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Combination of Methocarbamol and Diclofenac: A New Solution for Treating Low Back Pain

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Abstract

Introduction: Lower back pain (LBP) is a condition that restricts occupational activities of the patients suffering from it owing to pain and its perception, thus severely impacting functional capacity. The economic burden of LBP could be represented directly by the high costs of health care that one has to spend for the symptomatic relief from pain and indirectly due to decreased productivity owing to absenteeism. ***Material & Method:*** LBP can be acute, subacute or chronic in duration, however, with conservative measures that includes timely diagnosis and right treatment, the symptoms of low back pain typically improved within a few weeks from onset. Common attributes of LBP are muscular tension and spasms. ***Result:*** Pharmacological interventions for the treatment of LBP generally includes non-steroidal anti-inflammatory drugs (NSAIDs) and muscle relaxants, wherein both muscle relaxants and NSAIDs have proven efficacy and safety. Studies have shown that combining NSAIDs with a muscle relaxant could be a better treatment option than NSAIDs alone. One such example is Robi D, which is a combination of muscle relaxant methocarbamol and NSAID diclofenac, indicated for the relief of pain and inflammation associated with LBP along with rheumatoid arthritis, osteoarthritis, ankylosing spondylitis. ***Conclusion:*** Although there are no individual studies that have assessed the efficacy and safety of Robi D, the individual efficacy and safety of its components speaks volumes of its durability both in real world and clinical trial. Robi D Injection may be administered during acute or severe phase up to a maximum of 3 days or less until amelioration of acute symptoms, post while the patients could be kept on a maintenance therapy with oral Robinaxol D tablets that contain methocarbamol (muscle relaxant) + diclofenac potassium (analgesic) + paracetamol (analgesic).

Keywords: Methocarbamol; Diclofenac; Low Back Pain.

Introduction

Epidemiology of Low Back Pain

About 60%–80% of adults experience low back pain (LBP) at some point in their life that has an annual worldwide incidence of 15% and a point prevalence of 30%.[1,2] Studies indicate that LBP causes more disability than any other condition, accounting one-third of all work related disability. Interestingly, in the Indian scenario, LBP incidence provides a stark contrast among the general population, (6.2%) and the population working as construction workers (92%).[3] Additionally, in the countries sharing borders with India, the prevalence of LBP tells a similar picture observed across pan India. Countries like Bangladesh, Nepal, Pakistan and Sri Lanka have an overall prevalence of 64.8%, 69.5%, 40.6%, and 36.2%, respectively. Globally, the incidence of LBP has doubled in the last 25 years affecting 540 million people and is expected to increase due to ageing and increasingly obese population.[4] Further, lack of physical activity is another cause that leads to LBP.

Overall, burden of LBP owing to ergonomic exposures has been estimated to be 21.8 million (95% Confidence Interval [CI] 14.5–30.5) disability adjusted life years (DALYs) in 2010[5] Furthermore, in India near about 8% population years lived with disability (YLD) due to low back problem. Rate of change in DALYs with respect to low back pain has

increased from 1.2% to 2.3% between years 1990 to 2016 (Figure 1).[4]

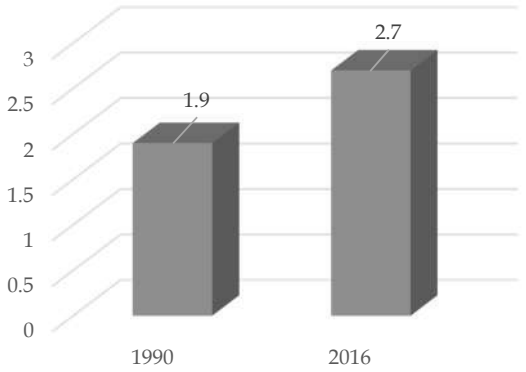

Fig. 1: Rate of Change in DALYs (1990-2016) of Lower Back Pain in India (Reproduced from Jana et al[4]).

Since the LBP restricts occupational activities owing to pain and its perception, it severely impacts functional capacity. The economic burden of LBP could be represented directly by the high costs of health care that one has to spend for the symptomatic relief from pain and indirectly due to decreased productivity owing to absenteeism. The burden of these costs are expected to rise even more in the next few years as per a 2006 review, wherein the total costs associated with LBP in the United States were expected to exceed $100 billion per year, two-thirds of which were the result of lost wages and reduced productivity.[4]

In addition to the physical elements for example lack of exercise or any injury, the risk factors for LBP could be psychosocial including such as stress, anxiety, depression, and monotony.[1] Furthermore, LBP can be acute, subacute or chronic in duration, however, with conservative measures that includes timely diagnosis and right treatment, the symptoms of low back pain typically improved within a few weeks from onset.

