

# Pain control in Extracorporeal Shock Wave Lithotripsy (ESWL): A narrative review based on pharmacological and non-pharmacological methods

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## Abstract

**Background:** Some cases of urinary lithiasis could be managed by a relatively none invasive procedure of ESWL; while it could be painful experience. This study aimed at systematically reviewing the different management methods of the pain during the ESWL.

**Methods:** In this narrative review, online databases were queried for studies reporting pharmacological and non-pharmacological methods of the pain management during the ESWL.

**Results:** Fifty-two articles were included in this study. In this article, pharmacological and non-pharmacological methods of pain control in ESWL were investigated. The drugs under review include: Tramadol, Acetaminophen/Paracetamol, Fentanyl, Pethidine, Remifentanyl, Morphine, Pentazocine, Dexmedetomidine, Diclofenac sodium, Ketorolac, Pregabalin, Lornoxicam, Parecoxib sodium, Melatonin, Inhalation gases (Entonex gas), and different gels of Piroxicam gel, Lidocaine gel, and EMLA. and non-pharmacological methods include: Prayer therapy, Sterile water, Acupuncture, TENS and Music therapy.

**Conclusion:** for pain management during the ESWL multiple options of both pharmacological and non-pharmacological interventions are available that are supported by high level evidences in RCTs. Physicians should select the options based on the condition of the patient to prevent the potential adverse events.

**Keywords:** ESWL, Pain, Pharmacological, Non-pharmacological.

## INTRODUCTION

Urinary lithiasis is the one of the most common urinary tract diseases (1-3). The prevalence of kidney stones in Asian countries is 1-5% (4) and in Iran it is 5.7% (6.1% in men and 5.3% in women) (5-6). Most of the patients are between 30 and 60 years old, and the highest incidence is in the age group of 35 to 45 years (6). Today, various surgical and non-surgical treatment methods are available to remove kidney stones, one of these non-surgical methods is ESWL (Shock wave lithotripsy extracorporeal) (7).

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Most of the patients experience pain during the stone breaking operation, which is due to the damage caused by the effects of low frequency sound waves and cavitation in the kidney tissue (8). To relieve pain, you can use two medicinal and non-medicinal methods (9-10). Among the advantages of non-pharmacological methods, we can mention the cheapness and convenience of these methods, their fewer side effects, increasing the patient's activity and ability to adapt, increasing the family's cooperation in patient care, reducing the patient's anxiety, reducing the cost of medical care, and reducing the occupancy of hospital beds (11-12). Despite the progress of new generations of stone breakers that cause less pain, in most cases, to control the pain caused by blows during stone breakers, it is necessary to use pain relievers, including; Various analgesic agents such as opioids including: morphine, pethidine and fentanyl and non-steroidal anti-inflammatory drugs such as: diclofenac, propofol, ketorolac and piroxicam and skin pain relievers such as EMLA )Eutectic Mixture of Local Anesthetic( alone or in combination with drugs Another is that each of these cases has advantages and disadvantages (13-14). By using pain relievers, the majority of the pain caused by the passage of waves through the skin can be relieved and the patient can be calm and immobilized. Therefore, pain is one of the problems during ESWL, which the anesthesiologist is trying to reduce (15). Therefore, the purpose of this study is to review the narrative of

pharmacological and non-pharmacological methods of pain control in ESWL.

### Method:

The present study is a narrative review. In this study, in order to find relevant articles, the researchers conducted a computer search in the Persian language SID, Magiran and English language databases, PubMed, Scopus, EMBASE and Science Direct with the keywords pain, pharmacological, non-pharmacological methods, ESWL. The search for studies was done without any time limit.

