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Clinical Evaluation of a Topical Patch for the Management of Acute and Chronic Osteoarticular Pain

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ABSTRACT

Pain is a symptom common to many pathological conditions that can affect all age groups, with greater incidence among adults and the elderly. It is an important clinical, social and economic aspect of all ages and has a negative impact on the quality of life. Pain therapy, also called antalgic therapy or pain medicine, aims to identify, evaluate and treat acute and/or chronic pain.

The objective of this observational study is to evaluate the effect of the "Tecnologia DUKTOR ionoattiva" iPatchMed ZeroDol patch in reducing in the short-term painful symptoms in case of local acute and chronic inflammatory states. The patch is a topical product to be applied on the affected area in order to create a hydro-active environment. The mechanism of action consists in the generation of micro-currents and micro-electromagnetic fields that promote ion exchange and the passage of micro-currents in the cutaneous tissues, increasing the use of oxygen by the cells and the restoration of the cell membrane. This results in both cellular reinvigoration and a high antalgic effect.This single-arm monocentric investigation has 50 subjects with acute and chronic pain.The pain measurement was recorded through the Numerical Rating Scale (NRS) at selected time points: at baseline (T0) and after 2, 8 and 24 hours. The use of the "Tecnologia DUKTOR ionoattiva" iPatchMed ZeroDol patch significantly promotes a decrease in acute and chronic pain; furthermore, no adverse effects were recorded, thus demonstrating that the medical device is optimally tolerated.

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Introduction

The objective of this observational study is to clinically evaluate the effect of the "Tecnologia DUKTOR ionoattiva" iPatchMed ZeroDol patch designed for topical application in the treatment of pain. The patch creates a hydro-active environment and, through an electrochemical reaction, exploits the endogenous body bioelectric potential that, in contact with the copper and zinc filaments present in the tissue of the patch, produces micro-currents which increase the bio-availability of the nutrients of the cells, promoting the absorption of the plant extracts of Arnica and Devil's Claw present within the adhesive matrix. The pain measurement was recorded through the Numerical Rating Scale (NRS) before and after the application of the patch on patients with acute and chronic pain.

Pain is a complex sensation resulting from a perceptive component (nociception) related to the transmission of the painful stimulus to the brain and a component related to the experience that depends exclusively on the subject, or the way he perceives and experiences the sensation of pain. In 1979 the International Association for the Study of Pain (IASP) described pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [1]. Pain is a symptom common to many pathological conditions that can affect all age groups, with greater incidence among adults and the elderly. It represents an important clinical, social and economic aspect of all ages and has a negative impact on the quality of life [2].

Pain can be classified into: acute, chronic and procedural. Acute pain has the function of alerting the individual to the current tissue injury and is normally localized, lasts for a few days, tends to decrease with healing. Its cause is generally clear: linked to surgery, trauma, infectious pathology [3]. Currently the therapeutic options available for the control of acute pain are multiple and effective in the vast majority of cases. Chronic pain is long-lasting, often determined by the persistence of the harmful stimulus and/or by self-maintenance phenomena, which maintain the nociceptive stimulation even when the initial cause has been limited. It is accompanied by an important emotional and psycho-relational component and limits the physical and social performance of the patient. It is mainly represented by the pain that accompanies chronic diseases (rheumatic, bony, oncological, metabolic). It requires a comprehensive approach and multidisciplinary and repeated therapeutic interventions [4,5]. Procedure pain accompanies multiple diagnostic/therapeutic investigations, represents in every setting, situation and age, a particularly feared and stressful event. Pain is associated with anxiety and fear and frequently its presence significantly affects the perceived quality of care, as well as the quality of life. Numerous intervention options (pharmacological and non-pharmacological) and effective and efficient organizational models are currently available, as described in table I.

