



Collective Reviews  
Preemptive and  
Preventive Analgesia

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Advisor : Capt. Grit Wattanaboonyongcharoen ,MD.

# outline

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Introduction

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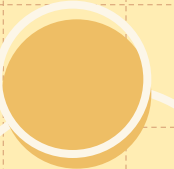
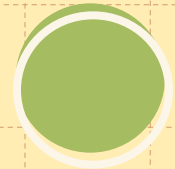
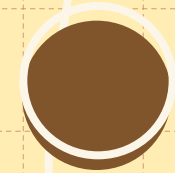
Management

...

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Clinical Study

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# Introduction



# Acute perioperative pain

## Goals of Management

- ☺ Relieve suffering
- ☺ Achieve early mobilization after surgery
- ☺ Reduce length of hospital stay
- ☺ Achieve patient satisfaction

# Characteristics of Pain

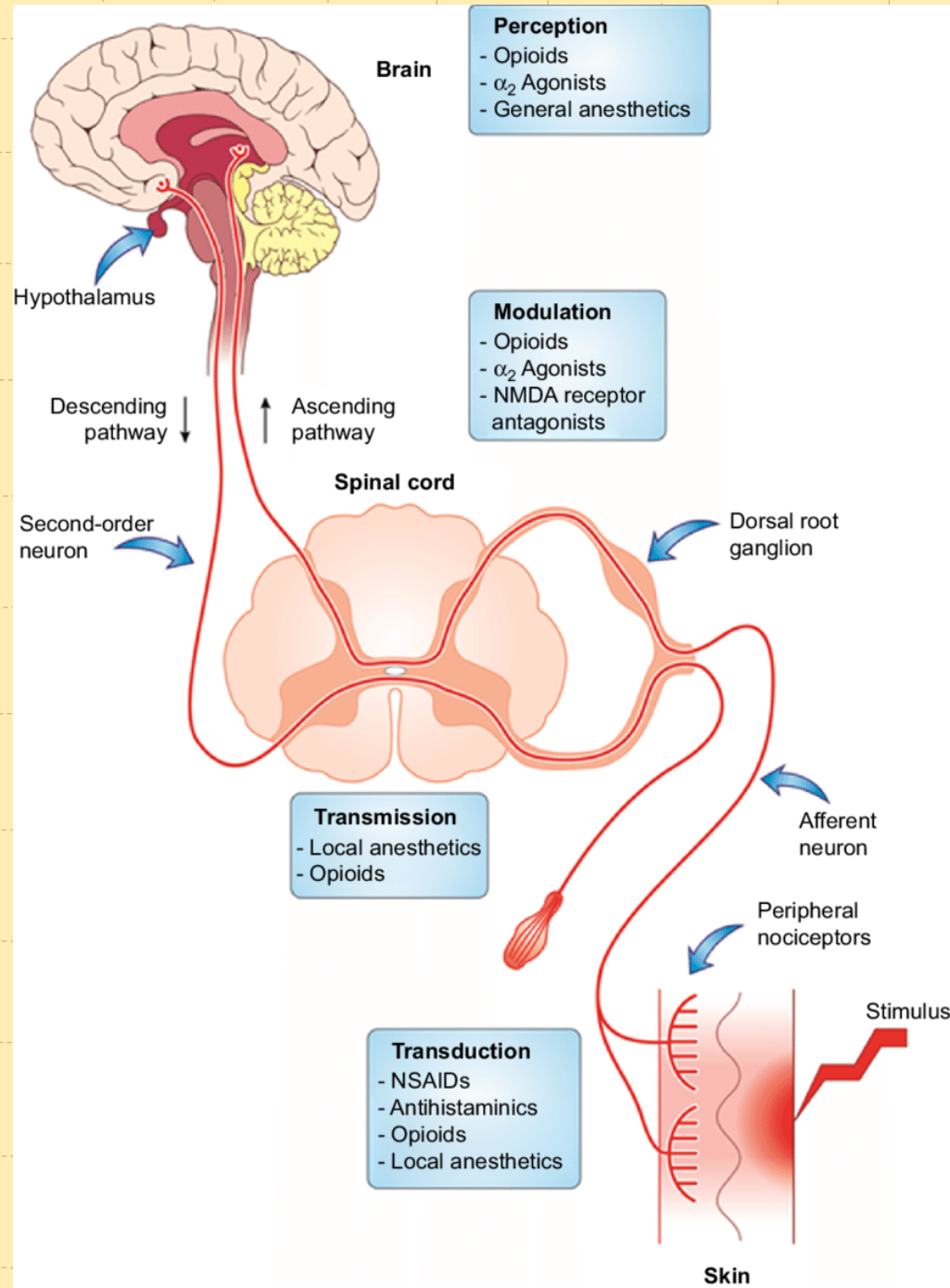
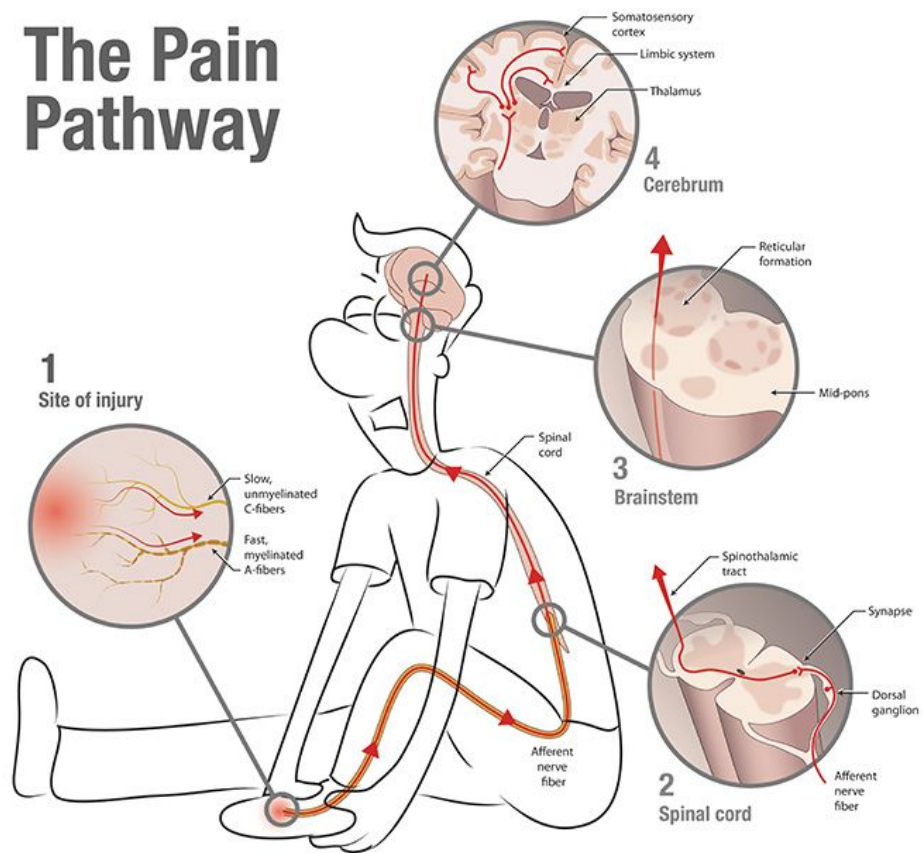
- 👤 **Nociceptive Pain** : acute pain setting
  - 👤 Somatic pain : sharp, well localized area with tissue injury
  - 👤 Visceral pain : dull cramping or colicky, poorly localized area
- 👤 **Neuropathic pain** : a result of nerve injury secondary to cutting, traction compression, or entrapment
  - 👤 Continuous burning, paroxysmal shooting, or electric pain with associated allodynia, hyperalgesia and dysesthesia
  - 👤 Delay onset, nondermatomal distribution