Material & Method

Lower Back Pain: Definitions and Classification

Medically LBP is defined in various ways. Some of the authors define LBP as 3digits ICD-9 and ICD-10 codes, lumbar and other intervertebral disc disorder with radiculopathy, LBP (M54.5), and dorsalgia (M54.5). Bartholomeeusen et al. and Spijker-Huiges et al. reported LBP as symptom/complaint (LO3), back syndrome without radiating pain (L84), and back syndrome with radiating pain (L86) for LBP definition. The Dutch Classification for Occupational Health Care and Social Affairs defines nonspecific LBP as acute (L101, M545), subacute (L102, M545) and chronic (L103, M545).[5] Clinical trials defines chronic LBP as presence of continuous pain for a period of three or more months.[6]

Altogether, LBP can be classified as nonspecific low back pain, associated with radiculopathy or spinal stenosis, and back pain correlated with another specific spinal cause (i.e., malignancy, infection, or vertebral fracture).[7]

Majority of population presents the manifestation of non-specific low back pain with no specific cause and typically resolves in less than four weeks[8,9] Muscle tension and spasm are some of the most common attributes particularly, in patients with fibromyalgia. More so, LBP can also be attributed to radicular, facet joint, sacro-iliac, and discogenic pain, as well as spinal stenosis.[7,8]

Etiologies of Back Pain

Anatomic sources like nerve roots, muscle, fascial structures, bones, joints, intervertebral discs (IVDs), and organs within the abdominal cavity could be attributed for LBP.[8]

Some of the most common factors leading to LBP are highlighted below.[3,6,7,8]

- Back muscle strain or ligament strain due to lifting a heavy object, twisting, or a sudden movement
- Bad sitting or posture
- Over activity leading to muscular fatigue
- Arthritis
- Pregnancy
- Certain tumours
- Ovary problems
- Disc tear
- Spondylolisthesis (forward displacement of a vertebrae over a lower Segment)
- Osteoporosis (brittle bones) leading to vertebral fractures
- Spinal stenosis
- Scoliosis (Lateral Curvature of Vertebral column)

Additionally, micro motion instability and inflammation in ageing population due to dehydration of vertebral disks can also result in LBP. This happens when the inflammatory proteins of nucleus pulposus leaks out of the disc space that lead to inflammation of structures next to the disc (e.g. nerve roots) resulting in back pain (radiculopathy).[2]

Discussion

Diagnosis and Evaluation

The diagnostic evaluation of patients of LBP requires complex clinical decision-making mostly due to its non-specific nature and varied classifications. Although, clinical information is critical in driving the initial impression, the presence of various psychological factors that may arise due to stress, depression, and/or anxiety, may influence the decision of the clinician during the clinical evaluation. Patient history in those cases should also include substance use exposure, detailed health history, work, habits, and other psychosocial factors. Imaging techniques like magnetic resonance imaging (MRI) should only be considered in the presence of clinical elements that are definitely not clear or in the presence of neurological deficits or other medical conditions. American College of Radiology recommendations rules out performing imaging for LBP within the first 6 weeks unless red flags are present. Further, clinical guidelines suggest that

when faced with LBP patients, the clinician should do a careful diagnosis of the mechanisms that sustain acute and/or chronic pain and the treatment should specifically complement to these mechanisms.

Thus the common mistakes of making the diagnosis of "simply low back pain", could be avoided and the improper treatment of a definition and not a complex disease. As chronic LBP could have simultaneous multiple pain generators, a multidisciplinary diagnosis and multimodal treatment is necessary.[8]

Lower Back Pain: Treatment

Treatment for LBP could be initiated once the patient's history type, severity of pain and etiology is decided, however, in most of the cases the LBP exercises forms the integral part of any treatment plan.[2,7] Pharmacological interventions for the treatment of LBP generally includes NSAIDS and muscle relaxants.