Regardless of its nature, origin and duration (acute or chronic), pain, from the pathophysiological point of view, is one of the main manifestations of inflammation. Pain therapy, also called antalgic therapy or pain medicine, aims to identify, evaluate and treat acute

and/or chronic pain. The treatment of pain can be more or less complex and more o less long depending on the cause and extent of the pain. In addition to muscle rest (especially indicated for acute pain), there are situations (subacute or chronic pain) where certain physical exercises can help maintain muscle function [6-8]. However, the elimination of the cause is in many cases the most advisable choice and it is generally recommended the administration of analgesics such as acetaminophen, nonsteroidal inflammatory drugs (FANS) or, in the case of more severe pain, opioids [9]. A list of available therapies for pain management is shown in table II. A valid alternative to pharmacological intervention, which unfortunately brings with it numerous side effects, is represented by palliative physical treatments that aim to improve the symptomatology of pain and that allow to shorten the time of resolution of the inflammation in a completely natural way. The use of medicinal herbs containing essential oils rich in antioxidants substances or the application of heat and/or cold conveyed through appropriate medications are often preferred for the treatment of joint pain, muscle and injuries (e.g. sports injuries, carrying of loads excessive, etc.) [10].

Table I: Different thypes of pain

Table 1

Different types of pain

Type	Pathophysiology	Characteristics	Examples
Based on underlying pathophysiology			
Nociceptive pain	Activation of nociceptors in response to noxious stimuli	Sharp, burning pain (somatic) or dull, aching pain (visceral)	Back pain, headaches, neck pain, shoulder pain, pain due to burns and injuries
Neuropathic pain	Central sensitization or neuronal damage	Severe, burning, shooting or numbing pain, increased sensitivity to stimuli (hyperalgesia and allodynia)	Peripheral neuropathy, diabetic neuropathy, trigeminal neuralgia, complex regional pain syndrome (CRPS), neuropathic pain due to spinal injury
Mixed pain	Nociceptive and neuropathic origin	Severe, shooting pain or dull, aching pain or pain with mixed characteristics	LBP with radiculopathy, cancer pain
Based on duration			
Acute pain	Activation of peripheral nociceptors, accompanied by release of COX enzymes and prostaglandins	Lasts from few seconds to less than 6 months	Injuries, headaches, sprains, postoperative pain, back pain
Chronic pain	Sensitization at the level of spinal neurons via multiple mechanisms	Lasts for ≥6 months	Chronic primary pain, cancer pain, posttraumatic and postsurgical pain, neuropathic pain, headache and orofacial pain, visceral pain, musculoskeletal pain
Breakthrough pain	Pain in a well-treated patient due to movement (incidental), spontaneous or resulting from weaning off of drugs or effect of drug	Lasts from few seconds to hours	Cancer pain
Based on etiology			
Cancer pain	Caused due to cancer itself (brain tumors, breast cancer), drug treatment (chemotherapy, radiation) or associated disease (neuropathy)	Acute or chronic pain of mild, moderate or severe intensity with/without breakthrough pain	All types of cancers
CNCP	May have multiple etiologies	Moderate-to-severe pain with/without restricted mobility	Rheumatoid arthritis, osteoarthritis
Based on location			
LBP	Caused due to bad posture, strains/sprains, underlying disease (malignancy or infection) or referred pain (kidney or gall stones)	Mild and moderate-to-severe pain with/without impaired movement or physical function	Acute LBP, herniated disk, spondylosis
Neck pain and shoulder pain	Caused due to strains, sprains, incorrect posture and compression of spinal cord or injuries	Mild and moderate-to-severe pain with/without impaired movement or physical function	Axial neck pain, cervical radiculopathy
Headaches	Caused due to incorrect posture, stress, migraine or underlying disease (tumors)	Headache associated with migraine may present additional symptoms (aura), visual problems or vertigo	Tension-type headaches, migraine headaches
Referred pain	Type of visceral pain that radiates to surrounding regions	May be sharp, pulsating pain or dull, aching pain depending upon the origin	Angina (jaws and shoulders), stones (abdomen and back)

Abbreviations: CNCP, chronic noncancer pain; COX, cyclooxygenase; LBP, low-back pain.