# Neuropathic Pain

- 🧑‍⚕️ It is critical to recognize patients who experience **neuropathic pain postoperatively** because they are **at increased risk of progressing to a chronic state**
- 🧑‍⚕️ High risk procedures
  - 🧑‍⚕️ Limb amputations
  - 🧑‍⚕️ Breast surgery
  - 🧑‍⚕️ Gall bladder surgery
  - 🧑‍⚕️ Thoracic surgery
  - 🧑‍⚕️ Inguinal hernia repair

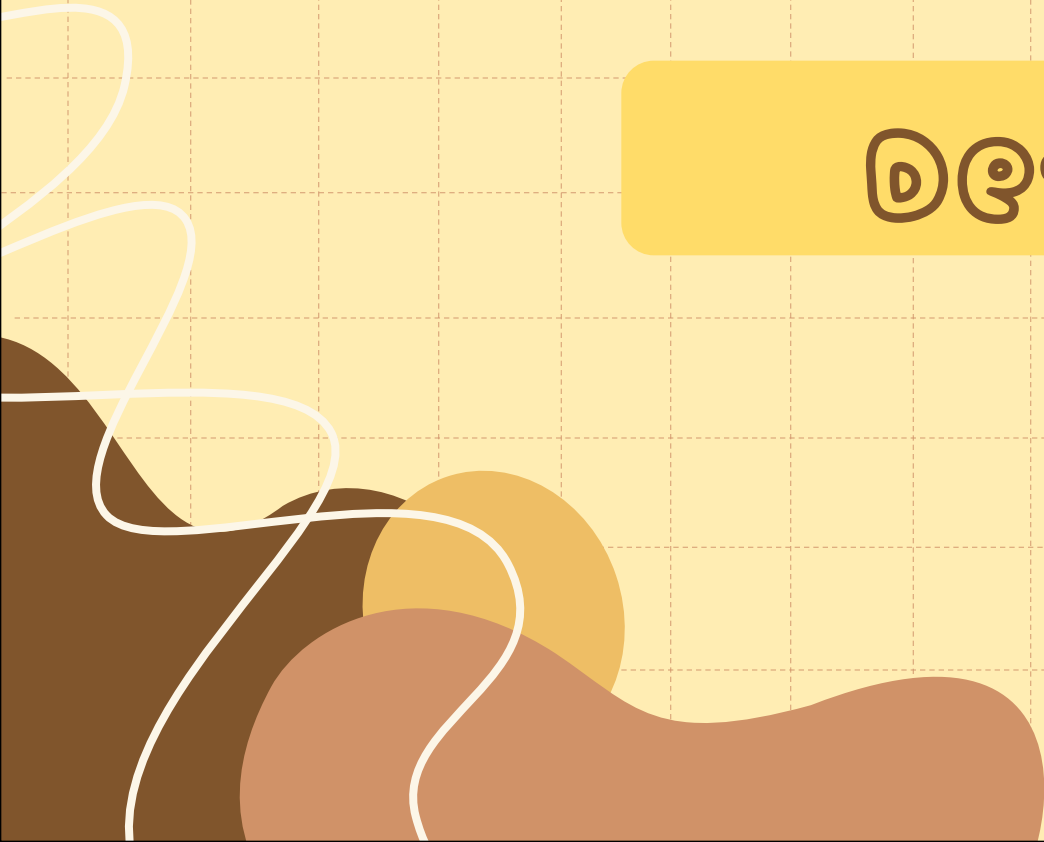
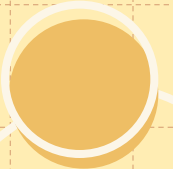
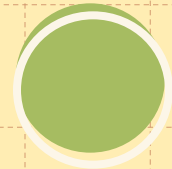
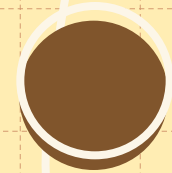
# Pain Pathway

