Section A-Research paper

A COMPREHENSIVE REVIEW OF CERVICAL STENOSIS DIAGNOSIS AND TREATMENT

GASI.SAI SRI LAKSHMI[1], Dr.CH.SUPRIYA[2], KONDUMAHANTHI.V N LAKSHMI[3], V.L.ANUSHA[3], P.SWARNA[4], P. BHANU SASANK[4], SK. SHARMILA[4], B.SRI DURGA[4], K. JAGADEESH[4], M. BHARATH CHANDRA SIVA SAI[4],

[1] Associate Professor, Department of Pharmaceutical Analysis, Nirmala College of Pharmacy, Mangalagiri,Guntur District, Pin 522503.

[2] Associate Professor, Department of Pharmaceutics, Nirmala College of Pharmacy, Mangalagiri, Guntur District, Pin 522503.

[3] Assistant Professor, Department of Pharmacology, Nirmala College of Pharmacy, Mangalagiri, Guntur District, Pin 522503.

[3]Associate Professor, Department of Pharmacology, Sims College of Pharmacy, Mangaldas Nagar, Guntur, Andhra Pradesh-522509.

[4] Nirmala College of Pharmacy, Mangalagiri, Guntur District, Pin 522503.

CORRESPONDING AUTHOR:

GASI. SAI SRI LAKSHMI
ASSOCIATE PROFESSOR
DEPARTMENT OF PHARMACEUTICAL ANALYSIS
NIRMALA COLLEGE OF PHARMACY
MANGALAGIRI.
522503
Email- sailakshmi405@gmail.com
PH.No. -8886789106

ABSTRACT

The condition known *as cervical stenosis* occurs when the spinal cord space is insufficient for the nerve roots and spinal cord. This may harm the spinal cord, a disorder known as *myelopathy*, or compress nerves as they leave the spinal canal, a condition known as *Radiculopathy*, with cervical spinal stenosis, the nerve roots are compressed by a variety of pathogenic conditions, resulting in symptoms like pain, weakness, and numbness. Each level of compression can result in a different set of symptoms depending on which region of the spine is being compressed, which calls for a specific type of treatment. This exercise

discusses the diagnosis and treatment of spinal stenosis as well as the function of the interprofessional team in enhancing patient care.

KEYWORDS: Cervical stenosis, prevention, epidemiology, pathophysiology, history, clinical anatomy, surgical treatment.

INTRODUCTION

Cervical stenosis is a common cause of neck pain. It takes place as changes take place in the neck's vertebrae and the joints that connect them. The development of bone spurs results in cervical spinal stenosis. The spinal canal becomes more constrained as the bone spurs spread, placing pressure on the spinal cord and nerves. The three primary forms are central spinal stenosis, lateral recess stenosis, and foraminal stenosis, each of which can affect the cervical, thoracic, or lumbar regions of the spine. In medical literature, cervical spinal stenosis is divided into two categories: congenital, which affects young, active patients, and acquired, which affects middle-aged and older patients. The mid-cervical spinal canal's typical sagittal diameter ranges from 17 to 18 mm. Relative stenosis is defined as less than 13mm, whereas absolute stenosis is less than 10 mm. (1)

CAUSES OF SPINAL STENOSIS

- The normal anatomy of the spine gradually deteriorates with age and age-related alterations to the spine over time.
- Arthritis. Spinal stenosis is frequently caused by arthritis as well (2).
- Genetic conditions.
- Causes of spinal stenosis include (3):
    - Bone spur
    - Herniated disks
    - Thick ligaments
    - Tumors
    - Spinal injuries

SYMPTOMS OF CERVICAL STENOSIS

- Degeneration, or wear and tear, affecting the anatomical components I your neck as a result of aging is a common cause of cervical spinal stenosis. Because of this, adults in their 50s and 60s who may have suffered from neck pain for a long time constitute the majority of patients with cervical spinal stenosis (figure 1) (4).
- As the illness worsens, coordination loss and weakness of the arms and hands are possible. Along with weakness and numbness in the legs and feet, which can make walking difficult, progressive cervical stenosis can also create issues with bowel and bladder function.