### Result:

Fifty-two articles were included in this study. In this article, pharmacological and non-pharmacological methods of pain control in ESWL were investigated. The drugs under review include: Tramadol, Acetaminophen/Paracetamol, Fentanyl, Pethidine, Remifentanyl, Morphine, Pentazocine, Dexmedetomidine, Diclofenac sodium, Ketorolac, Pregabalin, Lornoxicam, Parecoxib sodium, Melatonin, Inhalation gases (Entonox gas) and Non-pharmacological methods include: Piroxicam gel, Lidocaine gel, Prayer therapy, Sterile water, Acupuncture, TENS and Music therapy.

**Table 1:** Articles included in the study

Author/ Years	Country	Groups	Sample size	Pain measurement tool	Outcome
Abdullah Gul /2020 (16)	Turkey	sterile water injection/diclofenac sodium	524	VAS	Similar efficacy, lower AEs in intervention group
Bilal Eryıldırım/2008 (17)	Turkey	Cream EMLA/ Diclofenac sodium(DS) / DS + EMLA(DE)	120	VAS	Best efficacy in control group
Abdelwahab Hashem/2019 (18)	Egypt	Pethidine, Ketorolac, Lidocaine gel	132	NPRS	Highest efficacy in Ketorolac
Ali Çift/2020 (19)	Turkey	Music therapy	150	VAS	preferred music was effective
Gulgun Elif Akcali/2010 (20)	Turkey	Paracetamol/ Lornoxicam/ Tramadol	90	VAS	All interventions were effective and safe
Iraklis C Mitsogiannis/ 2008 (21)	Greece	Fentanyl/ Parecoxib	58	VAS	Better effects in Fentanyl group
Husnu Tokgoz/2010 (22)	Turkey	Diclofenac sodium / Dexketoprofen	70	VAS	dexketoprofen was better
Ayten Bilir/ 2008 (23)	Turkey	Placebo / Lornoxicam/ Tenoxicam	60	VAS	lornoxicam was better
Mehrdad Mesbah Kiaei/2018 (24)	Iran	Diclofenac suppository/ Placebo	158	VAS	Diclofenac was effective
Anup Kumar/2007 (25)	India	diclofenac sodium/ EMLA/ oral diclofenac sodium+ EMLA/	240	VAS	The use of a combination of oral diclofenac sodium and an occlusive dressing of EMLA cream during

					SWL provides adequate analgesia (25).
Yesil S/ 2014 (26)	Turkey	Diclofenac/ Dexketoprofen/ hyoscine plus paracetamol/ Saline solution	76	VAS	This study shows that reducing the pain with a single dose injection of intramuscular diclofenac sodium before SWL is superior compared to others
Mustafa Karalar/ 2016 (27)	Turkey	Controls/ music with NCHs/ music with non-NCHs/	89	VAS	Music therapy during SWL reduced pain. Music therapy with NCHs was more effective for pain and anxiety reduction. To reduce pain, nonpharmacological therapies such as music
Emma Marsdin/2012 (28)	United Kingdom	AV distraction via a wall-mounted television with wireless headphones/ No AV distraction	118	VAS	AV distraction significantly lowered patients' reported pain and distress scores
Sefa Resim/ 2005 (29)	Turkey	electro-acupuncture (EA)/ Tramadol midazolam (TM)	35	VAS	Our study shows that EA is an effective method for analgesia
Suna Akin Takmaz/ 2008 (30)	Turkey	saline solution/ I, 8 mg lornoxicam	60	VAS	Eight milligrams of intravenously administered lornoxicam 15 minutes before SWL provides pain Relief and patient satisfaction during the procedure
Alpaslan Akbas/ 2015 (31)	Turkey	music therapy	400	VAS	The effect of music therapy during shockwave lithotripsy on patient Pain perception
Erdal Yilmaz/ 2005 (32)	Turkey	Fentanyl / placebo cream and fentanyl / EMLA cream + fentanyl / placebo cream + fentanyl + occlusive dressing/ EMLA cream + + occlusive dressing.	160	VAS	EMLA + occlusive dressing + low fentanyl was best option
Faramarz Mohammad Alibeigi/ 2011 (33)	Iran	pethidine/ lidocaine /piroxicam	159	MC Gill	topical piroxicam or lidocaine was best
Maasoumeh Torki/ 2020 (34)	Iran	Prayer/ Control	120	McGill	Prayer therapy was effective.
Rahim Taghavi Razavizadeh/ 2014 (35)	Iran	EMLA Cream/ Control	80	VAS	EMLA cream was effective.
Tavakoli K/ 2014 (36)	Iran	True Acupuncture/ Sham acupuncture	100	VAS	Acupuncture was effective.
M. Sadegh Sanie/ 2017 (37)	Iran	Melatonin/ Pregabalin/ Control	45	VAS	Similar effects.
Behrouz Karkhanehei/ 2017 (38)	Iran	Diclofenac Sodium/ Acetaminophen Codein	90	Four Scale point	Similar effects.
Mehrabi S/ 2011 (39)	Iran	fentanyl/ pethidine + midazolam	89	VAS	Similar effects.
Randa Ali Shoukry/ 2019 (40)	Egypt	Transcutaneous Electric Nerve Stimulation (TENS)	60	VAS	TENS is effective and safe.
Esma Ozsaker/ 2014 (41)	Turkey	Transcutaneous Electric Nerve Stimulation (TENS)	50	VAS	TENS is effective
Alper Kararmaz/ 2004	Turkey	TENS	66	VAS	TENS is effective