Regardless of its nature, origin and duration (acute or chronic), pain, from the pathophysiological point of view, is one of the main manifestations of inflammation. Pain therapy, also called antalgic therapy or pain medicine, aims to identify, evaluate and treat acute and/or chronic pain. The treatment of pain can be more or less complex and more o less long depending on the cause and extent of the pain. In addition to muscle rest (especially indicated for acute pain), there are situations (subacute or chronic pain) where certain physical exercises can help maintain muscle function [6-8]. However, the elimination of the cause is in many cases the most advisable choice and it is generally recommended the administration of analgesics such as acetaminophen, nonsteroidal inflammatory drugs (FANS) or, in the case of more severe pain, opioids [9]. A list of available therapies for pain management is shown in table II. A valid alternative to pharmacological intervention, which unfortunately brings with it numerous side effects, is represented by palliative physical treatments that aim to improve the symptomatology of pain and that allow to shorten the time of resolution of the inflammation in a completely natural way. The use of medicinal herbs containing essential oils rich in antioxidants substances or the application of heat and/or cold conveyed through appropriate medications are often preferred for the treatment of joint pain, muscle and injuries (e.g. sports injuries, carrying of loads excessive, etc.) [10].

Table II: Avaible therapies for treatment of pain

Table 2

Available therapies for treatment of pain

Class	Molecules	Indications	Dosage	Common adverse events
Aniline analgesics	Acetaminophen	Acute/chronic pain	500–1,000 mg every 4–6 h; max dose of 4,000 mg/d	Hepatotoxicity
NSAIDs-Salicylate	Aspirin	Acute/chronic pain	500–1,000 mg every 4–6 h; max dose of 4,000 mg/d	GI upset/irritation, hepatic and renal dysfunction, fluid retention, hypersensitivity reaction
NSAIDs-Aryl acetic acid derivative	Diclofenac	Acute/chronic pain	50–100 mg/d; max 150 mg/d	GI upset/irritation, nausea and vomiting, weakness, headache, dizziness, hepatic and renal dysfunction, hypersensitivity reaction
NSAIDs- Propionate	Ibuprofen	Acute pain	400–800 mg every 6–8 h; max dose of 3,200 mg/d	GI upset/irritation, hepatic and renal dysfunction, fluid retention, hypersensitivity reaction, cardiovascular events in high-risk patients
	Naproxen	Chronic pain	250–500 mg every 8–12 h; max dose of 1,500 mg/d	GI upset/irritation, hepatic and renal dysfunction, fluid retention, hypersensitivity reaction, cardiovascular events in high-risk patients
COX-2 inhibitor	Celecoxib	Acute/chronic pain	200–400 mg every 12–24 h; max dose of 400 mg/d	GI upset/irritation, hepatic and renal dysfunction, fluid retention, hypersensitivity reaction, cardiovascular events in high-risk patients
	Rofecoxib	Acute/chronic Pain	12.5–50 mg once a day	GI upset/irritation, hepatic and renal dysfunction, fluid retention, hypersensitivity reaction, cardiovascular events in high-risk patients
Opiate	Codeine	Chronic pain	30–60 mg every 4 h as needed	Constipation, nausea, vomiting, sedation and pruritus; less common effects include dry mouth, mental confusion, urinary retention and respiratory depression
	Hydrocodone	Chronic pain	5–10 mg every 4 h as needed	Constipation, nausea, vomiting, sedation and pruritus; less common effects include dry mouth, mental confusion, urinary retention and respiratory depression
	Oxycodone	Chronic pain	5–10 mg every 4 h as needed	Constipation, nausea, vomiting, sedation and pruritus; less common effects include dry mouth, mental confusion, urinary retention and respiratory depression
	Morphine	Chronic pain	5–30 mg every 4 h	Constipation, nausea, vomiting, sedation and pruritus; less common effects include dry mouth, mental confusion, urinary retention and respiratory depression
	Tramadol	Acute/chronic pain	5–100 mg every 4–6 h; max dose of 400 mg/d	Constipation, somnolence, dizziness, nausea, vomiting and pruritus
Antiepileptic	Gabapentin	Acute/chronic pain	300–900 mg thrice daily; max dose of 3,600 mg/d	Dizziness, somnolence and peripheral edema
	Pregabalin	Acute/chronic pain	50–300 mg/d	Dizziness, somnolence and peripheral edema
	Carbamazepine	Acute/chronic pain	200–600 mg twice daily	Somnolence, mental confusion, dizziness and nausea
	Oxcarbazepine	Acute/chronic pain	1,200–2,400 mg/d	Changes in vision, dizziness, confusion and depression
Tricyclic antidepressants	Amitriptyline, nortriptyline	Acute pain	10–150 mg/d (amitriptyline), 25–100 mg/d (nortriptyline)	Drowsiness, dry mouth, dizziness and constipation
SNRIs	Duloxetine, venlafaxine	Chronic pain	40–60 mg/d (duloxetine), 150 mg/d (venlafaxine)	Nausea, gastrointestinal bleeding and increase in hepatic enzymes