Non-steroidal Anti-inflammatory Drugs in Lower Back Pain

Acetaminophen and other nonsteroidal anti-inflammatory drugs (NSAIDs) as first-line treatment for most patients has been recommended by the American Pain Society and the American College of Physicians published guidelines in 2007 for low back pain. This recommendation has been made primarily due to the favorable side-effect profile NSAIDs compared with other options as opposed to superior efficacy. In the event of failure of first-line agent, skeletal muscle relaxants, benzodiazepines, and opioids could be administered based on evidence of temporary additional pain relief.[7]

Muscle Relaxant in Lower Back Pain

Although skeletal muscle relaxants owing to their antispasticity and antispasmodic action are useful in patients with LBP, they are not recommended as primary treatment. Overall, only 35% of patients are prescribed muscle relaxants, while 18.5% receive initial muscle relaxant therapy for nonspecific LBP. Many patients have experienced pain relief within several weeks of starting therapy with muscle relaxants for the treatment of acute back pain.[9,10] Skeletal muscle relaxants were found to be effective in the short-term relief of acute low back pain when compared with placebo in a systematic review.[10]

Is Combination of NSAID with Muscle Relaxant Effective in LBP?

Studies indicates that the combination of an NSAID with a muscle relaxant to be better than the NSAID alone.[11] In a study the combination of muscle relaxants plus analgesics or NSAIDs put together were found to be more effective than placebo plus analgesics or NSAIDs in patients with acute LBP for short-term pain relief along with the decrease of muscle spasm after 3 to 4 and 7 to 8 days. Furthermore, the combination of muscle relaxant plus NSAID group were found to have a statistically significantly fewer disability days than the placebo plus NSAID group. Another trial showed statistically significantly greater decrease of muscle spasm for muscle relaxant plus NSAIDs after 14 days, but no differences on pain intensity and global efficacy.[10]

Result

Robi-D: Potent Formulation for Instant Relief in Low Back Pain

Robi-D injection is a combination of methocarbamol (muscle relaxant) 300 mg and diclofenac sodium (analgesic) 50 mg intended to provide instant relief from LBP (Figure 2).

Fig. 2: Robi D Injection.

Clinical objective of Robi-D injection is to provide immediate therapeutic benefit from low back pain. Subsequently (after 3 weeks) Robinaxol D tablets will provide continuous therapeutic benefit in low back pain for long term.

Methocarbamol which is an oral and parenteral centrally acting muscle relaxant, is indicated as an adjunct to physical therapy for the relief of acute musculoskeletal pain. Methocarbamol is approved by the USFDA and has been in use since last 50 years without any serious adverse effects. Methocarbamol can be helpful specifically in patients who cannot tolerate the stronger sedative effects of other muscle relaxants.[9,12]

Methocarbamol is indicated in conditions wherein painful muscle spasms are needed to be reduced for patient comfort (intervertebral disc disease, for example). Additionally, methocarbamol is also indicated as treatment of choice for metaldehyde (snail bait) poisoning, a condition causing severe muscle twitching[13] Methocarbamol is also used indicated in tetanus and strichnine poisoning (characterized by stiffness and seizures)[14] and is well-established for the treatment of LBP associated with myofascial components.[15]

Methocarbamol acts on the internuncial neurons of the spinal cord resulting in a diminution of skeletal muscle hyperactivity without concomitant alteration in normal muscle tone.[16] Methocarbamol centrally inhibit muscle spasm thus give relief from low back pain. Since it is centrally acting it acts only on poly synaptic reflex (Figure 3).

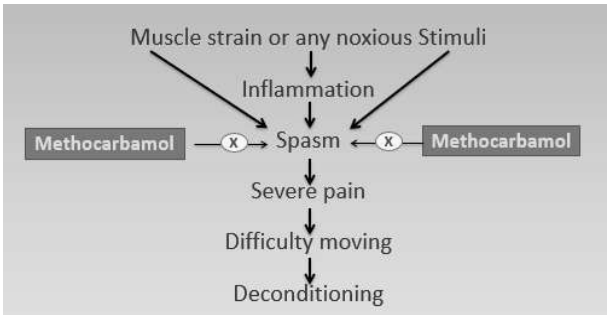

Fig. 3: Mechanism of Action of Methocarbamol.

On oral administration, methocarbamol is quickly and completely absorbed, andextensively metabolized by dealkylation and hydroxylation. The most common adverse events are light-headedness, dizziness, and drowsiness. The table showed that compared to its peers it showed faster onset of action and less adverse effects (Table 1).

Table 1: Methocarbamol Compared to its Peers Muscle Relaxants.