(42)						
Hulya Basar/ 2003 (43)	Turkey	Fentanyl/ sodium/ EMLA cream containing lidocaine and prilocaïne	Diclofenac Tramadol/	100	VAS	Same efficacy
Hamid Mazdak/ 2007 (44)	Iran	inhalational intravenous inhalational air	Entonox/ pethidine/ compressed	150	VAS	Entonox is effective
D Gallego Vilar/ 2012 (45)	Spain	EMLA + pethidine + cream	pethidine/ placebo	434	VAS	EMLA cream + pethidine was better.
S Rogenhofer/ 2004 (46)	Germany	Acupuncture		90	VAS	Acupuncture was effective.
Mahvash Agah/ 2004 (47)	Iran	Acupuncture		100	Score	Acupuncture was effective.
Medina/2005 (48)	Netherlands	Remifentanil		200	VAS	Remifentanil was effective.
Han/2003 (49)	Taiwan	Morphine / Pentazocine		100	VAS	pentazocine + lorazepam was better.
Zeyneloglu/2008 (50)	Turkey	Dexmedetomidine/ midazolam/fentanyl		49	VAS	Dexmedetomidine was better
Kaygusuz/2008 (51)	Turkey	Dexmedetomidine/ propofol		46	VAS	dexmedetomidine + fentanyl was better
Sepidkar/ 2017 (52)	Iran	Fentanyl and Pregabalin- Fentanyl		141	VAS	fentanyl was better

## Pharmaceutical methods

### Narcotics:

Opioids are the most common type of pain relievers used during stone-breaking surgery, but despite their good effect, their use may cause depression of the respiratory center, gastrointestinal complications, and hypotension (53).

### Tramadol:

Tramadol as a central analgesic, could modify pathways of nerve transmissions for painful stimulus (54). Tramadol is a sedative with central effects and a dual action mechanism, which includes weak agonistic effects on  $\mu$ -type opioid receptors and also a neurotransmitter reuptake inhibitor (55). Various studies indicate that the use of tramadol controls pain after surgery (56-58). In the study conducted by Gulgun

Elif Akcali (20), the effectiveness of tramadol in controlling pain in SWL has been proven.

### Acetaminophen/Paracetamol:

Today, intravenous acetaminophen with the brand name of Apotel is widely used to control the pain of patients. The mechanism of its effect is preventing the secretion of prostaglandins in the CNS, reducing environmental anti-inflammatory effects, reducing fever with a direct effect on the temperature control center in the hypothalamus (59-60). Various studies indicate that the use of acetaminophen (paracetamol) controls pain after surgery (61-63). In the study conducted by Karkhanehei (38), the effectiveness of acetaminophen in controlling pain in SWL has been proven.

