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Article

NegEnt Spray: an Original CE Medical Device, based on Liposomal Cannabidiol and Chamomile Hydrolate, for the Treatment of Muscles and Joints

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Abstract: Musculoskeletal disorders are a common occurrence in Europe, affecting millions of people and costing billions of euros in social security services. Traditional treatments using drugs like non-steroidal anti-inflammatory drugs (NSAIDs) can cause gastric damage, making prolonged use difficult. To address this issue, the Author has developed NegEnt Spray - Muscles and Joints, a topical medical device that uses liposomal cannabidiol and chamomile hydrolate to reduce inflammation and pain in musculoskeletal disorders. The liposomal technology used in NegEnt Spray allows for better bioavailability and a more targeted action, while chamomile hydrolate provides a natural anti-inflammatory and soothing effect. The spray is non-greasy, absorbs quickly, and can be used under any circumstances. Its pocket-sized design makes it easy to carry and use throughout the day. With NegEnt Spray, patients can alleviate discomfort and pain associated with musculoskeletal disorders without worrying about the side effects of traditional treatments.

Keywords: musculoskeletal disorders; cannabidiol; liposomal technology; chamomile hydrolate; topical treatment

Introduction

The incidence of musculoskeletal disorders in Europe is, unfortunately, very high, with millions of people affected and an estimated cost of billions of Euros to social security services, not to mention the personal and family distress of patients (European Agency for Safety and Health at Work - EU-OSHA, 2020).

Such disorders include a wide range of health problems, from mild discomfort and pain to more serious medical conditions that may require absence from work and specialised medical care. In particular, pathologies such as sprains, contusions, fasciitis, arthritis and arthrosis are now very common, also in relation to the increase in the average age of the population, and can be aggravated by physical, biomechanical, organisational, psychosocial and individual risk factors (Società Italiana di Reumatologia - SIR, 2021).

Regarding the incidence of musculoskeletal disorders in Europe, the following data are recorded (EU-OSHA, 2019).

For adulthood:

In Europe, 25% of workers suffer from back pain and 23% complain of muscle pain. 30% of European workers complain of back pain; 17% of muscle pain in their arms and legs; 45% report working in painful or tiring positions; 33% have to carry heavy loads at work.

For old age:

The prevalence of these conditions increases with advancing age and exhibits marked gender differences. Among the over 75s, 68.2% of women and 48.7% of men claim to suffer from arthrosis and/or arthritis.

These data highlight the importance of preventive and therapeutic interventions to manage the impact of musculoskeletal disorders in different age groups.

Topical treatments, for musculoskeletal disorders, implemented with the use of class I medical devices, constitute an important therapeutic resource, since the most commonly used drugs, at the

moment, are the so-called NSAIDs, i.e. non-steroidal anti-inflammatory drugs, which, if taken orally, can be unwieldy, due to the high potential for gastric disturbances and lesions, especially in prolonged treatments. For this reason, many medical devices proposed as NSAID-based creams and ointments have been developed and are currently on the market. However, although applied locally, the NSAIDs contained in these medical devices can be absorbed and be poorly tolerated (Grattagliano, Ubaldi, 2012).

For this reason, remedies have been developed to be applied to the skin in order to treat muscular and osteoskeletal problems. (Lin, Wiles, Waller, Goucke, Nagree, Gibberd, O'Sullivan, 2020).

Cannabidiol, a substance derived from the inflorescences of the industrial variety cannabis sativa light, appears to be an effective and well-tolerated remedy that can reduce inflammation and pain in musculoskeletal disorders. (Frane, Stapleton, Iturriaga, Ganz, Rasquinha, Duarte, 2022).

At Herbal Neurocare, we set out to develop a medical device for topical use based on cannabidiol. After years of technological and clinical research, we developed NegEnt Spray - Muscles and Joints (Scrimali 2020).

NegEnt Spray - Muscles and Joints is composed of liposomal cannabidiol diluted in chamomile hydrolate.

Liposomal cannabidiol is a component extracted from the inflorescences of the industrial variety cannabis sativa, known for its anti-inflammatory, analgesic and muscle-relaxing properties. Thanks to liposomal technology, cannabidiol has been encapsulated within microscopic lipid vesicles that promote better bioavailability and a more targeted action at the site of application.

Chamomile hydrolate is a natural extract obtained by distilling chamomile flowers, renowned for its anti-inflammatory, soothing and calming properties.

NegEnt Spray - Muscles and Joints comes in a professional dispenser, made as an unbreakable 50 ml plastic bottle, designed and manufactured for pharmaceutical preparations, equipped with a precise and ergonomic pressure spray pump that allows fine atomisation of the preparation on the skin.