## The Pain Pathway



2

Definition

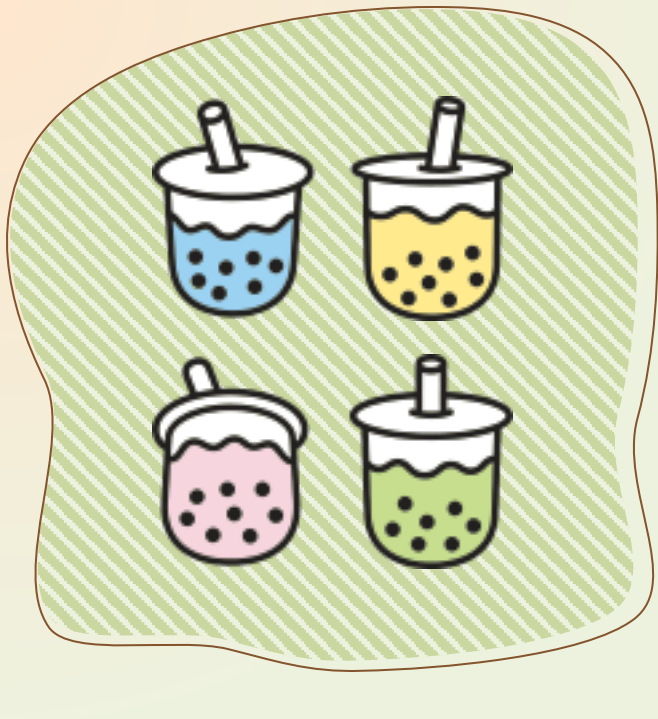




# Preemptive Analgesia

- 😊 More effective in relieving postoperative pain
- 😊 Administered **before** the surgical incision
- 😊 **Prevents** the establishment of **central sensitization** resulting from incisional injury

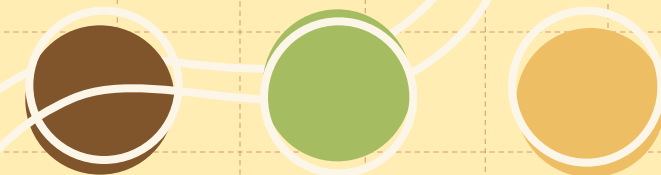
## Mechanism of action



- ☹️ Preventing NMDA receptor activation in the dorsal horn that is associated with windup, facilitation, central sensitization expansion of receptive and long term potentiation → chronic state

