

Pain Management: An Overview

Mehjabeen Fatimah¹, Rahida Hilal^{2*}, S.S.Alam¹, Junaid Nazir Dandroo¹, Samreen Khan³

¹Department of Jarahiyat, NIUM, Bangalore-91,

²Department of Jarahat, AKTC, AMU, Aligarh,

³Department of IBT, NIUM, Bangalore-91,
India.

*Email: rahidahilal@gmail.com

Abstract

Pain is an unpleasant sensory and emotional experience caused by actual or potential tissue damage. This damage is nature's warning that something is not well within the body. This condition causes loss of workforce and also affects the patients family members in socio-economical and psychological terms. There is an increase in knowledge regarding pain management in recent years. These developments in pain management may provide different opportunities to the patient and their families to lead a more comfortable and productive life. Managing pain is not about making it disappear rather it is about keeping it under control. The aim is not to stop pain in its stride, but to avert the damage caused by it. Prolonged pain is demoralising and debilitating and should be controlled as fast as possible and with all possible means. For this reason in addition to pharmacological treatment now a days non pharmacological treatment options are on rise.

Keywords

Pain, Tissue damage, Pharmacological interventions, Non-pharmacological interventions.

1. INTRODUCTION

According to International Association for

the study of pain (IASP), pain is “ an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (IASP, 1979).

The word pain comes from the Latin word ‘Poena’, meaning punishment. From times immemorial, pain was considered as form of punishment meted out by God for the sins committed by man. The word pain brings to one's mind misery and suffering.

The physician Albert Schweitzer, proclaimed in 1931 that, “pain is a more terrible lord of mankind than even death itself” (Ranjani, 2016).

Although there is an increase of knowledge and developments in technological resources regarding the pain, many patients still experiences it. This situation causes for reduction in living quality and functional situations of the patients, increase in the fatigue levels and impairment in daily life activities in working capacity and social interactions (Nash *et al.*, 1999; McMillan, 2000).

There are various remedies for pain management, either pharmacological or non pharmacological interventions, but they all do not necessarily work for everyone. As people respond differently to the same pain stimuli according to their respective thresholds, an

analgesia which can produce dramatic pain relief in one person, may be perceived as relatively ineffective by another.

Pain is known as *Waja'* in Unani system of medicine, it is an Arabic word and described as disturbed perception of body. According to Jalinoos (Galen), the main cause of pain is breach in continuity only, but Ibn Sina (Avicenna) stated that any changes in the temperament (*Sue Mizaj Mukhtalif*) or/and breach in continuity (*Tafarruqe Ittesal*) as well is the cause of pain.

The *Sue Mizaj Mukhtalif* may be *sada* (simple) or *maddi* (humoral). *Sue Mizaj Maddi* which is associated with the substance or matter may be *Sue Mizaj har Maddi* (abnormal hot temperament with humoral involvement) and *Sue Mizaj barid Maddi* (abnormal cold temperament with humoral involvement).

According to Jalinoos (Galen) breach in the continuity may be developed by some external and internal causes. The external causes which directly produce *tafarruqe ittesal* may be stretching force, tear, burn, crush, and prick. While the internal causes are *khilt laazeh* (irritant humour), *khilt akkal* (corrosive humours), *ghaleez riyah* (viscous pneuma), *ghaleez khilt* (viscous humours) (Sina, 1993; Rushd, 1987; Mirza, 2014).

1.1. Classification of Pain

Physiological Classification of Pain

Nociceptive Pain: (nocere – injure, Latin). Nociception is the activity of peripheral nervous system that transmits or processes the information about noxious events associated with tissue damage to central nervous system. Nociceptive pain is of following types:

- i) Somatic pain: Irritation or damage to musculoskeletal system, originating from bone, muscle, connective tissue etc. This type of pain can be described as aching,

sharp, stabbing, throbbing and is well localized.

- ii) Visceral pain: Originating from body organs such as pancreas, liver, gastro-intestinal tract etc. This type of pain is described as cramping, dull, colicky and squeezing. It is diffused, poorly localized, and may be referred to other areas.

Neuropathic pain: It is caused by an injury or dysfunction of the peripheral or central nervous system. It is often described as: burning, shooting, stabbing, numbness or tingling. It has the following types:

- i) Central neuropathic pain as in post stroke pain, spinal cord injury, multiple sclerosis and syringomyelia
- ii) Peripheral neuropathic pain may be focal, multi focal, symmetrical for example trigeminal neuralgia, carpal tunnel syndrome, nerve root fibrosis, post-herpetic neuralgia, vasculitis etc. Other sensations of neuropathic pain – Dysesthesia (bugs crawling on the skin, pins and needles). Allodynia (pain to a non painful stimulus). Hyperalgesia (increased pain sensation to a normally painful stimulus).