The absence of oily and creamy substances and the formulation in chamomile hydrolate, made possible by the liposomal preparation of cannabidiol, make the spray fresh and soothing on the skin, while facilitating the absorption of cannabidiol into the muscle tissue, muscle strips and joint and bone tissue.

The skin is immediately cool, dry and pleasantly scented with chamomile. Since NegEnt Spray - Muscles and Joints is non-greasy and absorbs almost immediately, it can be used under any circumstances. It does not stain clothes and leaves the skin fresh and dry.

The small size of the bottle and its safety closure make it pocket-sized for easy portability and repeated use, even multiple times during the day and in any scenario, including work or social.

Subjects, Materials and Method

The clinical research on NegEnt Spray - Muscles and Joints was conducted at the ALETEIA Clinical Centre, with the collaboration of patients who provided informed consent to the trial. The study design was observational, applying the experimental protocol with NegEnt Spray- Muscles and Joints when patients presented spontaneously at the Centre's outpatient facilities.

The clinical research work was carried out following the single case study series design, with systematic single-case studies of patients suffering from different diseases.

Importantly, NegEnt Spray - Muscles and Joints was offered free of charge to patients for the duration of the treatment, thus ensuring accessibility of the product and equity in study participation.

To assess the efficacy and tolerability of the product, we used two validated instruments that allowed us to collect quantitative and qualitative data on patients' experience with the treatment. The two instruments used were:

Pain Self-Assessment Questionnaire

For the research carried out by Herbal Neurocare. with NegEnt Spray - Muscles and Joints, the McGill Pain Questionnaire in the Italian version edited by Maiani and Sanavio (1984) was used.

The McGill Pain Questionnaire is a widely used psychometric instrument with a good reputation in the field of algology, developed to assess the multidimensional experience of pain. The Italian version, translated and adapted by Maiani and Sanavio in 1984, preserves the original structure of the questionnaire, offering a detailed measurement of the different qualities of pain through carefully selected verbal descriptors. This test is particularly useful for clinicians and researchers in identifying the nature and intensity of pain, thus enabling a more targeted and personalised therapeutic approach. Its widespread application in various clinical and research contexts makes it an effective and efficient tool in the field of patient self-assessment of pain in clinical research.

Questionnaire for Self-Assessment of Side Effects of Treatments

As part of the research on possible side effects of products, at Herbal Neurocare we use the Italian version of the Patient-Reported Outcomes - Common Terminology Criteria for Adverse Events (PRO-CTCAE), in the Italian version carried out at the National Cancer Institute National Cancer Institute. (PRO-CTCAE, 2024).

Fibromyalgia

A syndrome characterised by widespread muscle pain and fatigue.

The patient, a 47-year-old woman, had been diagnosed with fibromyalgia after a long period of non-specific symptoms, including widespread muscle pain and fatigue, and had embarked on a multidisciplinary treatment pathway that included lifestyle modifications, physical therapies, psychological support and targeted pharmacological treatment. To the treatment based on paroxetine and systemic NSAIDs was added NegEnt Spray - Muscles and Joints, applied three times a day on the painful parts. Thanks to the introduction of NegEnt Spray Muscles and Joints into the treatment plan, the patient experienced a significant improvement in pain management and quality of life, being able to resume her daily activities with greater ease and less discomfort, both physical and psychological.

Traumatic Contusion of a Finger of the Hand

Attributable to an injury caused by a direct impact of a sliding door leaf. The patient, a 36-year-old woman, had suffered a traumatic contusion to a finger of her hand when she was struck by a sliding door leaf. Despite initial pain and swelling, an X-ray excluded bone fractures. Initial treatment included immobilisation with a brace and the

application of ice to reduce the swelling. After a few days, NegEnt Spray - Muscles and Joints, applied three times daily to the bruised area, was introduced to manage pain and promote recovery. Regular use of NegEnt Spray, together with targeted physical therapy, allowed the patient to regain full finger function within a few weeks, without long-term complications.

This case demonstrates the effectiveness of a combined therapeutic approach, including the use of NegEnt Spray - Muscles and Joints, for the treatment of traumatic finger contusions.

Traumatic toe contusion with lacerated injuries

Female, 28 years old, patient presents following direct trauma to her toe caused by impact with a blunt, sharp object. She reports acute pain and difficulty walking. Examination reveals small lacerated and bruised wounds on the affected toe, with surrounding oedema and redness. No bony deformations or changes in the normal anatomy of the finger are observed. The diagnosis of Traumatic toe contusion with small lacerated-concused wounds is made.