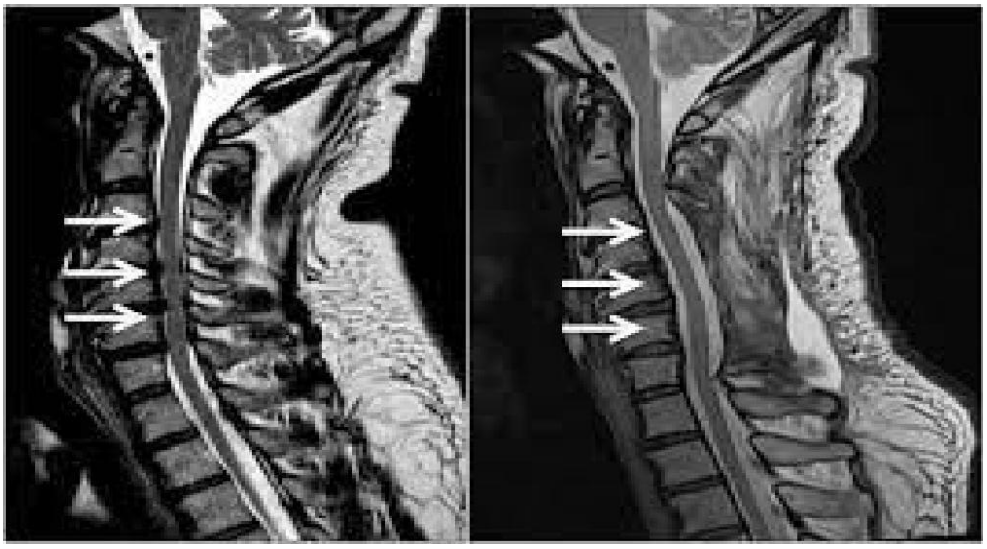

Figure 1: Site of stenosis occurring at Cervix of spinal cord

- Cervical stenosis can affect CSF flow, which can lead to a rise in intracranial pressure and the accumulation of waste materials. Headaches and other neurological flaws are the symptoms that follow. Additionally, it can exacerbate dementias such as Alzheimer's.

PREVENTION OF CERVICAL STENOSIS

- ✓ Your back is to maintain excellent posture and to use the right body mechanics. It's important to always maintain good body mechanics, whether you're standing, or lifting something heavy, the greatest techniques to stop stenosis from getting worse, and to maintain health or even sleeping (5).
- ✓ Physiotherapy is a successful method of reducing cervical stenosis symptoms.

EXERCISE FOR CERVICAL STENOSIS

i. Cervical flexion. Tilt your head down until your chin just about reaches your chest.
ii. Side bends. Tilt your head slowly to one side until your ear almost touches your shoulder.
iii. Cervical rotation.
iv. Chin tuck.
v. Median nerve slider.
vi. Shoulder shrugs.

EPIDEMIOLOGY INCLUDING RISK FACTORS

- Cervical spondylosis is a common condition in asymptomatic people, with prevalence rates between 14% and 24.2% reported in more recent investigations (6).
- Individuals displaying symptoms have been reported to have prevalence rates close to 81%.
- Research in *Hong Kong*that included samples of older individuals found that 98% of them had degenerative abnormalities in at least one level of their cervical spine (7).

- Risk factors for developing cervical stenosis include aging, female sex, obesity, playing American football, soccer, rugby, or riding horses are all risk factors for cervical stenosis, as are serious trauma and cerebral palsy with dystonic muscle tone (8),(9).

PATHOPHYSIOLOGY

Numerous ideas regarding the pathophysiology of spinal stenosis suggest several confluent mechanisms:

- ✓ The compression of local vascular systems can cause arterial insufficiency and venous stasis, which can result in spinal cord ischemia.
- ✓ Osteophytic bones and ligamentous hypertrophy can directly compress the spinal cord.
- ✓ Particularly in an unstable spine with many degrees of subluxations, a herniated disc can cause repeated local trauma to the spinal cord or nerve root during repetitive flexion and extension movements.
- ✓ Segments C5-6 and C6-7 of the cervical spine are frequently impacted (10).
- ✓ Mechanical and ischemic spinal cord insults both contribute to neuronal degeneration in cervical stenosis.
- ✓ Early issues with walking, balance, and proprioception may beexplained by dynamic shortening of the posterior cord(dorsal columns) in extension.
- ✓ Upper extremity (i.e., hand) symptoms are mostly caused by grey and white matter demyelination, which is a result of chronic *Cervical SpondyloticMyelopathy*(CSM).
- ✓ This is a result of the cervical spinal cords somatotopic organization, which makes the ventral horn motor neuron cell bodies more lateral and the lateral cortical spinal tracts more medially suspectable to mechanical compression.
- ✓ The anterior spinal artery's compressed arterioles contribute to cord ischemia that results in secondary free radical-mediated cell damage and apoptosis.

HISTORY

Natural History of Mild Cervical Spondylotic Myelopathy:

- ❖ Osteoarthritic degeneration of the cervical spine is referred to as cervical spondylosis. Radiculopathy or myelopathy symptoms, according to Brain et al., could be the result of disc protrusion and related soft tissue abnormalities (11,12)
- ❖ Even though degeneration can develop as a result of numerous factors, years of motion and activity, sometimes known as "wear and tear," is the most typical cause. Numerous studies have demonstrated in both human and animal models that recurrent micro trauma and excessive motion hasten degenerative processes (13,19).
- ❖ The cervical spine's canal diameter and sagittal mobility are also impacted by the accumulating degenerative alterations (20). Additionally, having a congested, narrow spinal canal may make someone more susceptible to developing CSM (21-24).