#### Fentanyl:

Fentanyl is a fat-soluble narcotic that is effective and safe in causing analgesia as a single dose or as a continuous infusion (64-65). Various studies indicate that the use of fentanyl controls pain after surgery (66-69). In the study conducted by Iraklis C Mitsogiannis (21), Mehrabi (39), the effectiveness of acetaminophen drug in controlling pain in SWL has been proven.

#### Pethidine:

Pethidine is a synthetic narcotic that has about one-tenth the strength of morphine and has a duration of effect of 2 to 3 hours. Due to its high solubility in fat (it is more soluble in fat than morphine) and rapid brain effects, it is highly possible to abuse it, and it may be preferred to morphine when rapid control of acute pain is necessary (70). Various studies indicate that the use of pethidine controls pain after surgery (71-73). In the study conducted by Mehrabi (39), the effectiveness of pethidine drug in controlling pain in SWL has been proven.

#### Remifentanyl:

Remifentanyl is a synthetic drug with a rapid effect on the  $\mu$  receptor. Due to its ester composition, remifentanyl is susceptible to non-specific esterases in plasma and cold, which leads to its rapid metabolism. Based on this, remifentanyl is known as an ultra-short-acting narcotic for creating analgesia. In addition, since it has very little hepatic and renal metabolism compared to other drugs, its use in patients with kidney involvement (such as kidney stones) seems very appropriate (74). Various studies indicate that the use of remifentanyl controls pain after surgery (75-79). In the study conducted by Medina (48), the effectiveness of remifentanyl in controlling pain in SWL has been proven

#### Morphine:

Morphine is an alkaloid opioid that prevents the release of ACTH and causes the release of histamine from sympathoadrenal activity (79). Narcotic drugs cause analgesia by inhibiting the release of substance P in the spinal cord and also directly affecting the narcotic receptors in the posterior horn of the spinal cord (80). Various studies indicate that the use of morphine controls pain after surgery (81-84). In the study conducted by Medina (48), the effectiveness of remifentanyl in controlling pain in SWL has been proven.

#### Pentazocine:

Pentazocine is a K-opioid receptor agonist and  $\mu$ -opioid relative antagonist, which is used as an analgesic in various surgeries (85-86). Various studies indicate that the use of pentazocine controls pain after surgery (87-88). In the study conducted by Han (49), the efficacy of pentazocine in controlling pain in SWL has been proven

#### Alpha-2 agonists

##### Dexmedetomidine:

Alpha 2 adrenergic receptors are part of a large family of adrenergic receptors that perform their actions by binding to G inhibitory proteins (GI) (89). Dexmedetomidine has a strong anesthetic and analgesic effect (90-92). Various studies indicate that the use of dexmedetomidine controls pain after surgery (93-97). In the study conducted by Zeyneloglu (50), Kaygusuz (51), the effectiveness of dexmedetomidine in controlling pain in SWL has been proven.

#### NSAIDs (Non-steroidal anti-inflammatory drugs)

##### Diclofenac sodium:

Diclofenac is a non-steroidal, non-inflammatory drug in the phenylacetic acid class, which has antipyretic, anti-inflammatory, and analgesic effects. Diclofenac has a higher ability to suppress cyclooxygenase 2 than cyclooxygenase 1 (98). Diclofenac, apart from its direct analgesic and anti-inflammatory and anti-edema effects, relieves pain due to a series of indirect effects caused by reducing the release of painful substances and chemical mediators involved in the creation of analgesic impulses (99). It has been observed in studies that the use of diclofenac reduces postoperative pain (102-100). Various studies indicate that the use of diclofenac controls pain after surgery (103-104). In the study conducted by Kiaei (24), Yesil (26), Karkhanehei (38), the effectiveness of diclofenac in controlling pain in SWL has been proven.