Mixed pain: Neuropathic pain may coexist with nociceptive pain. In some disease conditions, patients may have mixed pain consisting of somatic visceral and neuropathic pain all at the same time or each separately at different times. Examples include trauma that damages tissue and nerves, burns (that affect skin as well as nerve endings), and cancer that causes external nerve compression as well as damaging nerves by infiltration.

Classification Based on Duration of Pain

Acute pain: Is of sudden onset, is felt immediately following injury, is severe in

intensity, but is usually for short time period. It arises as a result of tissue injury stimulating nociceptors and generally disappears when the injury heals.

Chronic pain: Is continuous or recurrent pain that persists beyond the expected normal time of healing. Chronic pain may begin as acute pain and persist for long periods or may recur due to persistence of noxious stimuli or repeated exacerbation of an injury. Chronic pain may also arise and persist in the absence of identifiable pathophysiology or medical illness. Chronic pain can negatively affect all aspects

of daily life, including physical activities, school attendance, sleep patterns, family interactions and social relationships and can lead to distress, anxiety, depression, insomnia, fatigue or mood changes, such as irritability and negative coping behaviour (Ranjani, 2016; PMG, 2012; Arthur *et al.*, 2005).

1.2. Classification of Pain According to Unani System of Medicine

Jalinoos (Galen) and Ibn Sina (Avicenna) categorised pain into different types as shown Table 1.

Table 1: Classification of Pain with Body Sites Affected

Unani classification (Waja')	Nature of pain	Body sites affected
<i>Ayayi</i>	Fatigue	Whole body
<i>Hakkak</i>	Pruritic	Skin
<i>Khadri</i>	Neuropathic	Nerves
<i>Khashin</i>	Rough	Skin (Psoriasis)
<i>Laazeh</i>	Irritant	Stomach (Heart burn)
<i>Misalli</i>	Stabbing	Large Intestine
<i>Mufassikh</i>	Incisive	Muscles
<i>Mukassir</i>	Bony	Skeletal
<i>Mumaddid</i>	Distension	Stomach
<i>Nakhis</i>	Pricking	Lungs (Pleurisy)
<i>Rikhu</i>	Dull ache	Soft tissue muscles
<i>Saqeel</i>	Heavy	Liver and spleen
<i>Saquib</i>	Perforating	Colon
<i>Zaghit</i>	Compression	Heart
<i>Zarbani</i>	Throbbing	Acute inflammation, (Migraine)

Sina (1993).

Analgesics

There are three groups of agents which alleviate pain: 1) Some contrary to the cause of pain which removes the cause e.g. anethum, linseed made into a poultice and applied over the painful area. 2) Any agent which counteracts the acrimony of the humours, induces sleep or dullness or soothes the sensitive faculties and decrease activity e.g. inebriants milk, oil, aqua dulcis etc. 3) An agent which infrigidates and dulls the sensation in the painful part e.g. all narcotics and somniferous drugs (Sina, 1993).

1.3. Pain Pathway: (Nociception)

There are four main components of the pain mechanism: i) Transduction, ii) Transmission, iii) Modulation and v) Perception.

Transduction: During transduction, which occurs in the periphery, the damage to human tissue causes nociceptive stimulations which activate nerve endings i.e. primary afferent nociceptors.

Transmission: During the transmission the information is conveyed from the peripheral nervous system to the dorsal horn of the spinal cord where nerve cells activate and the information is then processed to higher centres i.e. to the brainstem. It is believed that the thalamus forwards the message to the frontal cortex which assigns meaning to the pain. The information is then conveyed to the somatosensory cortex, which identifies and localises the pain and finally to the limbic system where the information is interpreted as pain.

Modulation: Modulation is interaction between pain-transmitting and non-pain transmitting neurons i.e. pain control in the nervous system. The activation of non-pain transmitting neurons at the spinal cord can

interfere with signals from pain fibres and inhibit or modulate an individual's experience of pain. Modulatory inter-neurons in the spinal cord are either inhibitory or excitatory.