# Preemptive and Preventive Analgesia

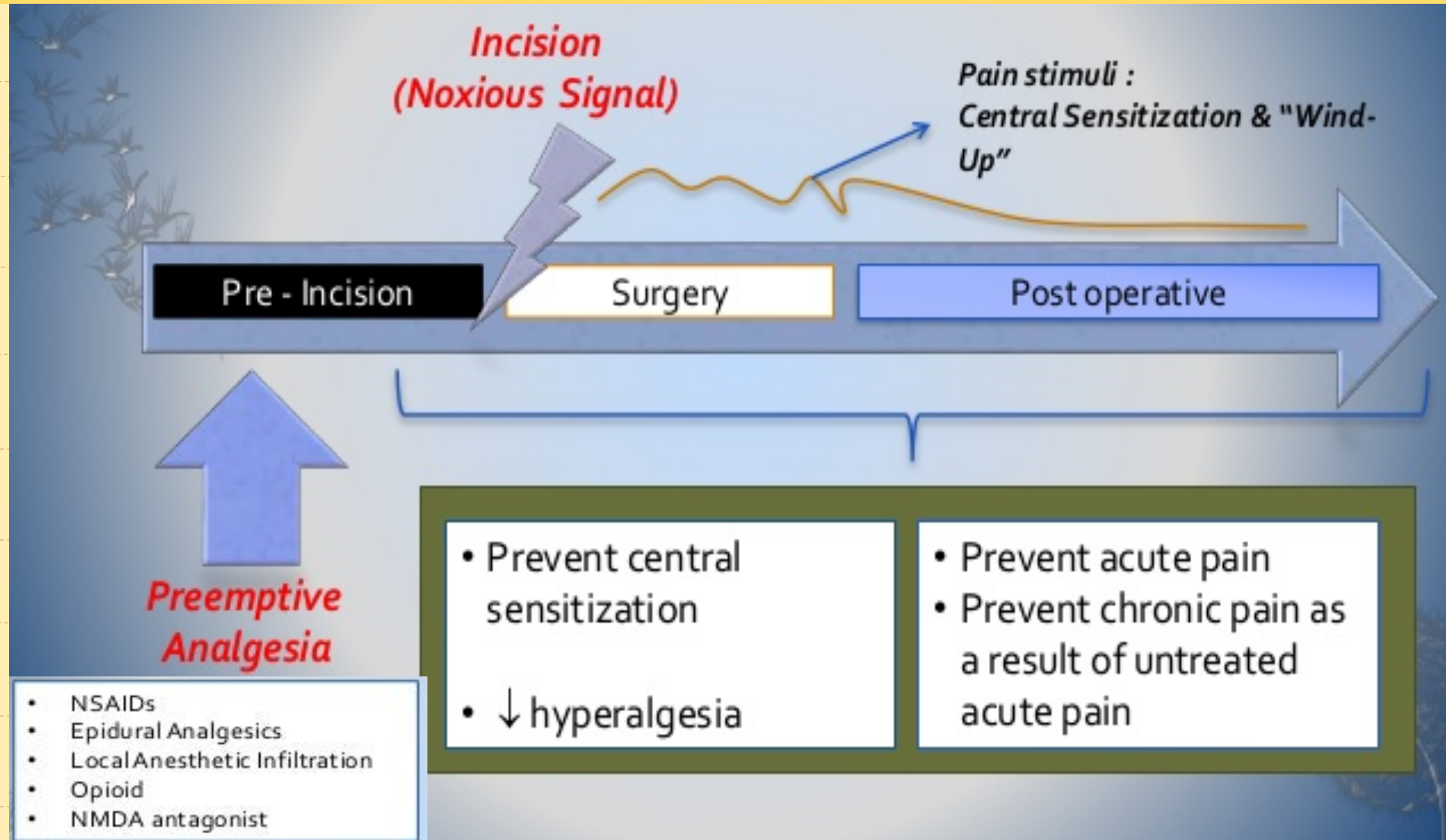
## Different?



# Preemptive Analgesia

- 🕒 Occur prior to the incision of surgery
- 🕒 Ideal
- 🕒 not always possible in some clinical setting(eg, traumatic injury)