- According to current knowledge, cervical spondylosis includes degenerative alterations that affect the facet joints, intervertebral discs, uncovertebral joints, and other soft tissues and bony parts of the cervical spine.
- Spondylosis has been demonstrated to frequently start at lower levels and develop into involve numerous spinal levels, even though it may only affect one level(25).
- While the advice for surgical treatment of patients with severe, progressing myelopathy seems apparent, it is less clear how to treat individuals with cervical spondylosis and extremely modest myelopathy symptoms.
- Many publications have description have provided descriptions of the clinical trajectory of patients with cervical spondylosis symptoms. Author at first endorsed clinical stability in this group of patients (26).
- *Clarke and Robinson* described 120 in retrospect. 26 patients with CSM received conservative care. Approximately 80% of these individuals had sensory loss or paralysis in one or more limbs, and 18% had discomfort.
- According to *Clarke and Robinson's* research, while two-thirds of patients exhibited mild clinical decline during periods of stability, about 75% of patients exhibited episodic progressions of symptoms with intervening stability.
- 20% of patients had a gradual decline in health. In 5% of cases, there was a long period of stability without any further deterioration after the onset of symptoms and signs (26).
- Overall, the clinical course of almost half of the patients with conservative management improved.
- According to a review of the literature, cervical myelopathy has a variable clinical history, and most individuals with modest symptoms may benefit from stabilizing or improving their symptoms with conservative therapy (27-31).
- It is still challenging to predict the clinical course of a single patient, even if some evidence indicates that younger patients and those with modestly better chances of symptom improvement exist (32).

CLINICAL RELEVANT CERVICAL ANATOMY

The neural components often have ample area in the cervical spinal canal. With height and between individuals, the spinal canal's sagittal diameter varies. The spinal cord occupies almost 50% of the spinal canal and the first cervical vertebral body(C 1) is 21.8 mm high. On the other hand, the spinal cord occupies roughly 75% of the spinal cord at C 6, which is around 17.8 mm tall(figure2) (33).

- At all levels, the average anterior-posterior canal diameters are 14.1 +/- 1.6 mm.
- With a median diameter of 14.4 mm, canal diameter ranges from 0.9 to 20.9 mm.
- At every level, men's cervical spinal canals are noticeably larger than women's (34).

Space-occupying lesions frequently have subsequent effects, such as stenosis, for example:

- Progressive disc generation with disc protrusion,
- Spondylophyte development in the ventral region,
- Thickening of the ligament flavum, and dorsal facets hypertrophy.

The spinal canal and cord's diameter are influenced by movement:

- In flexion and extension, the spinal canal's diameter decreases.

- The ligamentum flavum folds during extension, significantly narrowing the spinal canal.
- The spinal cords length is influenced by changes in the spinal canal's size as well. For instance, the spinal cords shortening in extension is associated with an increase indiameter and can suffer further harm from movement. It is compressed between the lamina or ligamentum flavum of the caudal segment and the pincers of the posteroinferior end of one vertebral body (figure 3) (34).