Perception: Perception of pain is a neurophysiologic phenomenon comparable to the sense of heat or touch when the neurons transmit pain and evoke a subjective response to pain. The emotional response to the perception (e.g., depression, fear, anxiety, suffering), and the pain behaviour in response to those emotions and perceptions guide the observer to believe the individual is suffering from pain i.e. talking about pain, grimacing or moaning (Ylinen *et al.*, 2009; Ylinen *et al.*, 2007).

1.4. Pain Assessment

The Visual Analogue Scale (VAS)

It is presented as a 10 cm line, anchored by verbal descriptors, usually 'no pain' and 'worst imaginable pain'. The patient is asked to mark a 100 mm line to indicate pain intensity. The score is measured from the zero anchors to the patient's mark. Using a millimetre scale to measure the patient's score will provide 101 levels of pain intensity.

The Numerical Rating Scale (NRS)

It is a 11, 21 or 101 point scale where the end points are the extremes of no pain and pain as bad as it could be, or worst pain. The NRS can be graphically or verbally delivered. When presented graphically the numbers are often enclosed in boxes and the scale is referred to as an 11 or 21 point box scale depending on the number of levels of discrimination offered to the patient.

The Verbal Rating Scale (VRS)

The VRS comprises a list of adjectives

used to denote increasing pain intensities. The most common words used being: no pain; mild; moderate; and severe or intense pain (Williamson *et al.*, 2005).¹

Pain Meter (PAULA)

Pain meter uses 5 coloured emoticon faces on the front of a ruler and corresponding VAS score on the back. Patients are allowed to move a slider to mark the pain which they are

experiencing. Use of this pain meter resulted in less variance than pain scores obtained from standard VAS (Machata *et al.*, 2009).

1.5. Pharmacotherapy of Pain Pharmacological Pain Management in Unani System of Medicine

In Unani system of medicine drugs that are used for analgesia are presented in Tables 2 and 3.

Table 2: Unani Analgesics with Botanical Name and Dose

Classical name	Botanical name	Dosage
<i>Afyoon</i>	<i>Papaver somniferum</i> L.	25-50 mg
<i>Bazrul Banj</i>	<i>Hyoscyamus niger</i>	15-60 mg
<i>Dhatura</i>	<i>Datura stramonium</i>	500 mg
<i>Shokran</i>	<i>Conium maculatum</i> Linn.	1 g
<i>Suranjan</i>	<i>Colchicum luteum</i>	125-375 mg
<i>Tukhme kahu</i>	<i>Lactuca scariola</i> Linn.	3-5 g

Ghani (2008) and Rafiquddin (1985).

Table 3: Adjuvant Unani Analgesics with Botanical Name and Dosage

Classical name	Botanical name	Dosage (g)
<i>Baboona (Muhallilat)</i>	<i>Maticaria chamomilla</i>	2-3
<i>Katan (Moaddelat)</i>	<i>Linum usitatissimum</i>	2-4
<i>Nakhoona (Muhallilat)</i>	<i>Trigonella uncata</i>	5
<i>Shibt(Moaddelat)</i>	<i>Anethum graveolens</i>	3

Ghani (2008) and Rafiquddin (1985).

1.6. Pharmacological Pain Management in Conventional System of Medicine WHO – Step Analgesics Ladder

The WHO 3 step guidelines were first published in 1986 and are considered to be the gold standard for managing pain in advanced cancer. This analgesia ladder has been modified for acute pain, chronic non cancer pain and cancer pain. This revised ladder integrates a fourth step which includes nerve blocks, epidurals and neurolysis (phenolisation, alcoholisation) (Vargas, 2010).

- Step 1: Non opioids ± adjuvants
- Step 2: Non opioids + Weak opioids ± adjuvants
- Step 3: Non opioids + Strong opioids ± adjuvants
- Step 4: Nerve Blocks, Epidurals

Adjuvant analgesia tend to be drugs that are licensed for indications other than pain. Hence, they are not primarily classified as analgesia even though they may relieve pain that is usually not responsive to standard analgesia which include antidepressants, anticonvulsants, antispasmodics and steroids etc (Vargas, 2010; WHO, 1986).

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

These drugs are the corner stone of the treatment for mild to moderate pain. All NSAIDs are analgesic, anti inflammatory and antipyretic effects. They modify the nociceptive responses induced by the polypeptide bradykinin, and also inhibit the enzymatic synthesis of prostaglandins from long chain fatty acids (Tables 4 and 5).