# Clinical application of Preemptive Analgesia

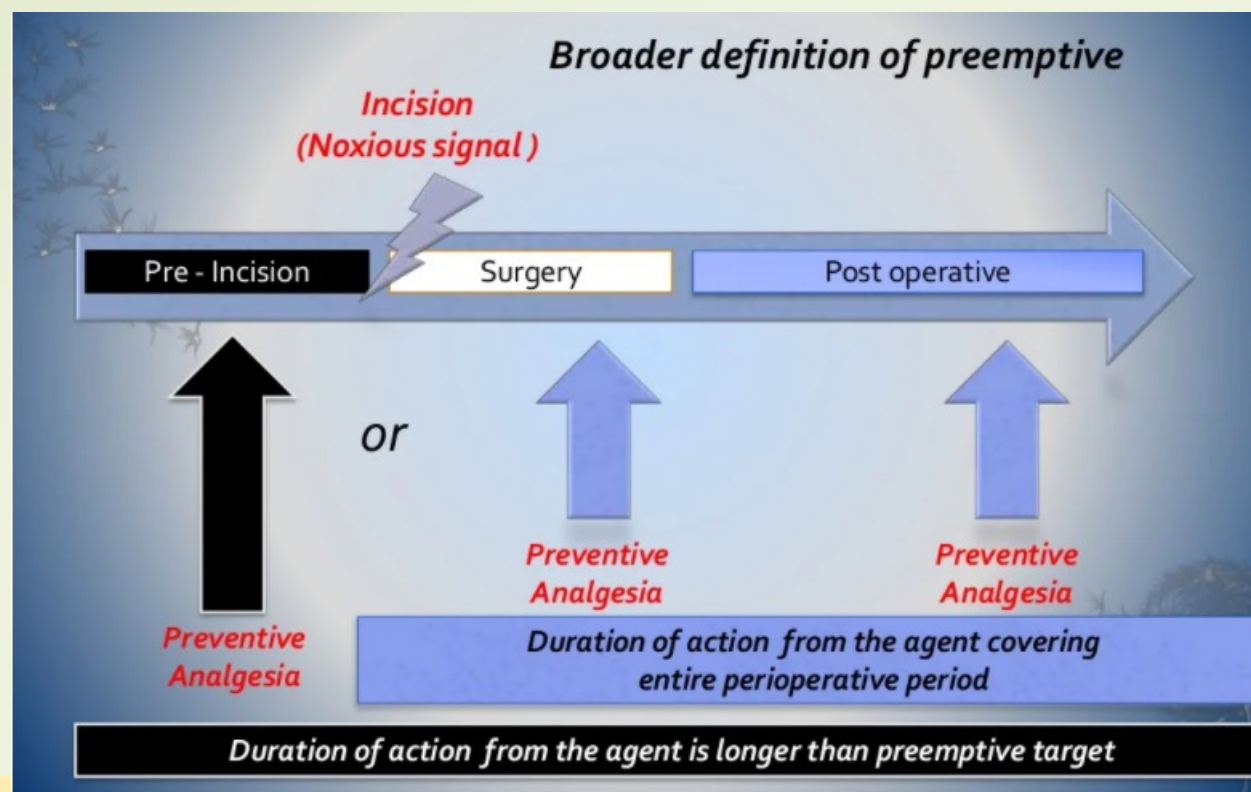


# Preventive Analgesia

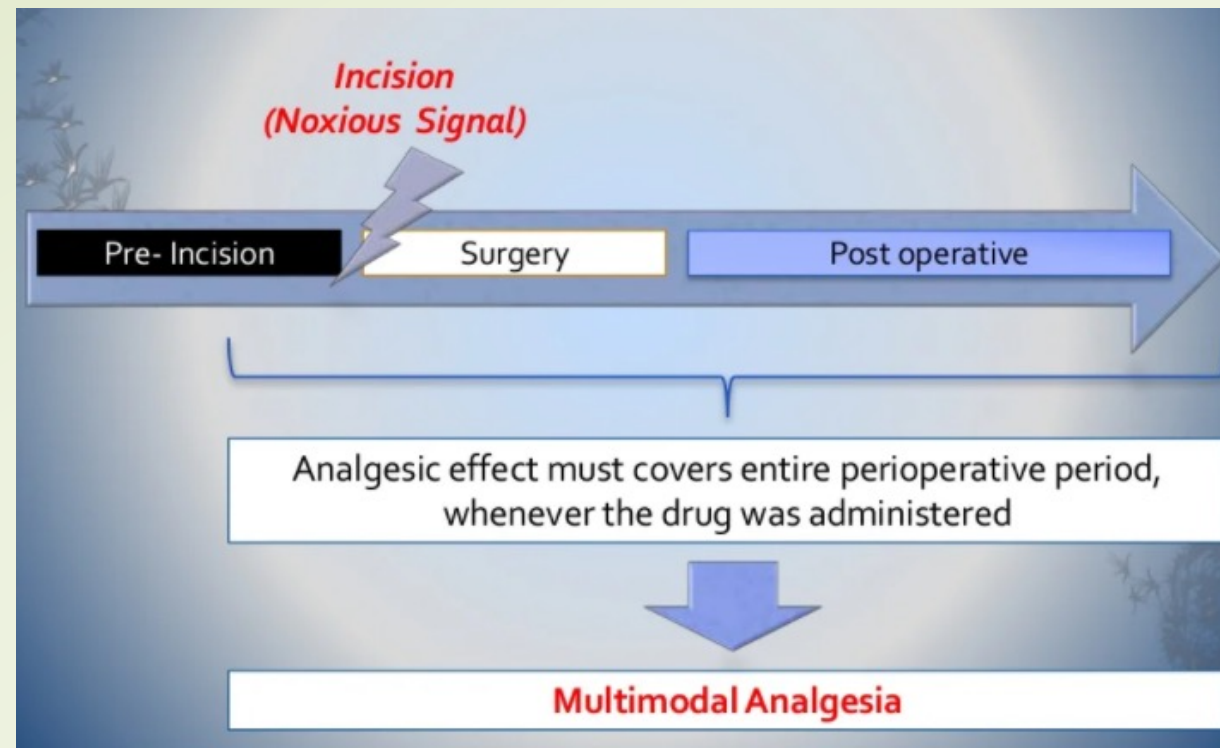
- 🕒 Perioperative intervention as it may occur prior to, during and immediately after the event
- 🕒 Duration of action from agent is longer than preemptive target

<b>Preemptive</b>		
Before surgical incision	During surgery	After surgery
<b>Preventive</b>		

# Preventive Analgesia



# Preventive Analgesia





# The principle to be successful

- ☹️ **Block all nociceptive input surgery**
- ☹️ **Entire surgical field**
- ☹️ **Duration of analgesia** must include **both the surgical and postsurgical periods.**
- ☹️ Patients with pre-existing chronic pain may not respond as well to these techniques