	Onset of Action	Adverse Effects	Dosage Forms
Methocarbamol	30 mins	Drowziness (rare), Dizziness	Oral, IM and IV
Thiocolchicoside	60 mins	Drowziness, Dizziness, Nausea, Headache, Epileptogenic	Oral and IV
Chlorzoxazone	60 mins	Hepatotoxicity, Gastric irritation	Oral
Tizanidine	60 mins	Hypotension	Oral

Apart from the US, methocarbamol is also approved and available for the 1st-line treatment of patients with muscle-related LBP in Germany and is the only approved muscle relaxant by the European Medicines Agency (EMA).[17]

Unlike other carbamates, methocarbamol is not known for its abuse potential.[9] Furthermore, studies comparing methocarbamol to Lorazepam (Ativan) and diphenhydra-mine (Benadryl), observed that methocarbamol causes increased "liking" responses along with mild sedative-like effects, and minor impairment of psychomotor and cognitive performance suggesting it be safe and non-habit forming.[19]

Diclofenac is an NSAID that acts by inhibiting prostaglandin synthesis by blocking of cyclooxygenase (COX). Diclofenac is used to treat pain and inflammatory disorders including musculoskeletal complaints.[20] On oral administration, diclofenac is rapidly and completely absorbed. The area under the plasma concentration-time curve (AUC) of diclofenac is proportional to the dose for oral doses between 25 to 150mg. Substantial concentrations of drug are attained in synovial fluid, which is the proposed site of action for NSAIDs.[21]

Robi-D, as a combination of muscle relaxant methocarbamol and NSAID diclofenac potentially breaks pain spasm pain cycle. As shown in Fig 4, methocarbamol inhibits muscle spasm and diclofenac sodium inhibits pain.

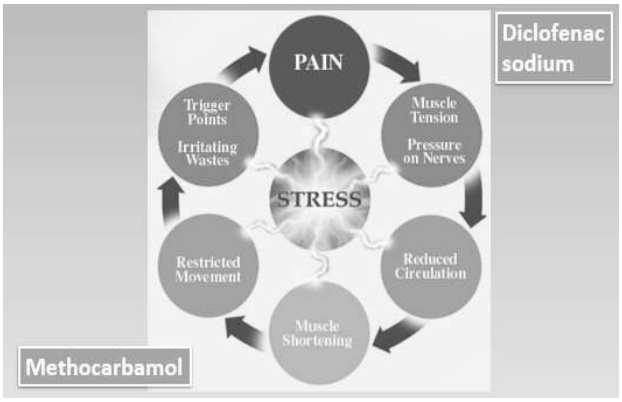

Fig. 4: Mechanism of Action of Robi-D.

Robi-D injection is indicated for the relief of pain and inflammation associated with Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis. Low back pain and other acute musculoskeletal disorders such as periarthritis, tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations and post-operative pain are other indications for use of Robi-D injection.

Robi-D Injection may be administered during acute or severe phase upto a maximum of 3 days or less until amelioration of acute symptoms. It should be replaced/continued by oral therapy subsequently i.e. Robinaxol D. For the indications mentioned, one ampoule of 3 mL can be administered thrice daily.

Intramuscular therapy with Robi D should be replaced by oral therapy subsequently. Robinaxol D oral tablets are available for oral administration. Robinaxol D oral tablets contain methocarbamol (muscle relaxant) + Diclofenac Potassium (analgesic) + paracetamol (analgesic).

Both active ingredients of Robi-D are approved from US FDA for therapeutic use. methocarbamol – US FDA approved muscle relaxant. Diclofenac sodium – US FDA approved analgesic. Khandelwal Labs has applied for Robi-D patent (Patent No. 416 MUM 2004) for Robi-D injection.Low back pain always needs immediate symptomatic relief for pain followed by the treatment of cause. Robi-D injection is the potential option for providing immediate relief from pain.

Conclusion

Robi-D is a combination of muscle relaxant methocarbamol and NSAID diclofenac that potentially breaks pain spasm and pain cycle. Robi-D injection is indicated for the relief of pain and inflammation associated with rheumatoid arthritis, osteoarthritis, ankylosing spondylitis.

Robi D Injection may be administered during acute or severe phase upto a maximum of 3 days or less until amelioration of acute symptoms. Both active ingredients of Robi D are approved from US FDA for therapeutic use. Methocarbamol – US FDA approved muscle relaxant. Diclofenac sodium – US FDA approved analgesic. Khandelwal Labs has applied for Robi D patent (Patent No. 416 MUM 2004) for Robi D injection. Low back pain always needs immediate symptomatic relief for pain followed by the treatment of cause. Robi-D injection is the potential option for providing immediate relief from LBP.