Notes: Data from American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons (2009),29 Patel et al.38 McPherson et al (2004),239 Bell and Schnitzer (2001),240 Antman et al (2007),241 Dworkin et al (2010),242 and Cleeland and Ryan.243,244

Abbreviations: d, day; h, hour; max, maximum; COX, cyclooxygenase; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRI, serotonin–norepinephrine reuptake inhibitor.

Materials and Methods

A monocentric observational study on the "Tecnologia DUKTOR ionoattiva" iPatchMed ZeroDol patch was conducted in San Raffaele Hospital (Milan, Italy). All subjects, enrolled in a single cohort, provided a written informed consent prior to entering the study. The trial was run in accordance with the Declaration of Helsinki (2013) and with principles of Good Clinical Practices.

Healthy subjects (n=50), with an average age of 53 years, some with chronic pain, in particular with the presence of osteoarthritis, and others with acute pain, in particular with the presence of distortion, muscular tear and tendinitis, were selected for the investigation. In contrast, subjects with ulcers and/or surgical wound dehiscence were eliminated from the study.

Method of application of the test samples

Samples of the tested product were applied to the painful area for a period of 24 hours.

Clinical evaluation

The pain evaluation was recorded through the Numerical Rating Scale (NRS) at selected time points: at baseline (T0) and after 2, 8 and 24 hours. NRS is a one-dimensional scale consisting of a numerical scale from 0 to 10, where 0 indicates no pain and 10 indicates maximum pain. The values between 1 and 9 indicate a severe increase in pain [11]. (Figure 1)

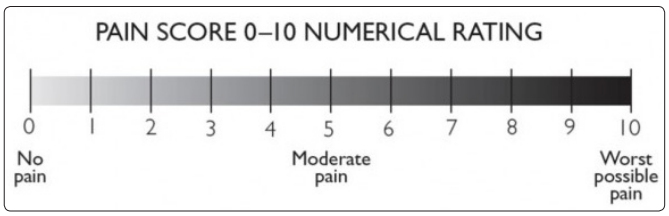

Figure 1: Numeral Rating Scale (NRS)

Statistical evaluation

Sample data on pain sensation were described using the usual position and dispersion measurements: median and interquartile range. For the analysis of the endpoint was used a non-parametric approach, the Friedman rank sum test, followed by sign test Bonferroni corrected to compare differences in the parameter evaluated among different timepoints. The significance level was set at 5%. All analyses were carried out using RStudio Version 1.1.456 – © 2009-2018 RStudio, Inc.

Results

During the trial, no subjects developed any adverse effects or breached the established inclusion/exclusion criteria. There were also no drop-out cases. Therefore, the analyses refer to a sample of 50 subjects, of average age 53 years, with presence of acute and chronic pain. Each subject of the study was asked to apply the patch on the affected area for a period of 24 hours.

As shown in the graph 1 and in the table III, compared to the baseline value (median value of 9,0 - Q1 8,0 and Q3 9,0), there is a significant reduction in the pain already at 2 hours (median value of 4,0 - Q1 4,0 and Q3 5,0) that remains constant up to 8 hours (median value of 4,0 - Q1 3,0 and Q3 4,0) and then further decreases to 24 hours (median value of 2.0 - Q1 1.0 and Q3 2.0). The Friedman rank sum test result indicates that there is a statistically significant difference between the groups analyzed (pain sensation at different times of analysis). In particular, the results of the sign test indicate that there is a statistically significant difference between all the couples examined, table IV. Therefore the sensation of pain is significantly reduced in each time analyzed compared to the previous, index of the effect in reducing the pain of the "Tecnologia DUKTOR ionoattiva" iPatchMed ZeroDol patch.