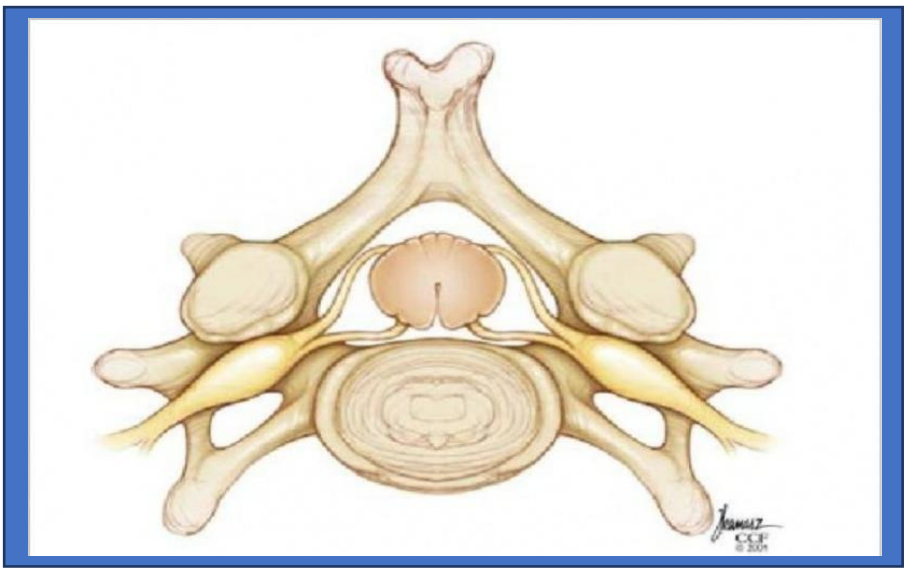

Figure 2: Normal Cervical Vertebrae

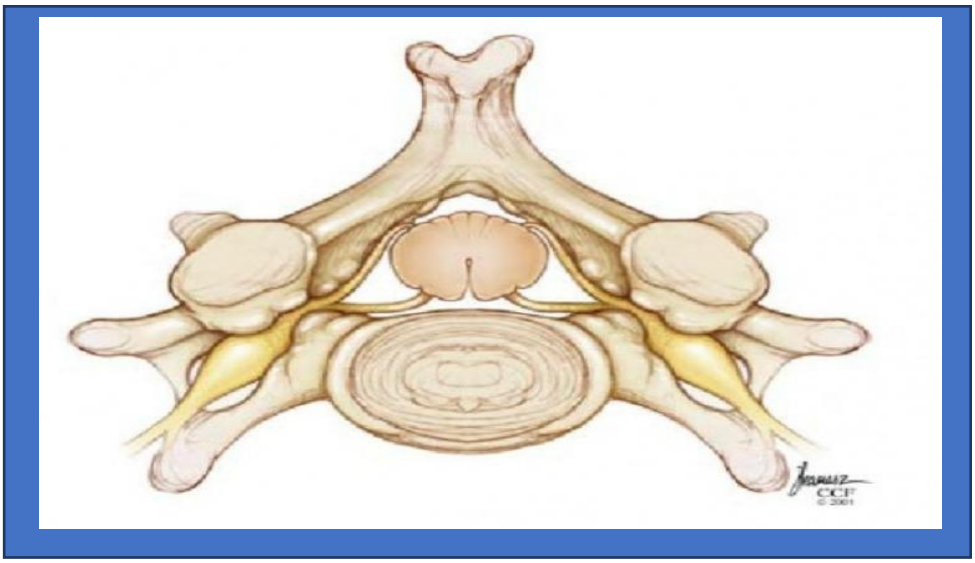

Figure 3: Cervical stenosis

CLINICAL PRESENTATION

A thorough history of symptoms and physical examination with an emphasis on sensation, motor function, reflexes, and gait are frequently the first steps in a patient with spinal stenosis's initial evaluation (35).

- While symptoms may be brought on by cervical stenosis, they are more likely to be brought on by concomitant cervical radiculopathy or cervical myelopathy.
- Gait disruption, lower extremity weakness, and ataxia are symptoms of cervical spondylotic myelopathy, which can be present in patients with more than 30% spinal constriction.

Radiculopathy symptoms depend on the level affected, for example, a C5 disc herniation results in C6 radiculopathy. Cervical spinal stenosis can cause myelopathy owing to spinal cord compression and nerve root compression can cause radicular symptoms.

- Shoulder paresthesia and deltoid weakness might result from a herniated C4-5 disc. The head, neck, and shoulder are some areas where patients may have pain and paresthesia.
- The most frequent type C6-7-disc herniation causes a wrist drop and paresthesia in the second and third digits.
- The next most frequent condition is C5-6-disc herniation, which causes paresthesia in the thumb and radial forearm as well as weakness in forearm flexion.
- A C7-T1 disc herniation may cause numbness and weakness in the fourth and fifth fingers of the hand.

Possible signs include (36), (37), (38):

- Ache in the arms or neck
- Hand weakness
- Stiffness, or clumsiness weakened
- Leg having trouble walking
- Recurring falling urinary urgency that could eventually affect the bladder and intestines incontinence of the urine diminished proprioception.

The following variations in symptom progression may also occur:

- A constant deterioration over time development up to a point, then stabilization accelerating decline.

SURGICAL TREATMENT

- **Cervical corpectomy:** cervical cleft palate to stabilize the spine, a portion of the vertebrae and discs are removed and replaced with a bone graft or a metal plate and screws. Depressive laboratories the vertebral column's roof, also known as the lamina, is removed surgically.
- **Anterior Cervical Discectomy and Fusion (ACDF):** For many years, this procedure has been regarded as the gold standard for treating stenosis. For the right indications and with competent surgical technique, it is typically quite successful.
- **Endoscopic Spine Surgery:**Endoscopic spine surgery is a true game-changer; this ultra-minimally invasive procedure relieves the excruciating nerve pressure and allows you to resume your normal activities.
- **Decompressive Laminectomy:** The most popular and effective for treating lumbar spinal stenosis symptoms is a decompressive laminectomy.

TREATMENT

ORAL MEDICATIONS:

- ✓ **Nonsteroidal anti-inflammatory medications(NSAID) –** such as ***Ibuprofen***(Advil, Motrin), ***Naproxen*** (Aleve), ***Aspirin, or Acetaminophen***(Tylenol) can help relieve inflammation and provide pain relief from spinal stenosis.
- ✓ Best options include ***Baclofen, Cyclobenzaprine, and Methocarbamol. Baclofen*** is an antispastic drug that's widely used to treat muscle spasms in spinal cord conditions, including lumbar spinal stenosis.

IBUPROFEN

Ibuprofen (figure 4) is a nonsteroidal anti-inflammatory medicine that is used to treat inflammation, fever, and pain. This includes rheumatoid arthritis, migraines, and painful menstrual cycles. It can be used to close a premature baby's patent ductus arteriosus. It can be administered intravenously or orally.Usually, it starts working after an hour (39). It is a weaker anti-inflammatory agent than other NSAIDs (40).