Opioid Analgesics

The term opium is derived from the Greek term for juice, the drug being derived from the juice of poppy plant, *Papaver somniferum*. Drugs such as morphine mimic endogenous

opioid chemicals known as enkephalins, endorphin, and dynorphins. Enkephalin in the dorsal horn of the spinal cord and endorphin in the periaqueductal gray region of the brain are neurotransmitters involved in “closing the pain gate, “thereby, inhibiting the pain transmission.

These are drugs conventionally used for indications other than analgesia, but may be analgesic in specific circumstances. These drugs include antidepressants, anticonvulsants, benzodiazepines, corticosteroids, etc. (Table 6).

1.7. Non-pharmacological Pain Management

Cognitive behavioural therapies

Relaxation – respiration techniques – It is provided to focus on the respiration and avoid disturbing thoughts by taking a deep breath slowly through the nose and giving it back in a long time through the mouth

Distraction: Getting the attention away from the pain reduces its severity. The aim in using that technique is to increase the tolerance for pain and decrease the sensitivity towards pain. This method includes listening to music, watching television, reading books and dreaming.

Meditation and Praying: In the traditional meaning, meditation is generally focusing on the moment. This act is realized with an individual focusing on respiration, a word or picture. Sometimes arbitrary connection with God while praying may also works wonder in pain relief.

Hypnosis: It is the state of conscious change similar to sleep. Hypnosis requires the body to relax and the patient to focus on an object, a stimulant or memory. Hypnosis is “the deep physical relaxation state during which subconscious can be reached and important abilities are suspended”.

Aromatherapy: It is using the essential oils that are obtained from flowers, herbs and trees to improve health and well being. These

Table 5: Non-steroidal Anti-inflammatory Drugs Dosage for Adults

Generic name	Dosage (mg)	Half life (hours)
Aspirin	75-325 QID	2-20
Celecoxib	100-200 BID	10
Diclofenac	50 BID	2
Ibuprofen	200-800 TID	2
Indomethacin	25-50 TID	5
Ketoprofen	50-75 TID	3
Ketorolac	15-30 QID	2
Naproxen	250-500 BID	13
Piroxicam	20 QID	50

Twice a day (BID); Thrice a day (TID); and Four times a day (QID)
Gehdoo (2013).

Table 4: Opioid Analgesics Dosage for Adults

Drug	Route	Dose	Schedule
Codeine (weak opioid)	Oral	30-60 mg	4-6 hourly
Fentanyl	IV	1-2 µg/kg	30-40 min.
Morphine	Oral/IV	10 mg	4 hourly
Pentazocine	Oral/IM	50-100/30-60 mg	4-6 hourly
Pethidine	Oral/IM	50-100 mg	4 hourly
Tramadol	Oral/IV/IM	1-2 mg/kg	4-6 hourly

Gehdoo (2013) and Jain (2013).

Table 6: Adjuvant Drugs Used in Conventional System of Medicine for Neuropathy

Drug	Dosage per day	Time to be effective
Amitriptyline (Antidepressants)	10-75 mg	6-8 week
Nortriptyline (Antidepressants)	70-100 mg	6 week
Pregabalin (Anticonvulsant)	75-600 mg	4-6 week
Gabapentin (Anticonvulsant)	100-3600 mg	4 week
Diphenhydramine (Sedative)	200 mg	–
Promethazine (Sedative / Antipsychotic)	100 mg	–
Prednisone (Steroid)	5 mg	–

Tripathi (2013).

oils are applied by being respired through oily gauze that is placed under the nostrils of the patient or as massage oils being applied on skin (Williams *et al.*, 2009; Richardson *et al.*, 2006; Jackson *et al.*, 2008).

1.8. Peripheral Therapies (Physical Agents/Skin Stimulation) **Transcutaneous Electrical Nerve Stimulation (TENS)**

Pain is reduced when the area is rubbed or stimulated due to activation of non nociceptive fibers inhibiting the nociceptive response in the dorsal horn of the spinal cord. TENS uses electric current produced by a portable device to stimulate the nerves for therapeutic purposes. In TENS, non nociceptive fibers are selectively stimulated with electrodes in order to produce this effect and thereby inhibiting pain. People using cardiac pacemaker should be excluded for this therapy (Sluka *et al.*, 2003).

Acupuncture and Acupressure

Acupuncture, one of the important components of Traditional Chinese Medicine (TCM) is acceptable worldwide as a scientific treatment method. It provides the body to restore balance by means of stimulating some special points on the body with needles. Acupoint stimulation such as manual acupuncture involves the penetration and manipulation of a fine needle through the skin into specified points on the body to evoke a sensation. More than 360 acupoints are located along 14 meridian channels that cover the body in a web like interconnecting matrix (Lin *et al.*, 2009; Chen *et al.*, 2014).

