beginning of 1864, several papers and magazines in the United States revealed that Dr. Lussing cured a man with canine rabies in eight days with the use of intermittent galvanic electricity [17]. On the basis of data reported by available literature, we know that the patient showed evident symptoms of rabies, such as restlessness, will to bite, and repulsion of water. In this case, the negative pole was placed around the feet with a copper wire, while the positive pole, in line with throat and spine, so that electricity passed through a sponge soaked in a vinegar and sea salt solution. Initially Lussing noted that symptoms came back after thirty minutes. He later repeated the electrical shock treatment for thirty minutes at regular intervals and noted that symptoms decreased; after twelve hours of treatment the patient was able to drink and sleep. When symptoms appeared again, Lussing

performed another application of electricity and after eight days the patient was definitively cured.

Considered the lack of any other effective alternative treatments, with the exception of cauterization, and on the basis of Lussing's success, the Commission of the Maggiore Hospital decided to put this into practice, approving the project for the treatment of hydrophobic patients through the use of electricity.

The practice to use electricity in diseases regarding nervous system started to be tested after the failure of traditional treatments. From the Eighteenth Century on, literature provides an important basis for academics in order to explain and understand the nature and functions of the CNS and fluid, considered as a sort of *phenomenization* of universal and vital fluid that could permeate matter, albeit not instilling refreshing properties. In this regard, we should note the study on electricity carried out by B Franklin (1706-1790), which argues the existence of a natural electricity in the atmosphere that can be transmitted to the animal body through the use of special metal tools, causing muscular movements.

Morever, we should also mention the work of Luigi Galvani (1737-1798), who contributed to a doctrinal basis on electrophysiology and, therefore, therapeutic applications of electricity. In his work, based on frogs experiments, Galvani demonstrates the existence of electricity in animals and compares the action of the nerves on the muscles and muscle motion with the famous Leyden Jar.

The Leyden Jar is one of the first electrostatic devices that was able to store electricity, consisting of a bottle filled with water and a metal wire conductor.

A fundamental aspect for the theoretical construction of the electrotherapy – and shock therapy / is the work of Alessandro Volta (1745-1827), who argues that muscle contractions are likely to be caused by residues left in tissues by metals and, consequently, shows that the contact between metals of different nature produces electricity. When explaining the differences between positive and negative energy, also in terms of alkalis and acids, Volta provides the basis for a chemical and physiological interpretation of electricity and in doing so, for electrotherapy in general.

Starting in the first decades of the Nineteenth Century, the electricity began to be used for the treatment of diseases that were defined as altered/

cut nervous and muscular functions, such as paralysis, deafness, or severe form of asthenia. These new electro dynamic devices created by physicists were used for this type treatment.

When the news of the success achieved by Lussing in the treatment of rabies spread among the scientific community, electrotherapy had already been tested in the treatment of tetanus. Due to the lack of a specific medical nosology on tetanus, this practice was used on the basis of the fact that the symptoms of this pathology appeared similar to those of the other CNS diseases. It is therefore important, regarding this issue, to mention the study conducted by the physicist Carlo Matteucci (1811-1868) on electricity in living organisms. According to this author, galvanic current should be considered as a powerful means for revitalization of nerves and tetanic muscles.

Initially, the protocol followed by the Milanese Commission of Maggiore Hospital employed a magnet electric device with perpetual electricity, but later, due to the news of the success reached by doctor Lussing, the Commission decided, using Plinio Schivardi's request (1833-1908) (author of a handbook on electrotherapy and important author among the major supporters of therapeutic application of electricity) to adopt the same device that Dr. Lussing had used: a device with intermittent electricity (Ducheen's Device), with the goal of allowing for faradization (faradic electrical current) and prevent the cauterization of tissues.

Experiments conducted at The Maggiore Hospital of Milan

Between 1865 and 1866, four experiments with electricity were conducted on rabid patients in the Maggiore Hospital of Milan. Patients analyzed varied from 2 to 40 years old.

Before reporting the Milanese experiments, we should state that at that time other experiments were also conducted with electricity, resulting in unsuccessful outcomes. In 1864, for example, two young patients (respectively 15 and 20 years old) who had undergone faradization treatments in the Austrian Hospital of Lemberg both died after an initial regression of rabid symptoms and further organic worsening. While the first patient underwent electric applications at regular intervals of 10 minutes, the second patient received applications every half hour. The protocol required the use of a Grove battery consisting of two elements, with the positive pole placed on the spine and the negative one on the lower limbs.

Similar to the case just mentioned above, we should also mention the case of a 70 year old woman suffering from canine rabies who was admitted to the Santa Maria Nuova Hospital of Florence on June 15th, 1864, again without success. The woman was bitten a month and a half before being admitted to the hospital [18].

The first experiment at Maggior was performed on the 18th of February, 1865, on a 40 year old man, named Giuseppe Pavesi. The man – who was affected by clear symptoms of rabies – went to the Hospital after a total of 5 months after being bitten. He did not do any precautionary therapy – not even cauterization – limiting his home treatment to the washing of these wounds. The first symptoms appeared 4 days before his admission to the hospital.