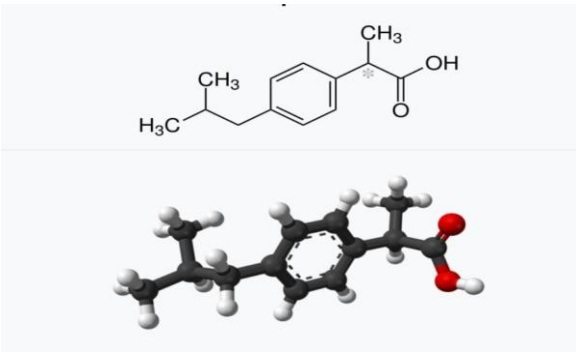

Figure 4: Structure of Ibuprofen

MECHANISM OF ACTION:

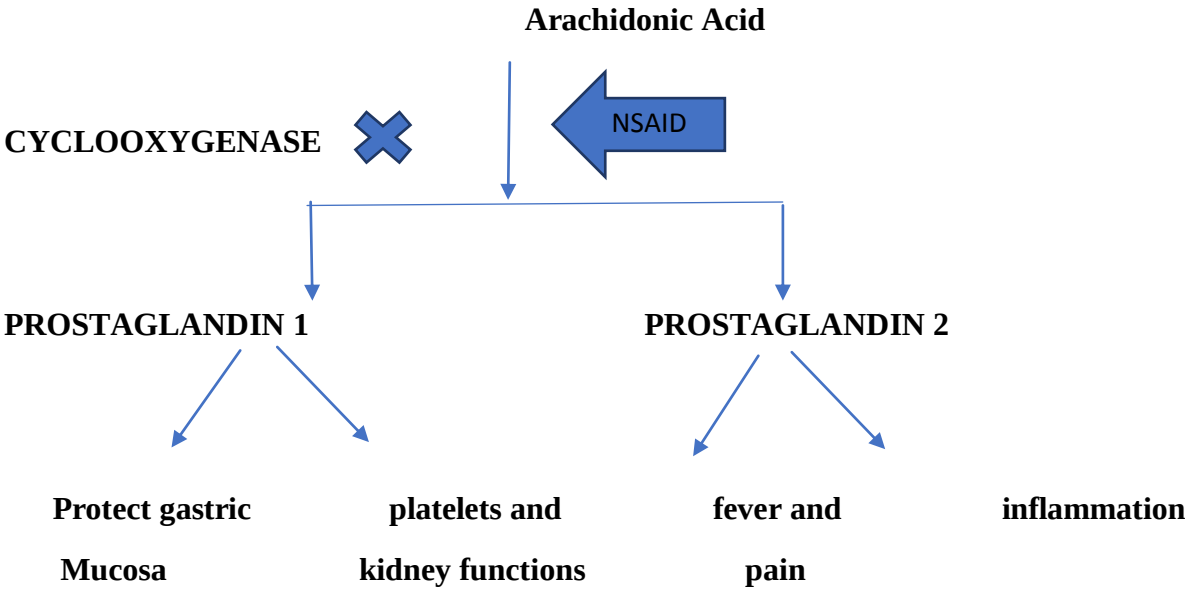

Figure 5: mechanism of action of ibuprofen

NAPROXEN

Naproxen (figure 6) is anNSAID used to treat pain, menstrual cramps, and inflammatory illnesses such as rheumatoid arthritis, gout, and fever. It is also marketed under the trade name Aleve among others. It is consumed orally. It is offered in formulations for both immediate and delayed release. Effecbeginins take action within an hour and can last up to twelve hours (41).

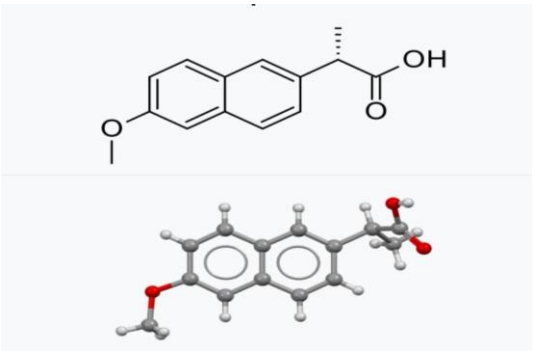

Figure 6: Structure of Naproxen

ASPIRIN

Acetylsalicylic acid (ASA), generally known as aspirin (figure 7), is anNSAID used to treat inflammation, fever, and or pain as well as a blood thinner. Aspirin is used to treat a variety of inflammatory disorders, including Kawasaki disease, pericarditis, and rheumatic fever (42). In 2020, it was the 36th most commonly prescribed medication in the United States, with more than 17 million prescriptions (43).