Graph 1: Box-plot of clinical pain evaluation

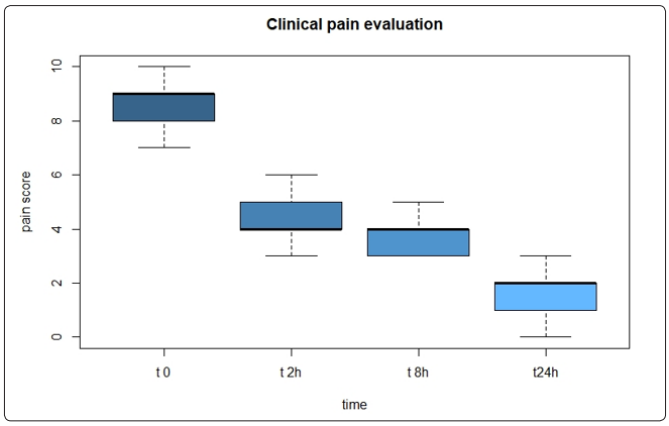

Table III: Descriptive analysis

Descriptive analysis				
Survey times	Median	(IQR)		
T0	9,0	8,0	-	9,0
T2h	4,0	4,0	-	5,0
T8h	4,0	3,0	-	4,0
T24h	2,0	1,0	-	2,0

Table IV: Friedman rank sum test and sign test

Friedman rank sum test	
p-value and significance	
p-value <0,01	yes

Pairwise comparison using sign test						
p-value and significance						
	T0		T2h		T8h	
T2h	<0,01	yes				
T8h	<0,01	yes	<0,01	yes		
T24h	<0,01	yes	<0,01	yes	<0,01	yes

Discussion

The purpose of this study is to evaluate the clinical effect of the "Tecnologia DUKTOR ionoattiva" iPatchMed ZeroDol patch, a product designed for topical application for the treatment of pain. In particular, the results of the short-term application of the product were analyzed in patients with acute and chronic pain. The tested medical device consists of a "Textronik" fabric patch, which in turn is made up of alternating copper and zinc tracks inserted between cotton and polyester tracks impregnated with colloidal silica. The presence of natural hydration factors, such as glycerol and urea, in association with the arnica and devil's claw contained in the patch, favors a greater cutaneous tolerability during the application of the product as well as creating in association with the electrolytes and the composition of the adhesive matrix the interface needed to create the electric field. The evaporation that would occur under normal physiological conditions ceases, from the moment the patch is applied which, creating an occlusive barrier, causes the rise of the surface temperature of the skin on the treated area. Furthermore, the presence of this barrier, which creates a kind of closed system, favors the continuous passage of

ions between the skin layers and the surface in order to allow the constant generation of the electrical flow during the entire period of application of the device. Once applied to the area of the body to be treated, the peculiar tissue containing alternating copper and zinc tracks comes into contact with the electrolytic salts contained in the normal sweat of the skin, generating a barrier of light, harmless and painless micro-currents. This screen increases the occlusive effect of the patch and acts as a reflective surface, on which the caloric energy of the body is refracted, being retransmitted to the body itself, giving relief from pain.

The data reported in this observational study have shown that the application of the patch contributes to improve the quality of life of patients by giving a fair perception of relief from osteoarticular pain already after 2 hours from the application of the product. This result is remarkable because the application of the patch not only significantly relieves the sensation of pain, but also stimulates cell renewal, an interesting aspect also to increase the healing capacity of the skin wound. In fact, a similar antalgic effect can be expected also on pain at different genesis; however, the evaluation requires specific clinical studies. In addition, the product showed optimal tolerability as it did not have any adverse effects.

Conclusions

The use of the ”Tecnologia DUKTOR ionoattiva” iPatchMed ZeroDol patch significantly promotes a decrease in acute and chronic pain; moreover, no adverse effects have been recorded, thus demonstrating that the medical device is optimally tolerated.

In conclusion, the use of this medical device for the control of osteoarticular pain has shown, in the observed clinical cases, an excellent antalgic effect also thanks to the exclusive technical characteristics of the patch, such as the particular adhesiveness, adaptability and resistance to water. Both for the technical characteristics but also from the clinical analysis the patch is free of side effects.

Disclosure

There are no conflicts of interest to declare.

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