3

Management

# Multimodal Analgesia

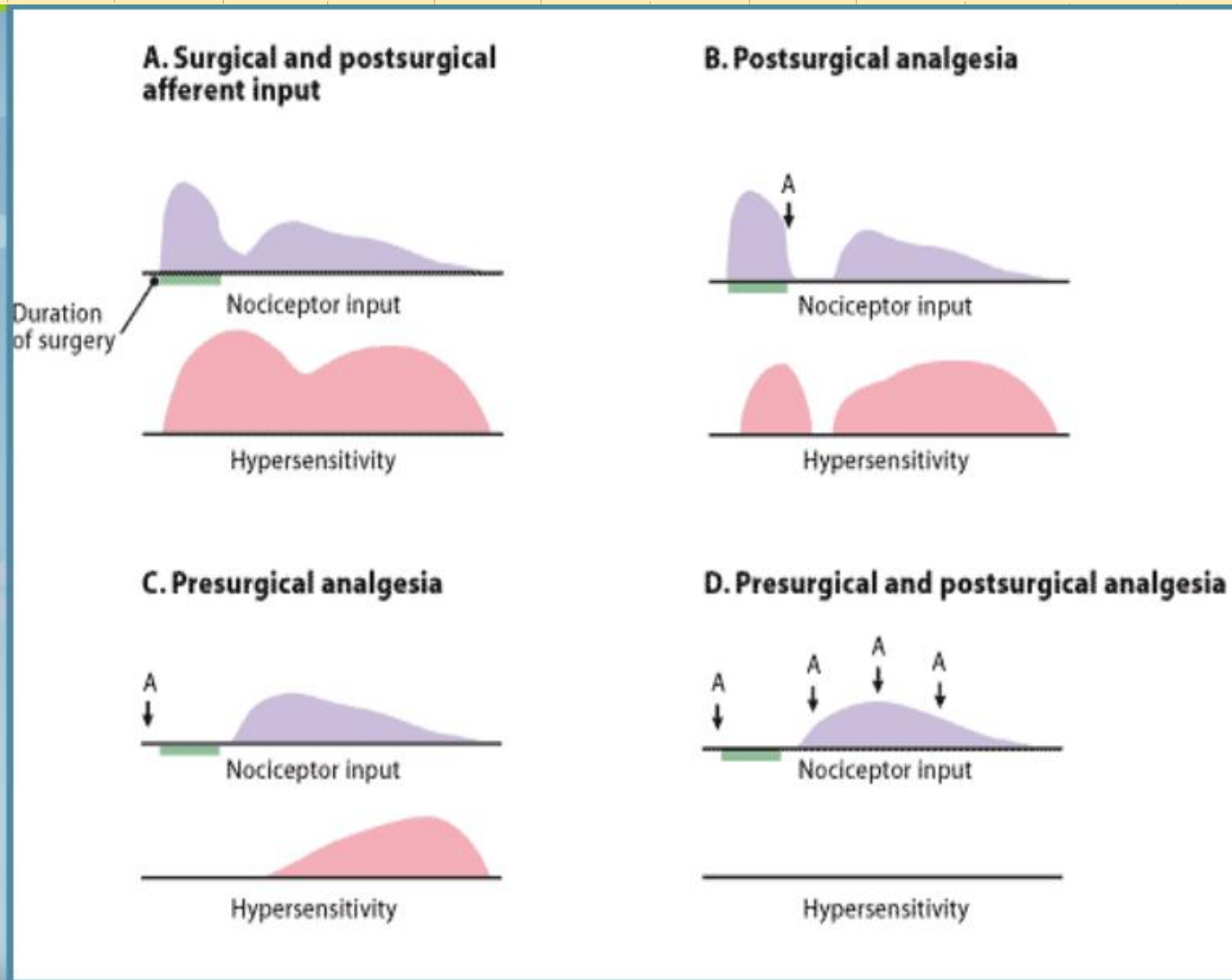
- ☺ Systemic pharmacologic therapy
- ☺ Regional analgesia
- ☺ Local analgesia
- ☺ non-pharmacological technique

# Preemptive and Preventive Analgesia



- ☹️ To decrease postoperative pain
- ☹️ Decreasing the consumption of analgesics after surgery
- ☹️ Reduction of long-term pain sensitization

# Preemptive Analgesia



4

Clinical study

OPEN

# Impact of Preemptive Analgesia on inflammatory responses and Rehabilitation after Primary Total Knee Arthroplasty: A Controlled Clinical Study

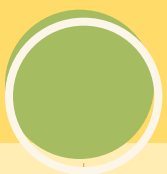
Received: 04 March 2016

Accepted: 20 June 2016

Published: 31 August 2016

Xu Jianda<sup>1</sup>, Qu Yuxing<sup>2</sup>, Gao Yi<sup>3</sup>, Zhao Hong<sup>3</sup>, Peng Libo<sup>3</sup> & Zhao Jianning<sup>4</sup>

- ☺ 75 patients with unilateral primary knee osteoarthritis
- ☺ Two groups(MMA with/without preemptive analgesia group)
  - ☺ **Preemptive oral analgesic regimen : celecoxib 400 mg po within 1 hr before operation**
  - ☺ MMA : cocktail injection(ropivacaine 357.6 mg, morphine 5 mg, adrenaline 0.3 mg, ketorolac 30 mg) for pre- and post-cementation



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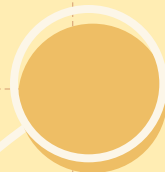
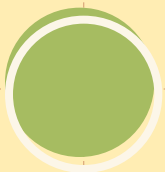
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☹️ The parameters to evaluate :