After thorough wound disinfection, a sterile dressing is applied. Analgesics and non-steroidal anti-inflammatory drugs are prescribed to control pain and inflammation. In addition, treatment is started with NegEnt Spray Muscles and Joints, applied directly on the bruised areas three times a day to promote pain relief and accelerate the healing process. It should be emphasised that in this case,

in which the skin was lacerated, the use of the class I medical device NegEnt Spray Muscles and Joints proved particularly beneficial given the antibacterial and healing-promoting properties of the cannabidiol it contains. The patient was re-evaluated after 7 days. The wounds showed signs of healing with no signs of infection. Pain has decreased and the patient reports improved walking ability. It is recommended to continue with the RICE protocol and closely monitor the wounds until complete healing. The use of NegEnt Muscle and Joint Spray was well tolerated and contributed to the improvement of symptoms.

The management of traumatic toe contusion with lacerated wounds requires a careful approach to prevent complications such as infection. Timely treatment, conservative measures such as the RICE protocol and the addition of NegEnt Spray Muscles and Joints contributed to a favourable outcome in this case. Further follow-ups are necessary to ensure complete resolution of the clinical picture.

This clinical case illustrates the importance of immediate intervention and appropriate follow-up in the treatment of traumatic contusions complicated by laceration injuries. The prognosis is generally positive if appropriate management is implemented, and the addition of topical treatments such as NegEnt Spray Muscles and Joints can be beneficial in the healing process due to its antibacterial effect, favouring skin wound healing, as well as anti-inflammatory and analgesic.

Arthrosis of the hands.

Female, 76 years old, the patient presents a history of arthrosis with progressive degeneration of cartilage in the joints of the hands. She reports chronic pain and stiffness limiting daily activities. On physical examination, swelling and reduced joint mobility are observed, without obvious signs of active inflammation as in the case of rheumatoid arthritis. A course of treatment with NegEnt - Muscles and Joints, a topical spray indicated for the relief of joint pain, was prescribed. The patient was instructed to apply the spray three times a day to the affected areas and to supplement the treatment with mobility and strength exercises for the hands.

After two weeks of treatment, the patient reported an improvement in pain and greater ease in daily activities. No side effects were reported. Encouraged by the improvement achieved with NegEnt Spray - Muscles and Joints, the patient subsequently started a programme of specific hand exercises, which further contributed to the improvement in function. Treatment with NegEnt - Muscles and Joints proved to be effective in reducing the symptoms of arthrosis in this clinical case. The combination of topical therapy and specific exercises improved the patient's quality of life.

Arthrosis of the knee.

Pain due to degeneration and inflammation of the cartilage of the knee joint.

The patient, a 51-year-old man, suffered from osteoarthritis of the knee, a degenerative condition that caused pain, stiffness and restricted movement. Despite following standard treatments, including analgesics and physiotherapy, he continued to experience significant symptoms that affected his quality of life. It was therefore decided to supplement his treatment regime with NegEnt Spray - Muscles and Joints, applied directly to the affected area four times a day. After the introduction of this topical treatment, the patient reported a noticeable improvement in pain management and an increase in joint mobility. This change allowed him to participate more actively in his daily and work activities, with a positive impact on his personal and professional life.

This case highlights the importance of a customised therapeutic approach and the effectiveness of NegEnt Spray - Muscles and Joints as a complement and supplement to conventional treatments for knee arthrosis.

Fasciitis

Inflammation of the plantar fascia, the tissue that connects the heel to the toes.

The patient, a 28-year-old woman, presented with symptoms of plantar fasciitis, characterised by acute pain in the heel and sole of the foot, especially in the morning. Despite standard conservative treatments, the symptoms persisted, limiting her daily activities. He therefore introduced NegEnt Spray - Muscles and Joints into his treatment plan, applied three times a day to the affected area. After the addition of this topical treatment, the patient reported significant pain relief and improved function, which allowed her to resume her activities, with intense relief from the previous discomfort.

This case highlights the effectiveness of NegEnt Spray - Muscles and Joints as a complement to traditional treatments for plantar fasciitis.

Cervical Pain

Treatment of a pain that was localised in the cervical region of the spinal column of the patient, which included the C4 to C6 vertebrae. The symptoms complained of by the patient included pain ranging from mild to severe, radiating pain to the shoulders, arms or hands, tingling or numbness due to nerve root compression or irritation.

Lumbar Pain

Lumbar pain occurring in the lower spine of a 25-year-old young woman. It was attributable to muscle contracture and ligament sprains rather than disc herniations, vertebral injuries, or other degenerative conditions of the spine. Symptoms consisted of dull, constant burning pain, often radiating to the buttocks or legs, as in the case of sciatica.

