PCCA Lipoderm®

Topical Pain Relief for Degenerative Disc Disease

SUMMARY: Lower back pain caused by degenerative disc disease (DDD) has a high incidence and prevalence, but there is no consensus on the standard management of the associated pain. The purpose of this case study is to evaluate the effectiveness of a transdermal formulation delivered by Lipoderm® in managing DDD associated pain and improving functionality in a patient. The Roland-Morris Disability Questionnaire (RMDQ) and a visual analogue scale for pain were used to measure the clinical outcomes. The patient reported decreased pain VAS from 10 to 2 as well as a reduction of RMDQ score from 15 to 6. This case study demonstrated the effectiveness and safety of this compounded formulation for pain management in a patient with DDD.

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Introduction:

Degenerative disc disease (DDD) is a chronic condition of lower back pain (LBP) caused by the degeneration of the intervertebral disc. It is ranked the fifth most common reason for a doctor's visit, and its associated LBP is the number one leading cause of disability in young people under the age of 45[1,2]. The annual incidence of adult DDD is 3.6% worldwide and 5% in the U.S., and the lifetime incidence of the associated LBP is 60-90% [1,2].

Pathophysiology of DDD is a multifactorial process involving three main phases: 1) Recurrent or excessive forces beyond threshold lead to microtrauma of the disc; 2) The loss of proteoglycans and subsequent loss of osmotic pressure and water occurs in the disc matrix due to an imbalance of extracellular matrix degradation; and 3) The associated change in collagen fibers further results in structural changes and instability of intervertebral disc, nearby ligaments and muscles, when the pain most likely to occur[2]. Systemic lupus erythematosus usually causes inflammation in joints and muscle, but the spine is generally spared from the attack due to the central nucleus pulposus (elastic core) being isolated by the annulus fibrosus and the cartilaginous endplate. However, once there is a tear or fissure to the outer barrier, patients with lupus will have a stronger autoimmune response that exacerbates the degeneration of the disc and related complications [3].

Patients with DDD commonly experience increased pain with activities that involve bending or twisting the spine, or holding certain position for an extended period. Muscle tension and spasm may also be triggered by the spinal instability.

There is a lack of consensus in regard to the management of LBP associated with DDD. Current available therapies include noninvasive physical therapy, biopsychosocial rehabilitation, drug therapy and invasive surgical procedures to replace the disc. Pharmacological therapies mostly focus on oral NASIDs, opioids, muscle relaxants, antidepressants, antiepileptics, benzodiazepines, and systematic corticosteroids. Corticosteroids can also be given with anesthesia via epidural injection, percutaneous intradiscal injection or trigger point injection, all of which are accompanied by limited evidence as well as inconsistent efficacy and safety [4].

The purpose of this case study is to present the effectiveness of a compounded topical formulation (Table 1.) in reducing pain and functional disability resulting from DDD in a patient.

Methodology:

The Roland-Morris Disability Questionnaire (RMDQ) was implemented to evaluate the activities of daily living, functional mobility and pain in the patient with DDD before and after using the compounded formulation. The RMDQ assesses the patient reported outcomes by asking 24 questions about how LBP is affecting functional activities. Each question that correctly describes the patient is worth one point, so the total score can range from 0 (no disability) to 24 (severe disability) [5,6]. The patient was instructed to complete the RMDQ retrospectively before and after treatment, and was also asked to score the overall pain level on a 1-10 Visual Analogue Scale (VAS).

Written informed consent was obtained from the patient for publication of this case study. The RMDQ is permitted to use in research and clinical practice by the original author.

Rx

Baclofen USP	2%
Bupivacaine Hydrochloride USP Monohydrate	* 1%
Ketoprofen USP, PCCA Special Micronized	10%
Ethoxy Digycol Reagent	10%
Base, PCCA Lipoderm®	q.s.

Table 1. Compounded formulation for DDD (PCCA F13625).