Although the protocol providing for the use of Duchanne's device was available, the Commission decided to employ another magnet electric device with perpetual induced electricity due to a technical problem that had occurred during the experiment. The positive electrode was placed on the nape, while the negative electrode was placed on the larynx and along the Vagus Nerve (also called pneumogastric nerve or tenth cranial nerve) in order to induce a descending and centrifugal current. The electrotherapy went on for around 11 hours with 18 applications, during which the intensity of electricity was regulated gradually, respecting the patient's conditions. In order to compensate for the loss of fluids and nutrients, the protocol provided for enemas of beef broth. During the first applications, the symptoms of rabies seemed to decrease, but later they returned stronger with delirium, anxiety, agitation, increased salivation, flushing, pharyngeal spasm, as reported by the Universal Annals of Medicine [19]. After the suspension of treatment, the patient died within in few hours. As a result, the first experiment did not produce the results they had hoped for, seeing that the patient died after the interruption of treatment. However, the analysis of serums and blood showed the presence of monads, vibrios and bacteria that were described by Polli as thymes or with thyme-shaped.

The second experiment was performed on April 16th, 1865, on a 17 year-old man named Aurelio Casnedi, who had been bitten by his dog two weeks before being admitted to the hospital. Just as inthe experiment described above, no prior therapy had been carried out. The experiment was conducted with the support of a device consisting of the Daniell's battery.

The positive pole was placed on the nape, while the negative electrode was applied between the last dorsal vertebras and first lumbar vertebrae [20]. The treatment continued for about 19 hours with 5 applications. Once again, initially the symptoms of the disease appeared to decrease, however they later appeared again, stronger than before, until the death of patient. Polli compared the patient's necroscopic examination and haematological analysis with those belonging to a woman who had died of apoplexy and a woman suffering from tuberculosis, however he did not find any particular similarity.

After this second experiment, the mechanism of virus' spread in the body still remained unclear, and the same can be said for the virus' specific actions and, above of all, an anatomophatological framework that could be useful in creating a specific nosological categorization of rabies.

The third experiment carried out at the Maggiore hospital was performed on February 28th, 1866, on a 9 year-old child named Angela Barozzi, who had been attacked by a dog on February 15th.

Although the child displayed clear clinical symptoms of rabies, no precautionary therapy or cauterization had been carried out prior.

The experiment was conducted using a device with perpetual galvanic electricity. In order to better balance intensity, the staff – made up of Mr. Plinio Schivardi, Felice dell'Acqua e L. Barzanò – decided to use the Daniell's battery with 26 pairs (torques) split in 2 sections. The positive pole was placed on the brow, while the negative one on the feet, based on the belief that the electricity would pass through the entire body.

The treatment was carried out for about 80 hours with only 2 interruptions, during which the symptoms appeared to completely disappear, however but later on the patient developed apathy and asthenia, falling into a coma (along with an intense stench of ammonia) until her death[21].

Although the patient died, the third experiment conducted in the Maggiore Hospital was considered a great success, leading physicians to verify the effectiveness of electrotherapy and, consequently, to hypothesize the pathophysiology of rabies. As argued by Schivardi, Angela Barozzi's case represents the first documented success of the electrotherapy. According to this author, in fact, tests performed have shown that the death of the child, which occurred two days after the suspension of electrical treatment, should be ascribed to a form of uremia or hyperammonemia caused by an excess of

urea that remains and accumulates in the blood, transforming into ammonium carbonate due the poison already found in the body.

Mr. Polli disapproved Schivardi's thesis, arguing that rabies could not be caused by poison, due to the fact that several cases showed that the incubation period could go on few months. Therefore, the death of the patient should be attributed not to poison, but rather to a sort of enzyme that Polli defined as a microorganism. Specifically, this rabies enzyme was described as a "ferment" that, when entering into contact with certain tissues and organic fluids, is able to find favourable conditions for development. For this reason, rabies did not alter the patient's condition immediately, from a chemical or structural point of view, but rather gradually with its own vital functions and products of development.

Furthermore, again according to Polli, the ferment later decomposes and transforms the element in which it takes root by appropriating the vital principles that are needed to grow and multiply, while leaving heterogeneous materials that can become toxic and harmful to the host organism.

The variabilities found in the timing on manifestation of anger therefore depends on the time required for this microorganism to penetrate tissues and grow, as determined by the state of both the virus and host conditions, and its virulence will be directly proportional to the amount of products of decomposition emitted. Polli describes rabies as a disease that develops in the blood, where the inoculated "rabid ferment" triggers a fermentation processes that produces toxic materials, altering the chemical composition of the host.

Necroscopies carried out on the three patients did not show a clearly defined pathological framework, except for widespread hyperaemia in cerebral vessels, whose the origin was unknown. On the other hand, analysis of sera and blood taken from the three patients showed the presence of monads, vibrios and bacteria.