Muscular and Joint Pain in the Shoulder

The patient, a 46-year-old man with an active and athletic lifestyle, presents complaining of persistent muscle and joint pain in the left shoulder region. He reports no recent traumatic events, but reports increased physical activity in recent weeks. On physical examination, the left shoulder shows signs of muscle tension and pain on palpation of the joints. Shoulder mobility is slightly limited due to pain, but there are no structural deformities or signs of acute trauma. A diagnosis of suspected rotator cuff tendonitis or muscle overload due to physical activity is made.

The patient is then advised to temporarily reduce the intensity of physical activity and apply the RICE (Rest, Ice, Compression, Elevation) protocol. For pain control and reduction of inflammation, treatment is started with NegEnt Spray Muscles and Joints, to be applied, directly on the affected area, three times a day. After one week of treatment, the patient reports a significant improvement in pain and greater freedom of movement in the shoulder. The treatment with NegEnt Spray Muscles and Joints was well tolerated and contributed to the functional recovery of the shoulder.

The clinical case just reported highlights the importance of a conservative approach in the treatment of muscle and joint pain in the shoulder. The use of NegEnt Muscle and Joint Spray has proven to be an effective treatment option to alleviate symptoms and aid the athlete's recovery. Further evaluation and a gradual return to physical activity will be necessary to prevent recurrence.

This single case study illustrates a multimodal therapeutic approach for the treatment of muscle and joint pain in the shoulder, emphasising the effectiveness of topical treatments such as NegEnt Spray - Muscles and Joints in combination with conservative measures.

Dysodontiasis of the third Molar Included

As NegEnt Spray - Muscles and Joints is non-toxic, if ingested, and even edible (Scrimali, 2023), it was also tested in a bone and connective tissue affection related to the mouth, with application on a tooth and gums. The patient presented with dysodontiasis of the third molar included, manifesting pain and discomfort in the left mandibular region. On clinical examination, swelling and redness was observed in the area of the impacted third molar, with difficulty in fully opening the mouth and pain on palpation. A provisional diagnosis was then made, pending specialist and radiographic examination, of dysodontiasis of the impacted third molar with symptoms of pericoronitis. In addition to standard oral hygiene measures, it was decided to supplement the treatment with the application of NegEnt Spray Muscles and Joints directly on the affected buccal mucosa and the gingiva surrounding the tooth. The product is applied three times a day, after main meals and before going to bed. In this case, reliance was also placed on the antiseptic and antibacterial potential of the product. After just three days of treatment, the patient reported a significant improvement in symptoms. Pain was significantly reduced and jaw mobility improved, allowing more comfortable chewing and a wider oral opening. The use of NegEnt Spray - Muscles and Joints showed a beneficial

effect in controlling the pain and inflammation associated with dysodontiasis of the third molar included.

Results

Participants in the experimental group treated with NegEnt Elixir Muscles and Joints reported a marked clinical improvement, subjectively perceived as a significant increase in psychophysical well-being. None of the subjects reported any side effects. The application of Fisher's test (1922) to the collected data showed a high statistical significance, with a 'p' value of less than 0.001%.

Discussion

It seems important to emphasise that these results, while promising, are only a preliminary indication. The limited sample size imposes caution when interpreting the data and emphasises the need to conduct larger and methodologically rigorous clinical trials. Such studies should include an adequate number of participants and control groups treated with placebo and/or other medical devices in order to definitively confirm the efficacy and safety of NegEnt Spray - Muscles and Joints, as well as the absence of side effects.

Conclusions

Precisely in order to extend the collection of clinical data on the efficacy and tolerability of NegEnt Spray - Muscles and Joints, we have decided to include in the package leaflet of the medical device an invitation to download free of charge from the Herbal Neurocare website (www.herbalneurocare.it) a copy of two tests for self-administration, one for the self-assessment of pain and the other for the detection and quantification of side effects, such as the PRO-CTCAE carried out in Italy at the National Cancer Institute. (PRO-CTCAE, 2024). and the McGill Pain Questionnaire (Maiani, Sanavio, 1984). Users of NegEnt Spray -Muscles and Joints are invited to contribute to clinical research on the product by completing questionnaires at the beginning of product use and at seven and fifteen day intervals. The inclusion of a clinical efficacy protocol in the packaging of a class I medical device, which involves the patient in monitoring the efficacy and absence of side effects of product use, is a promising development in the sales strategies of medical device companies.

Conflicts of Interest: The author is the scientific director of Herbal Neurocare, which will market NegEnt Muscle and Joint Spray.

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