References

1. Ganesan, Sudhir, et al. "Prevalence and risk factors for low Back pain in 1,355 young adults: a cross-sectional study." Asian spine journal 11.4 (2017): 610.
2. Biyani, Ashok, and Gunnar BJ Andersson. "Low back pain: pathophysiology and management." JAAOS-Journal of the American Academy of Orthopaedic Surgeons 12.2 (2004): 106-115.
3. Bindra, Supreet, A. G. K. Sinha, and A. I. Benjamin. "Epidemiology of low back pain in Indian population: a review." Int J Basic Appl Med Sci 5.1 (2015): 166-179.
4. Jana, Arumay, and Asish Paul. "Epidemiology of low back pain: A literature review." International Journal of Physical Education, Sports and Health 6(3) (2019): 233-237.
5. Fatoye, Francis, Tadesse Gebrye, and Isaac Odeyemi. "Real-world incidence and prevalence of low back pain using routinely collected data." Rheumatology international 39.4 (2019): 619-626.
6. Meucci, Rodrigo Dalke, Anaclaudia Gastal Fassa, and Neice Muller Xavier Faria. "Prevalence of chronic low back pain: systematic review." Revista de saude publica (2015): 49-73.
7. Chou, Roger, et al. "Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society." Annals of internal medicine 147.7 (2007): 478-491.
8. Allegri M, Montella S, Salici F et al. Mechanisms of low back pain: a guide for diagnosis and therapy [version 2; referees: 3 approved] F1000Research 2016, 5(F1000 Faculty Rev):1530.
9. Witenko, Corey, et al. "Considerations for the appropriate use of skeletal muscle relaxants for the management of acute low back pain"." Pharmacy and therapeutics 39.6 (2014): 427.
10. Van Tulder, Maurits W., et al. "Muscle relaxants for nonspecific low back pain: a systematic review within the framework of the cochrane collaboration." Spine 28.17 (2003): 1978-1992.
11. Roelofs, Pepijn DDM, et al. "Non-steroidal anti-inflammatory drugs for low back pain. Cochrane database of systematic reviews". Spine 33 (2008):1766–1774.
12. Sica, D. A., et al. "Pharmacokinetics and protein binding of methocarbamol in renal insufficiency and normals." European journal of clinical pharmacology 39.2 (1990): 193-194.
13. Dolder, Linda K. "Metaldehyde toxicosis." Veterinary Medicine 98.3 (2003): 213-215.
14. Utterback, Robert A., and Phillip H. Tenney. "Methocarbamol in the Therapy of Tetanus." Archives of neurology 9.5 (1963): 555-560.
15. Emrich, O. Milachowski, K. A. Milachowski, and M. Strohmeier. "Methocarbamol in acute low back pain. A randomized double-blind controlled study." MMW Fortschritte der Medizin 157 (2015): 9-16. [Abst.]
16. O'Doherty, Desmond S., and Charles D. Shields. "Methocarbamol-new agent in treatment of neurological and neuromuscular diseases." Journal of the American Medical Association 167.2 (1958): 160-163.
17. Überall, M. A., O. M. D. Emrich, and G. H. H. Müller-Schwefe. "Real-life efficacy and tolerability of methocarbamol in patients suffering from refractory muscle-related low/back pain-Results of a health care research project based on data from the German pain practice registry." MMW Fortschritte der Medizin 159.Suppl 7 (2017): 6-17.[Abst.]
18. Emrich, O. Milachowski, K. A. Milachowski, and M. Strohmeier. "Methocarbamol in acute low back pain. A randomized double-blind controlled study." MMW Fortschritte der Medizin 157 (2015): 9-16. [Abst.]
19. Preston, Kenzie L., et al. "Subjective and behavioral effects of diphenhydramine, lorazepam and methocarbamol: evaluation of abuse liability." Journal of Pharmacology and Experimental Therapeutics 262.2 (1992): 707-720. [Abst.]
20. Gan, Tong J. "Diclofenac: an update on its mechanism of action and safety pr1ofile." Current medical research and opinion 26.7 (2010): 1715-1731.
21. Davies, Neal M., and Keith E. Anderson. "Clinical pharmacokinetics of diclofenac." Clinical pharmacokinetics 33.3 (1997): 184-213. [Abst.]