Cryotherapy

The pain-relieving benefits of snow and ice were first documented by the Greek physician Hippocrates thousands of years ago. It is a relatively new form of treatment in which the

body is briefly exposed to very cold temperatures in order to promote healing and other therapeutic results. Cytotherapy has been shown to decrease inflammation of the body's tissues, muscles and joints. It can also help improve the body's circulation and healing, and also slow down cellular metabolism and reproduction. Cryotherapy can help to reduce pain and muscle spasms in the body as well as reduce the swelling of injuries. It promote and accelerate healing in joint, muscle and tendon injuries. The most common type of cryotherapy is an ice pack and most effective in crushed form because it conforms comfortably to the contours of the injured area (Saini, 2015).

Hammam (Turkish Bath)

Hamam is well known regimental therapy in Unani system of medicines. It consists of various rooms where facilities are available for a bath followed by shower and massage. It reduces pain and improves general health. It reduces the viscosity of the humours and improves health of the debilitated individuals. It improve metabolism, increase innate heat of the body and excrete waste products through skin (Hamdani, 2010).

Dalk (Massage Therapy)

Dalk is also an integral part of Unani system of medicine. By this diversion of morbid matter (*Imalae mawad, Tanqiya mawad*). Evacuation of morbid matters from the site of affected organ. It also induces sedation, analgesia and increase blood circulation. Unani medicine describes detailed types of massage e.g. Rough massage (*Dalk khishan*), smooth massage (*Dalk amlas*), prolonged massage (*Dalk kaseer*) or short duration massage (*Dalk qaleel*) (Lone *et al.*, 2011).

Hijamah (Cupping Therapy)

It a well known Unani regimental therapy

meaning “to suck”. *Hijamah* refers to a Unani regimental mode of treatment. It is an ancient method which was practically used among the Chinese, Babylonians, Egyptians, Greeks, Romans, Arabs and Indians. It is also used to relieve severe pain in any part of the body. This purpose is achieved either due to diversion of materials away from the site of pain or by dissolution of morbid material (Sheikh *et al.*, 2014).

2. CONCLUSION

Pain can be managed effectively with the combination of pharmacological and non-pharmacological therapies. Understanding of the pharmacology of all potentially useful agents, available therapeutic goals, patient conditions and adverse effects of the drugs used will greatly help to optimize outcomes. Unani drugs and regimens may play a vital role to mitigate pain due to its safety and efficacy inspite of controversial scientific status, insufficient facilities for clinical research and lack of updated literature. Unani System of medicine has tremendous potential in pain management. The role of non-pharmacological approaches to pain management is evolving, and some non-pharmacological and complementary therapies have an important contribution towards patient care however, some approaches have not been shown to be of benefit, so it is essential that for management of severe pain appropriate analgesics and adjuvant should be considered along with complementary therapies using evidence based approach.

3. REFERENCES

1. Chen, Y.W. and Wang, H.H. (2014). The effectiveness of acupressure on relieving pain: A systematic review, *Pain Management Nursing*. **15**(2):539-550.
2. Gehdoo, R.S.P. (2013). Pharmacotherapy in chronic pain. *World Clin Care Pain*. **1**(1):50-94.
3. Ghani, H.N. (2008). *Khazainul Advia*. Idara Kitabul Shifa, New Delhi, pp. 245-255, 317, 701, 861, 915, 1012.
4. Guyton, Arthur C. and Hall, John E. (2005). *Text Book of Medical Physiology*. 12th Edn. Pennsylvania Elsevier Publication, pp. 558-559.
5. Hamdani, S.K.H. (2010). *Usool Tib*. Urdu Council, New Delhi, p. 180.
6. International association for the study of Pain. (1979). Pain terms: a list with definition and notes on usage. Recommended by the IASP subcommittee on Taxonomy pain. **6**:249 [PUBMED]
7. Jackson, E., Kelley, M., McNeil, P., Meyer, E., Schlegel, L. and Eaton, M. (2008). Does therapeutic touch help reduce pain and anxiety in patients with cancer?. *Clin. J. Oncol. Nurs*. Feb. **12**(1):113-120.
8. Jain, S. (2013). Management of cancer pain. *World Clin. Anesth. Crit. Care Pain*. **1**(1):222-262.
9. Lin, J.G. and Chen, W.L. (2009). Review: Acupuncture analgesia in clinical trials, *The American Journal of Chinese Medicine*. **37**: 1-18.
10. Lone, A.H., Ahmad, T., Mohammed, A., Sofi, G. and Shamin, A.M. (2011). Role of massage therapy in the management and prevention of diseases: A case series of medicated massage. *International Journal of Research in Ayurveda and Pharmacy*. **2**(5):1474-1477.
11. Machata, A.M., Kabon, B., Willschke, H. *et al.*, (2009). A new instrument for pain assessment in the immediate postoperative period. *Anaesthesia*. **64**(4):392-398.
12. McMillian, S.C., Title, M., Hegan, S. and Laughlin, J. (2000). Management of pain and pain related symptoms in hospitalised veterans with cancer. *Cancer Nursing*. **23**(5):327-336.
13. Mirza Ghufuran Baig *et al.*, (2014). Pain alleviation in Unani medicine – A conceptual analysis. *IJPSR*. **5**(12):927-934.
14. Nash, R., Yates, P., Edwards, H., Fentiman, B., Dewar, A., McDowel, J. *et al.*, (1999). Pain and administration of analgesia: What nurses say. *J. of Clin. Nurs*. **8**(2):180.
15. *Pain Management Guidelines* (Sept. 2012). Ministry of Health, Republic of Rawanda. pp. 1-3 [www.moh.gov.rw]
16. Rafiquddin, M. (1985). *Kanzul Advia Mufrada*.