☹️ Knee flexion

☹️ Pain at rest and walking

☹️ Functional walk capacity (2 min walk test and 6 min walk test)





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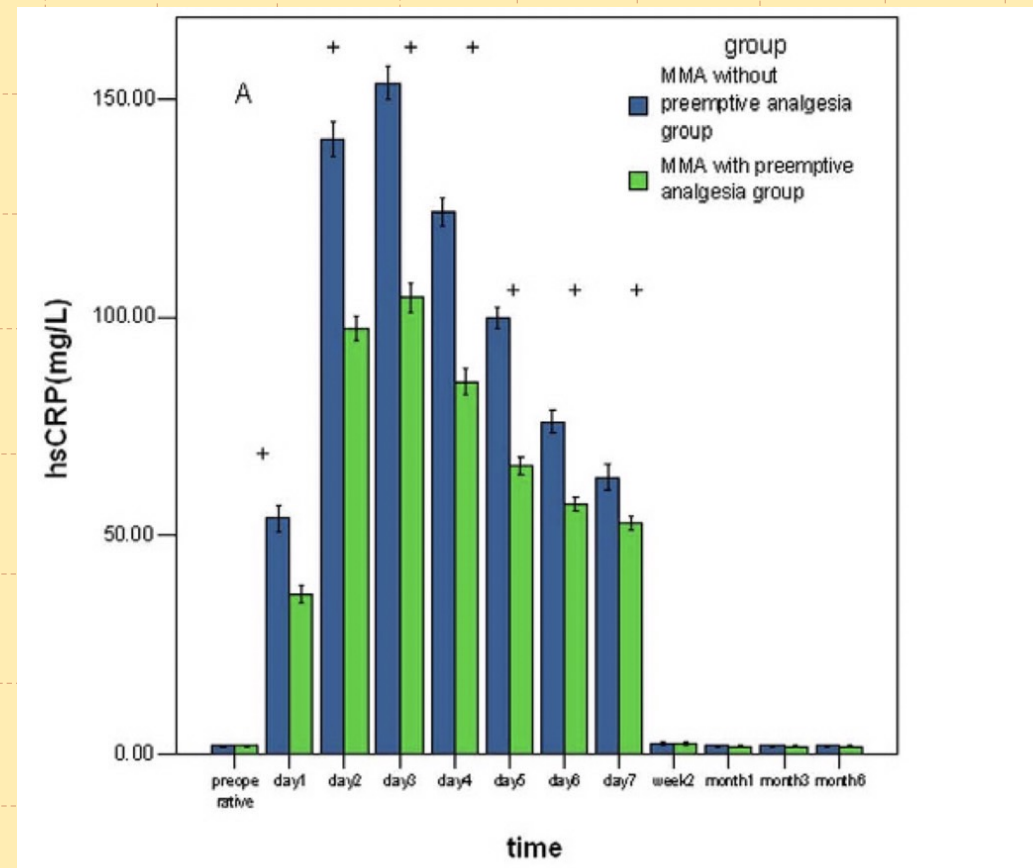
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☺ Patients in MMA with preemptive analgesia group

☺ **lower hs-CRP** during the first week postoperatively



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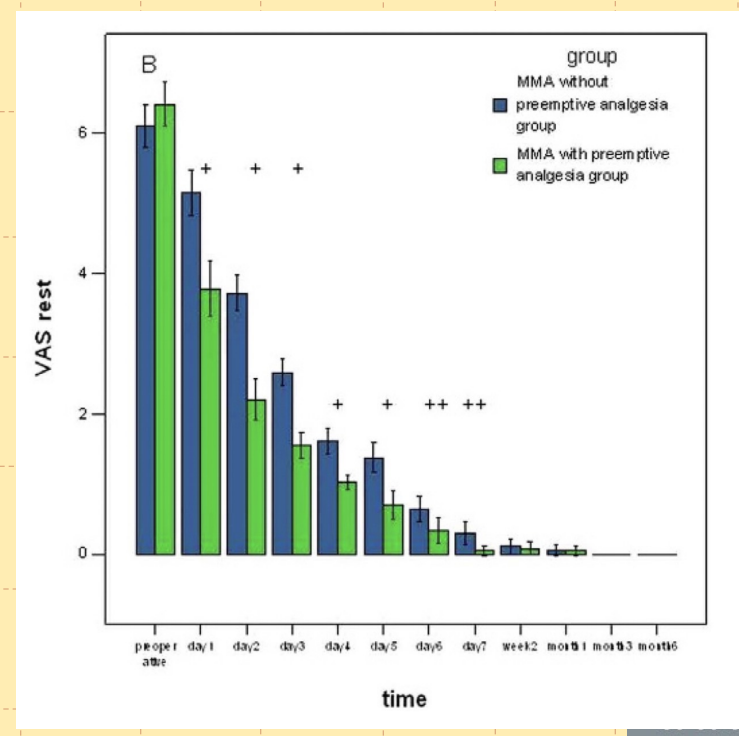
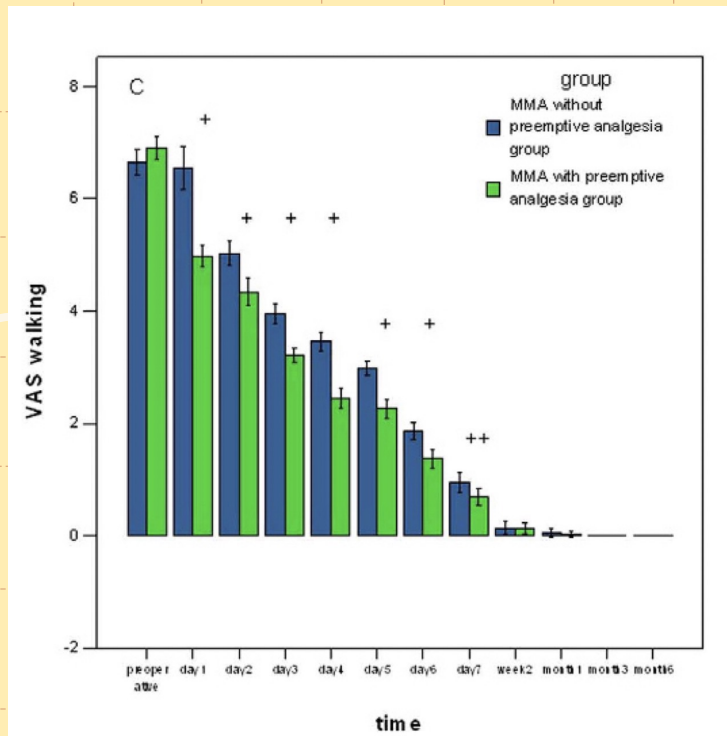
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Time	MMA with preemptive analgesia group	MMA without preemptive analgesia group	<i>P</i> -value between groups
0–24 h	13.25 ± 7.67	18.05 ± 8.57	0.017
24–48	19.08 ± 7.24	23.05 ± 9.24	0.023
total	43.28 ± 14.65	45.03 ± 15.42	0.113