##### Ketorolac:

Ketorolac, generically known as ketorolac trometamol, is a nonsteroidal anti-inflammatory drug (NSAIDs) that reduces pain and inflammation by inhibiting the activity of cyclooxygenase and prostaglandin synthesis (105). The main benefit of using Ketorolac is that this drug has analgesic properties (106), without depression of the central nervous system, which is seen in the use of opioids. The main advantage of using Ketorolac is its analgesic effects without reducing the function of the central nervous system, which is seen in opioids (107). Various studies indicate that the use of ketorolac controls pain after surgery (108-110). In the study conducted by Abdelwahab Hashem (18), the effectiveness of Ketorolac drug in controlling pain in SWL has been proven.

##### Pregabalin:

Pregabalin, which is an analog of gamma-aminobutyric acid (GABA), is known as an anticonvulsant, anti-anxiety and analgesic drug (111). The mechanism of its effect is the presynaptic connection to voltage-dependent calcium channels (112-114). Various studies indicate that the use of Pregabalin controls pain after surgery (119-115).

##### Lornoxicam:

Lornoxicam is one of the non-steroidal anti-inflammatory compounds (Nsaid) that can reduce acute pain after surgery

and can be used as a substitute or complement to narcotic analgesics in the treatment of postoperative pain (120-121). It is rapidly decomposed and has a short half-life of about 3-4 hours in plasma (122). Therefore, it seems to be suitable for short-term administration and cases of acute pain, including pain after surgery. Various studies indicate that the use of Lornoxicam for postoperative pain control is well tolerated by patients (123-130). In the study conducted by Gulgun Elif Akcali (20), Ayten Bilir(23), Suna Akin Takmaz (30), the effectiveness of Lornoxicam drug in controlling pain in SWL has been proven.

**Parecoxib sodium:**

Parecoxib sodium, a highly selective inhibitor of COX-2, that is being used as a painkiller (131). Various studies indicate that the use of paracoxib controls pain after surgery (132-137).

**Sleep Awake Cycle Regulator**

**Melatonin:**

While mostly being known for sleep awake cycle regulation, it also has analgesic effects (138-144).

## **Inhalation gases**

**Entonex gas:**

Entonex gas is an odorless and colorless inhalation sedative with a quick onset of action with a combination of O<sub>2</sub> and N<sub>2</sub>O in a ratio of 50-50. This gas is a safe, cheap and relatively effective pain reliever that is available and widely used in many countries (145-146). The quick-acting effect of Entonex gas, rapid elimination from the body, creating pain relief, and not requiring specialized personnel are among the advantages of this drug (147). Also, the peak anti-pain effect of Entonex is 50 seconds (148). Various studies indicate that the use of Entonex gas controls pain after surgery (149-152). In the study conducted by Mazdak (44), the effectiveness of Entonex gas in controlling pain in SWL has been proven.

**Piroxicam gel:**

Piroxicam is a prostaglandin synthesis blocker, which inhibits cyclooxygenase enzyme and causes pain relief, reducing fever and inflammation (153). Various studies indicate that the use of piroxicam gel controls pain after surgery (154-155). In the study conducted by Faramarz Mohammad Alibeigi (33), the effectiveness of Entonex gas in controlling pain in SWL has been proven.

**Lidocaine gel**

Lidocaine inhibits the conduction of nerve signals in neurons due to the block of fast-type voltage-dependent sodium channels in the membrane of neurons, which is responsible for signal transmission, and with the block of sodium channels, the neuron membrane is not depolarized after synapse and from pulse transmission. The nerve remains open and leads to its anesthetic effects (153).

Various studies indicate that the use of piroxicam gel controls pain after surgery (156-154). In the study conducted by Faramarz Mohammad Alibeigi (33), the effectiveness of Entonex gas in controlling pain in SWL has been proven.