- Aligarh University Publication Unit Sarfaraz House, Aligarh Muslim University, pp. 104, 106, 111, 132, 228, 258, 354, 438, 460.
17. Ranjani, S.S. (2016). *Handbook of pain management in practice*, 1st Edn. Jaypee Brother's Medical Publishers, New Delhi. 1.
 18. Richardson, J., Smith, J.E., McCall, G., Pilkington, K. (2006). Hypnosis for procedure-related pain and distress in pediatric cancer patients: a systematic review of effectiveness and methodology related to hypnosis interventions. *J. Pain Symptom Manage.* Jan, **31**(1):70-84.
 19. Rushd, I. (1987) *Kitabul Kulliyat*. 2nd Edn. CCRUM, Ministry of Health and Family Welfare, Govt of India, New Delhi, pp. 120-129.
 20. Saini, D. (2015). Cryotherapy – An inevitable part of sports medicine and it's benefits for sports injury. *International Journal of Applied Research.* **1**(4):324-327.
 21. Sheikh, H.M., Fasihuzzaman and Jabeen, A. (2014). *Hijamah* (cuppingtherapy): A noble method of treatment in unani medicine. *Int. J. Res. Ayurveda Pharm.* **5**(1):60-64.
 22. Sina, I. (1993). *Alqanoon Fit Tib*. Vol. 1, (English translation By Jamia Hamdard), Jamia Hamdard, New Delhi, pp.176-182, 379-382.
 23. Sluka, K.A. and Walsh, D. (2003). Transcutaneous electrical nerve stimulation: basic science mechanisms and clinical effectiveness. *The Journal of Pain.* **4**(3):109-121.
 24. Tripathi, K.D. (2013). *Essentials of Medical Pharmacology*, 7th Edn. Jaypee Publications, New Delhi, pp. 397-411.
 25. Vargas-schaffer, G. (2010). Is the WHO analgesic ladder still valid? Twenty four years of experience. *Can Fam Physician.* **56**(6):514-517.
 26. Williams, A.M., Davies, A. and Griffiths, G. (2009). Facilitating comfort for hospitalized patient using non-pharmacological measures: Preliminary development of clinical practice guidelines. *Int. J. Nurs. Prac.* Jun, **15**(3):145-145.
 27. Williamson, A. and Hoggart, B. (2005). Pain: A review of three commonly used pain rating scales. *Journal of Clinical Nursing.* Aug. **14**(7):798-804.
 28. World Health Organisation. (1986). *Cancer Pain Relief*, 1st Edn. World Health Organisation, Geneva: [whqlibdoc.who.int/publications/9241544821.pdf]
 29. Ylinen, E.R., Vehvilainen, J.K. and Pietila, A.M. (2009). Effects of patients' anxiety, previous pain experience and non-drug interventions on the pain experience during colonoscopy. *Journal of Clinical Nursing.* Jul. **18**(13):1937-1944.
 30. Ylinen, E.R., Vehvilainen, J.K. and Pietila, A.M. (2007). Nurses' knowledge and skills in colonoscopy patients pain management. *Journal of Clinical Nursing.* **16**:1125-1133.