Polli suggested that these organisms might be ferments that are similar to urea, described as a spherical torula that continues to grow only when it is in a context where it receives nutritional substances. Multiplying and spreading through bodily tissues, the ferment comes into contact with blood, turning into a type of ammonium salt or, more precisely, into ammonium carbonate. For this reason, Polli believed that ammonemia was the last and defining symptom of rabies after treatment with induced electricity [22].

Although the previous three experiments had not offered successful outcomes, on June 6th, 1866, the Hospital Commission approved the continuation of these experiments, while making some changes to the protocol, and also treating the patients with reverse current electricity.

Unlike Barozzi's case, this new protocol required the interruption of electrotherapy at regular intervals in order to allow the body to recover from potential electricity disorders. The protocol included the use of a medical device similar to that used for Ms. Barozzi, with the Daniell's Device working with twelve batteries to be regulated based on the patient's age, physical build, and restraint.

Certainly, the observation of clinical and symptomatic signs recorded during the electrotherapy performed on Ms. Barozzi was an important chance for the Commission rethink the sustainability of the electrotherapy. For this reason, several members of the Commission, along with physicians employed by the Maggiore hospital (including Mr. Polli), suggested testing electrotherapy on rabid dogs before starting again with human testing. With these tests, Polli wanted to verify the real side effects arising from electrotherapy: if the comatose state and hyperammonemia of Ms. Barozzi could be attributed to the treatment, and if the voltage along with lengthened intervals could have been too high on the basis of the patient's age and build. Tests were performed on selected rabid dogs and showed that the death of Ms. Barozzi was not related to this therapy. After these further tests and controls, the Commission decided to reinstate experiments on humans.

The fourth experiment was carried out on December 10th, on a 2 and half year-old child named Emilia Carniti, who had been bitten by a rabid dog 25 days before contacting the hospital. The procedure was directed by the hospital's leading doctors L. Barzanò and F. dell'Acqua.

Much like Barozzi's case, the positive electrode was placed on the forehead while the negative electrode was placed on the feet, so that the electricity could pass continuatively through the body. However, while Mrs. Barozzi received only two interruptions at irregular intervals, the treatment was suspended, at regular intervals, in order to enable body to recover from potential disorders caused by the treatment. Voltage was kept low, around on 10° - 12°, and applications was spread out over two or three hour intervals.

After the first day of treatment, the patient's conditions of worsened, and physicians decided to increase the voltage up to 16°. Nevertheless, the following day vital conditions did not improve and the patient died [23].

Conclusion

The results of the four experiments conducted at the Maggiore Hospital led the Commission to state that electricity was not an effective therapy for the treatment of rabies, due to the fact that it caused serious functional and organic alterations, resulting in the worsening of patient's general conditions.

More specifically, the Commission understood and accepted that the only available and safe therapy for rabies was the cauterization of wounds with a chlorine-based solution in order to prevent the spread of the virus in the blood.

Considering the scientific and historical context at that time, the Commission also confirmed the urgent need for a more prevention-oriented policies to prevent the risk of rabies through the control of animals, especially dogs, by isolating and killing them, and on the other hand the promotion of health education for the general population. Due to the failure of the previous experiments with electricity and the lack of a real and effective therapy, the idea to cure rabid patients with electricity was therefore abandoned, while the aetiology and pathological action of rabies remained unknown. The Commission, in fact, realized that the only therapeutic system that could stop the spread of the poison through the blood in the body was simply the old method of cauterization of wounds. As we know well, the rabies vaccine would be used successfully two decades later, in 1885 by L. Pasteur, after the discovery of the pathogenic microorganisms and how they carried out infection. Rabies then moved from the traditional and historical concept of a poison to that of the modern understanding of rabies as a contagious disease transmitted to humans from animals.

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Sažetak

Tijekom 19. stoljeća znanstvena osnova liječenja bjesnoće bila je slaba zbog nedostatka literature o specifičnom uzročniku bjesnoće te nespecifične i neučinkovite terapije. Elektroterapija je već predstavljala važan terapijski pristup kod bolesti živčanog sustava, iako ne specifično za bjesnoću.

U ovom radu autori raspravljaju o uporabi elektroterapije u liječenju ljudi oboljelih od bjesnoće u eksperimentalnoj studiji provedenoj u bolnici Maggiore u Milanu, s ciljem ustanovljenja otkrića moguće specifične terapije. Kroz analizu tiskanih znanstvenih izvora, dostupnih u knjižnici Braidense u Milanu, autori opisuju četiri pokusa provedena na pacijentima različite dobi. Istaknuti su simptomi i učinci tijekom i nakon elektroterapije. Prikazani pokusi pokazali su da struja nije učinkovita terapija u liječenju bjesnoće, već može uzrokovati ozbiljne funkcionalne i organske promjene kod pacijenata.

Analizirajući milanske pokuse, autori su prikazali specifično talijansku povijest znanstvenoga i medicinskoga pristupa bjesnoći na kraju 18. stoljeća, što je dovelo do promocije zdravstvenoga odgoja, ojačalo strategiju prevencije i otvorilo put prema eri cijepljenja.

Ključne riječi: *bjesnoća; struja; povijest medicine; medicinsko istraživanje.*