** Calculating the bupivacaine needed for the preparation has to use the water content and assay of Bupivacaine Hydrochloride USP Monohydrate, which can be obtained from the Certificate of Analysis for each lot number of the product.*

Case Report:

Patient KR is a 56-year-old female with systemic lupus erythematosus who was diagnosed with DDD after a series of injuries. She had a horse riding accident that resulted in temporary trauma paralysis. She was involved in a car accident that further injured her back, and the lower back pain became worse during patient care activities on her job as a nurse. She attempted to relieve the pain through chiropractic, physical therapies and yoga but only received temporary and minimal benefits. The pharmacological therapies prior to the compounded topical pain cream included OTC and prescription pain medications, and glucocorticoid injections. However, none of the treatments provided lasting effects. The patient's physical activity level used to be high but then decreased to very little only as necessary due to the pain. Later, KR was prescribed the topical pain cream containing 2% baclofen, 1% bupivacaine and 10% ketoprofen in Lipoderm. Patient reported instant relief of pain upon application. She was instructed to apply 1-2 pumps (0.5 – 1 g) four times daily as needed for pain. After 6 months, during a follow-up visit, her pain VAS reduced from 10 to 2, and RMDQ total score decreased from 15 to 6, indicating that the LBP was well under control and the limitation of her daily activities has been greatly lowered. She is now able to exercise for 6 minutes daily and continues using the formulation. The assessed daily functional impairments are shown in Table 2 and are compared between before and after treatment.

Patient reported no adverse reaction associated with the topical treatment.

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I. The Roland-Morris Disability Questionnaire	Before treatment	After treatment
I stay at home most of the time because of my back	√	
I change position frequently to try and get my back comfortable	√	√
I walk more slowly than usual because of my back	√	
Because of my back I am not doing any of the jobs that I usually do around the house	√	√
Because of my back, I use a handrail to get upstairs	√	
Because of my back, I lie down to rest more often is possible	√	
Because of my back, I have to hold on to something to get out of an easy chair		
Because of my back, I try to get other people to do things for me	√	√
I get dressed more slowly than usual because of my back	√	
I only stand for short periods of time because of my back		
Because of my back, I try not to bend or kneel down		
I find it difficult to get out of a chair because of my back		
My back is painful almost all the time	√	
I find it difficult to turn over in bed because of my back		
My appetite is not very good because of my back pain		
I have trouble putting on my socks (or stockings) because of the pain in my back		
I only walk short distances because of my back		
I sleep less well because of my back	√	√
Because of my back, I get dressed with help from someone else	√	
I sit down for most of the day because of my back		
I avoid heavy jobs around the house because of my back	√	√
Because of my back pain, I am more irritable and bad tempered with people than usual	√	
Because of my back, I go upstairs more slowly than usual	√	√
I stay in bed most of the time because of my back	√	
Total Score /24	**15**	**6**
II. **Visual Analogue Scale for Pain (1-10)**	**10**	**2**

Table 2. Clinical outcomes of DDD before and after treatment reported by the patient measured by the RMDQ and VAS for pain. The patient marked the sentences that described her during daily life.

Discussion and Conclusions:

Lower back pain resulting from DDD is one of the major causes of disability and has produced a heavy socioeconomic burden worldwide. Here we presented a potentially effective therapeutic strategy combining common agents for DDD into a topical cream, from which the agents are delivered into skin and underlying muscle and tissues to modify the pain pathways.

Muscle spasm can be very painful due to the body struggling to stabilize the DDD spine that is inflamed and instable. Baclofen, a $GABA_B$ receptor agonist, is a traditional therapy for spasticity. Percutaneous absorption of baclofen has been confirmed and topical baclofen at 2-5% dose has shown effectiveness in reducing acute and chronic pain while avoiding the CNS adverse effects from systematic therapy [7,8]. Local anesthetic injection provides short-term relief of pain; however, the pressurized injection may induce cytotoxicity on intravertebral disc cells shown by an *in vivo* study [9]. The long-acting efficacy and safety of topical bupivacaine, a sodium channel blocker, has been proven by multiple clinical trials [10], and it exerts no direct pressure or cytotoxicity to the disc cells, thus can be a viable option. Like many other pain conditions, DDD is as well associated with inflammation [11] which is even worse in a patient with lupus. Therefore, ketoprofen, a NASAID not only inhibiting COX-2, but also decreasing proinflammatory cytokine levels, becomes one of the most commonly used topical regimens for musculoskeletal pain and DDD, and is included in this formulation. The combination of all three agents may have synergistic effect in alleviating pain.

Prolonged and steady drug permeation through the skin to the pain site is key to ensuring therapeutic effect. Lipoderm, the transdermal vehicle to deliver the active ingredients, is a phospholipid emulsion system with permeation enhancers that facilitates drugs across the stratum corneum and entering cutaneous circulation with a prolonged and steady flux rate. The capability and kinetics of Lipoderm in transdermal drug delivery have been shown in multiple publications.

As a result, this compounded formulation successfully improved the daily functionality and reduced level of pain in a patient suffering from DDD. The reported therapeutic strategy may provide a flexible, convenient, effective and safe option for future DDD management.

References:

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