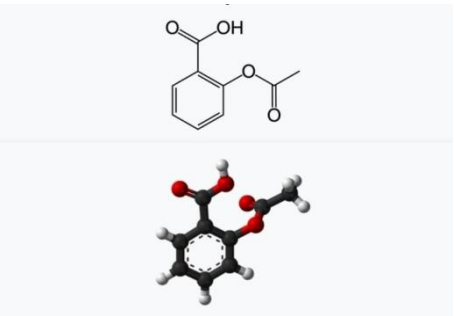

Figure 7: Structure of Aspirin

BACLOFEN

A drug called baclofen (figure 8), also known by the brand name *Lioresal*, is treat muscle spasticity, which can result from multiple sclerosis or a spinal cord injury (45), (46). Near the end of life, it can also be used for hiccups and muscle spasms. It can be administered orally or directly into the spinal canal (46).

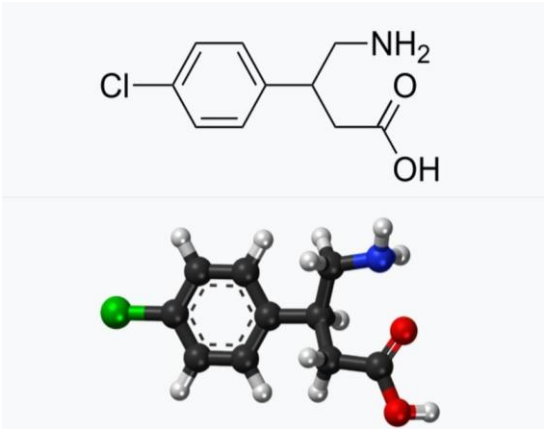

Figure 8: Structure of Baclofen

CYCLOBENZAPRINE

A muscle relaxant called *Cyclobenzaprine*(figure 9*)*, which is marketed under the trade names Flexeril and others, is used to treat sudden-onset musculoskeletal diseases that cause muscle spasms. In cerebral palsy, it serves no use. It is consumed orally. It is not advised to use it for longer than a few weeks (47).

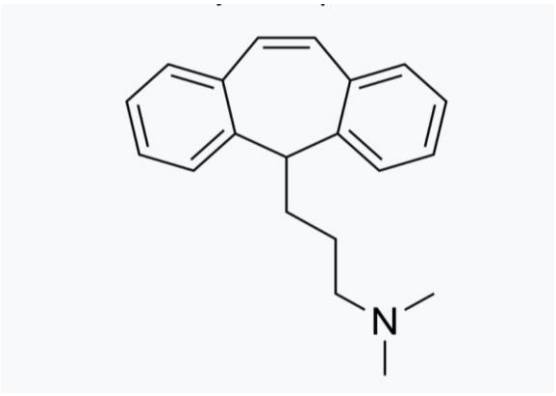

Figure 9: Structure of Cyclobenzaprine

METHOCARBAMOL

Methocarbamol (figure 10) is a drug used to treat temporary musculoskeletal discomfort; it is marketed under the trade names Robaxin and others. It can be combined with rest, physical treatment, and painkillers. In low back discomfort, it is less preferred. Its application in treating cerebral palsy and rheumatoid arthritis is restricted. Effects often start after 30 minutes. It can be consumed orally or administered intravenously (48).