**Prayer therapy:**

Prayer therapy is one of the non-drug methods to relieve pain and anxiety. The belief that faith and religious belief can be fruitful in the physical and mental improvement of people is not a new phenomenon. In all religions, it is common to appeal to God with special prayers and verses (157). Religious beliefs are more important in times of illness than at any other time. Religion helps people to bear the suffering and pain caused by illness. Among religious sources, prayer is the most source that people use to adapt to the situation; Because prayer increases human tolerance against diseases and problems and controls seemingly uncontrollable conditions. In fact, positive thoughts and tolerance are both components of prayer therapy (158). Various studies indicate that prayer therapy controls pain after surgery (159-160). Studies conducted in this field show the effectiveness of prayer therapy on the pain level of patients undergoing ESWL (161).

## **Non-pharmacological methods**

**Sterile water injection**

Various evidences show that injection pain can modify pain pathways during an acute pain (162-164). Various studies indicate that the use of sterile water controls pain after surgery (165-167). The studies conducted in this field show the effectiveness of sterile water on the pain level of patients undergoing ESWL (16).

**Acupuncture:**

Acupuncture is a traditional treatment method. In acupuncture, anatomical points along the body are stimulated for the purpose of treatment. By inserting the needles into the acupuncture points, vital energy enters the body along special channels. In most of the conducted researches, a strong emphasis has been placed on the analgesic property of acupuncture, from which two final conclusions can be drawn. First, the analgesic property of acupuncture for chronic treatments is much more effective than placebo. Secondly, the neural mechanism of acupuncture action is very clear and specific, as a result of needling, the small myelinated nerve fibers located in the muscles are activated and send stimuli to the spinal cord, and in this way three nerve centers (marrow, brain) medial, hypothalamus pituitary axis) is activated and they show their analgesic effects. Nowadays, instead of the old method of stimulating the needles by hand, they use low frequency (2 to 4 Hz) electrical stimulation (Electro Acupuncture) and it is no longer necessary for acupuncture specialists to stimulate the needles by hand during the entire treatment session (168). . Various studies indicate that the use of acupuncture controls pain after surgery (169-172). The studies conducted in this field show the effectiveness of

acupuncture on the pain level of patients undergoing ESWL (29, 36, 46, 47).

#### TENS:

Transcutaneous electrical nerve stimulation (TENS) is one of the alternative non-pharmacological methods. The main mechanism of TENS effect is still not fully known, but one of the mechanisms that most experts agree on is that this electric current activates the roots of many afferent nerves that stimulate the inhibitory nerves of the posterior horn or release endorphins. or both leads (173). Various studies indicate that the use of TENS controls pain after surgery (174-176). The studies conducted in this field show the effectiveness of TENS on the pain level of patients undergoing ESWL (40-42).

#### Music therapy:

Nowadays, the tendency to use non-medicinal methods for pain relief is increasing, one of these methods is the use of pleasant sound stimuli or therapeutic music (177). Using music to control pain in hospital wards; It is a safe, easy and low-cost method (178-179). Music provides positive auditory stimuli that can eliminate peripheral stimuli, affect biochemical production, and improve emotional health through normalization of an unfamiliar environment and provide a sense of hope, empowerment, and increased well-being (180). . Two separate stimuli in the nervous system at the same time can neutralize each other's effect, and in this way, a person who is focused on listening to music can neutralize other stimuli such as pain in the nervous system (181). Various studies indicate that the use of music therapy controls pain after surgery (182-184). The studies conducted in this field show the effectiveness of music therapy on the pain level of patients undergoing ESWL (19, 27, 31).

#### Conclusion:

for pain management during the ESWL multiple options of both pharmacological and non-pharmacological interventions are available that are supported by high level evidences in RCTs. Physicians should select the options based on the condition of the patient to prevent the potential adverse events.

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