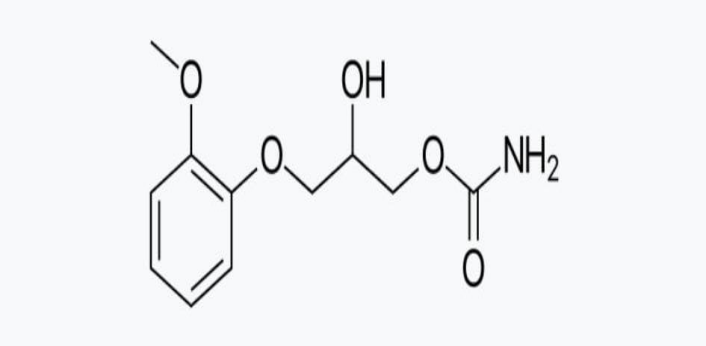

Figure 10: Structure of Methocarbamol

REFERENCES

1. Wolf BS, Khilnani M, Malis L. The sagittal diameter of the bony cervical spinal canal and its significance in cervical spondylosis. Journal of the Mount Sinai Hospital, New York. 1956; 23(3):283-292. Accessed March 13, 2021.
2. Spinal stenosis: In-depth. National Institute of Arthritis, Musculoskeletal and Skin Diseases. https://www.niams.nih.gov/health-topics/spinal-stenosis. Accessed May 9, 2022.
3. AskMayoExpert. Cervical spinal stenosis(causes). Mayo Clinic; 2021
4. Crandall PH, Batzdorf U. Cervical spondylotic myelopathy. J Neurosurg. 1966; 25:57-66. [Pub Med] [Google Scholar].
5. Smith SS, Stewart ME, Davies BM, Kotter MRN. The prevalence of Asymptomatic and Symptomatic Spinal Cord Compression on Magnetic Resonance Imaging: A Systematic Review and Meta-analysis. Global Spine Journal. Published online 2020.doi:10.1177/2192568220934496.
6. Wang X-R, Kwok TCY, Griffith JF, Yu BWM, Leung JCS, Wang YXJ. Prevalence of cervical spine degenerative changes in the elderly population and its weak association with aging, neck pain, and osteoporosis. Annals of translational Medicine. 2019;7(18):486-486. Doi:10.21037/atm.2019.07.80.
7. Kelly JC, Groarke PJ, Butler JS, Poynton AR, O'Byrne JM. The Natural History and clinical syndromes of Degenerative Cervical Spondylosis. Advances in orthopedics. 2012;2012:1-5. Doi:10.1155/2012/393642.
8. Lv Y, Tian W, Chen D, Liu Y,Wang L, Duan F. The prevalence and associated factors of symptomatic cervical spondylosis in Chinese adults: A community-based cross-sectional study. BMC Musculoskeletal Disorders.2018;19(1):1-12. Doi:10.1186/s12891-018-2234-0.
9. Raja A, Hanna A, Hoang S,Mesfin FB. Spinal Stenosis dec 2019.Available from:http://www.ncbi.nlm.nih.gov/books/NBK441989/ (last accessed 3.2.2020).
10. W.R. Brain, G.C. Knight, and J.W.D. Bull, "Discussion of rupture of the intervertebral disc in the cervical region," Proceedings of the Royal Society of Medicine, vol. 41, no.8, pp. 509-28, 1948. View at: Google Scholar
11. W.R.Brain, D.Northfield, and M. Wilkinson, "The neurological manifestations of cervical spondylosis," Brain, vol. 75, no. 2, pp. 187-225, 1952.
View at Publisher site/ Google Scholar.

12. J. Berge, B. Marque, J. M. Vital, J. Senegas, and J.M. Caille, "Age-related changes in the cervical spines of front-line rugby players," American Journal of Sports Medicine, vol. 27, no.4, pp.422-429, 1999. View Google Scholar.
13. S. Ebara, Y. Yamazaki, T. Harada, et al., "Motion analysis of the cervical spine in athetoid cerebral palsy. Extension-flexion motion," Spine, vol. 15, no.11, pp. 1097-1103, 1990.
View at: Publisher site/ Google Scholar
14. R. S. El-Mallakh, K. Rao, and M. Barwick, "Cervical myelopathy secondary to movement disorders: case report," Neurosurgery, vol. 24, no.6, pp. 902-905, 1989.
View at: Google Scholar
15. P. M. Olive, T. S. Whitecloud 3rd, and J. T. Bennett, "Lower cervical spondylosis and myelopathy in adults with Down's syndrome," Spine, vol. 13, no.7, pp. 781-784, 1998.
View at: Google Scholar
16. L. Pollak, J.Schiffer, C. Klein, Y. Mirovsky, L. Copeliovich, and J. M. Rabey, "Neurosurgical intervention for cervical disk disease in dystonic cerebral palsy," Movement Disorders, vol.13, no.4, pp.713-717, 1998.
View at: Publisher Site/ Google Scholar
17. K. L. Quarrie, R. C. Cantu, and D. J. Chalmers, "Rugby Union injuries to the cervical spine and spinal cord," Sports Medicine, vol. 32, no. 10, pp. 633-653, 2002.
View at: Google Scholar
18. E. Wada, S. Ebara, S. Saito, and K. Ono, "Experimental spondylosis in the rabbit spine: overuse could accelerate the spondylosis," Spine, vol. 17, no. 3, supplement, pp. S1-S6, 1992.
View at: Google Scholar
19. Y. Morishita, M. Naito, and J. C. Wang, "Cervical spinal canal stenosis: the difference between stenosis at the lower cervical and multiple segment levels," International Orthopaedics, vol. 35, no.10, pp. 1-6, 2011.
View at: Publisher Site/ Google Scholar
20. W. C. Edwards and H. La Rocca, "The development segmental sagittal diameter of the cervical spinal canal in patients with cervical spondylosis," Spine, vol. 8, no. 1, pp. 20-27, 1983.
View at: Google Scholar
21. D. R. Gore, "Roentgenographic findings in the cervical spine in asymptomatic persons: a ten-year follow-up," Spine, vol. 26, no. 22, pp. 2463-2466, 2001.
View at: Publisher Site/ Google Scholar
22. H. Hayashi, K. Okada, and M. Hamada, "Etiologic factors of myelopathy. A radiographic evaluation of the aging changes in the cervical spine," Clinical Orthopaedics and Related Research, vol. 214, no. 214, pp. 200-209, 1987.
View at: Publisher Site/Google Scholar
23. J. S. Torg, R. J. Naranja, H. Pavlov, B. J. Galinat, R. Warren, and R. A. Stine, "The relationship of developmental narrowing of the cervical spinal canal to reversible and irreversible injury of the cervical spinal cord in football players," Journal of Bone and Joint Surgery. Series A, vol. 78, no.9, pp. 1308-1314, 1996.
View at: Google Scholar

24. Ramu Samineni, G Ramakrishna, M Balaji, K Kondala Rao. Formulation and evaluation of sumatriptan succinate mouth disintegrating tablets. American J Advanced Drug Delivery. 2013; 1(5): 759-769.
25. Z.Kadanka, M Mares, J.Bednarik, et al., "Approaches to spondylotic cervical myelopathy: Conservative versus surgical results in a 3- year follow up study," Spine, vol. 27, no. 20, pp. 2205-2210,2002.
View at: Publisher site/ Google Scholar.
26. T. Shimomura, M. Sumi, K. Nishida, et al.,"Prognostic factors for deterioration of patient with cervical spondylotic myelopathy after nonsurgical treatment," Spine, vol. 32, no. 22, pp. 2474-2479,2007.
View at: Publisher site/Google Scholar
27. J. A. Epstein, Y. Janin, R. Carras, and L. S. Lavine, "A comparative study of the treatment of cervical spondylotic myeloradiculopathy. Experience with 50 cases treated using extensive laminectomy, foraminotomy, and excision of osteophytes during the past 10 years," Acta Neurochirurgica, vol. 61, no. 1-3, pp. 89-104, 1982.
28. P. Sampath, M. Bendebba, J.D. Davis, and T. B. Ducker, "Outcome of patients treated for cervical myelopathy: a prospective, multicenter study with the independent clinical review." Spine, vol. 25, no. 6, pp. 670-676, 2000.
29. R. Murthy, I. Moledina, L. Mc Evoy, et al., "The natural history of cervical myelopathy," European Spine Journal, vol. 19, no. 3, pp. 517, 2009.
30. D Srinivasa Rao, S Haranadh Reddy, S Ramu, E Rambabu. Preparation and evaluation of mucoadhesive microspheres of simvastatin by ionic gelation technique. American Journal of Advanced drug delivery. 2014; 2(5): 594-608.
31. Meyer F, Borm W, Thome C. Degenerative cervical strategies in diagnosis and treatment. DeutschesArzteblatt International. 2008 May;105(20):336.
32. Lee MJ. Cassinelli EH, Riew KD. Prevalence of cervical spine stenosis: an anatomic study in cadavers. JBJS.2007 Feb 1;89(2):376-80.
33. Raja A, Hanna A, Hoang S, Mesfin FB. Spinal Stenosis dec 2019. Available from: http://www.ncbi.nlm.nih.gov/books/NBK441989/ (last accessed 3.2.2002).
34. North American Spine Society Public Education Series. Cervical stenosis and myelopathy. http://www.spine.org/Documents/cervical_stenosis_2006.pdf (Accessed 22 November 2011).
35. Williams SK, et al. Concomitant cervical and lumbar stenosis: Strategies for treatment and outcomes. Semin Spine Surg 2007;19(3):165-176.
36. Countee RW, et al. Congenital Stenosis of the cervical spine: Diagnosis and Management. J Nati Med Assoc1979;71(3):257-264.
37. "Ibuprofen". The American Society of Health-System Pharmacists. Archived from the original on 9 September 2017. Retrieved 12 October 2016.
40. S Ramu, P Suresh, D Srinivasa Rao, G Ramakrishna. Formulation and Evaluation of Floating Microspheres of Rosiglitazone. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2015; 5(4): 907-918.
41. "Naproxen monograph for professionals". Drugs.com. AHFS. Retrieved 19 December 2018.
42. "Aspirin". American Society of Health-System Pharmacists. 29 November 2021. Archived from the original on 25 April 2017- via Drugs.com.
43. "The Top 300 of 2020". US Government. Retrieved 7 October 2022 – via ClinCalc.

44. S Ramu, P Chandra Gopal Reddy, D Srinivasa Rao, G Ramakrishna. Formulation and Evaluation of Lansoprazole Delayed Release Pellets. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2015; 5(4): 860-878
45. "Baclofen Monograph for Professionals". Drugs.com. American Society of Health-System Pharmacists. Retrieved 3 March 2019.
46. British National Formulary: BNF 76(76 ed.). Pharmaceutical Press. 2018. P. 1092. ISBN 9780857113382.
47. Ramu Samineni, Jithendra Chimakurthy, Sathish Konidala. Emerging Role of Biopharmaceutical Classification and Biopharmaceutical Drug Disposition System in Dosage form Development: A Systematic Review. Turkish Journal of Pharmaceutical Sciences. 2022; 19(6): 706-713.DOI: https://doi.org/10.4274/tjps.galenos.2021.73554
48. S Ramu, Y Ashok Kumar, D Srinivasa Rao, G Ramakrishna.Formulation and evaluation of Valsartan oral dispersible tablets by direct compression method. American Journal of Advanced Drug Delivery. 2014; 2(6): 719-733.