**Table 2.** Cumulative consumption of morphine after total knee arthroplasty.

- ☺ Patients in MMA with preemptive analgesia group
  - ☺ **Less cumulative consumption of morphine at 48 hr**
  - ☺ but no difference at total requirement



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- ☺ Patients in MMA with preemptive analgesia group
  - ☺ Had lower hs-CRP
  - ☺ Less pain at rest and walking during the first week postoperatively
  - ☺ 2 min walk test was significant better
  - ☺ Less cumulative consumption of morphine at 48 hr but no difference at total requirement



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## 🍪 Conclusion

- 🍪 Preemptive analgesia added to multimodal analgesic regimen improved analgesia
- 🍪 Reduced inflammatory reaction and accelerated functional recovery at the first week postoperatively
- 🍪 but not improved long-term function



# Preemptive analgesia for postoperative pain relief in thoracolumbosacral spine operations: a double-blind, placebo-controlled randomized trial

Linda S. Aglio, MD, MS,<sup>1</sup> Muhammad M. Abd-El-Barr, MD, PhD,<sup>2</sup> Vwaire Orhurhu, MD, MPH,<sup>4</sup> Grace Y. Kim, MD,<sup>1</sup> Jie Zhou, MD, MS, MBA,<sup>1</sup> Laverne D. Gugino, MD, PhD,<sup>1</sup> Lisa J. Crossley, MD,<sup>1</sup> James L. Gosnell, RN, BSN,<sup>1</sup> John H. Chi, MD, MPH,<sup>3</sup> and Michael W. Groff, MD<sup>3</sup>

👤 99 patients in 3 groups

👤 Group 1 : epidural placebo with NSS 10 ml

👤 Group 2 : epidural with hydromorphone 0.5 mg alone

👤 Group 3 : epidural with bupivacaine 31.25 mg with hydromorphone 0.5 mg

receive a single shot before surgery at preoperative holding area



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## 😊 Primary outcome

- 😊 opioid sparing and rescue time

## 😊 Secondary outcomes

- 😊 Length of stay at PACU
- 😊 Pain score at PACU
- 😊 Opioid dose
- 😊 Hospital length of stay

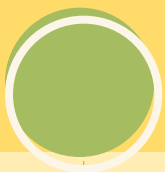


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## 🍪 Results

- 🍪 **Opioid sparing was significantly higher** in group 2 and 3 in the first demand
- 🍪 **Recue time was significantly higher** in group 2 and 3
- 🍪 There were no significant differences in secondary outcomes





# Preemptive analgesia for postoperative pain relief in thoracolumbosacral spine operations: a double-blind, placebo-controlled randomized trial

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## 🍪 Conclusion

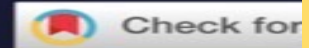
- 🍪 Preemptive analgesia in thoracolumbosacral surgeries can significantly **reduce analgesia requirements in the immediately postoperative period** as evidenced by **reduced request for opioid medication**



# Preemptive Analgesia in Minimally Invasive Gynecologic Surgery

Jaime B. Long, MD   • Kristin Bevil, MD • Dobie L. Giles, MD, MS


Published: July 28, 2018 • DOI: <https://doi.org/10.1016/j.jmig.2018.07.018> •



- 🧐 Review articles from Pubmed, Cochrane and Embase from inception through Feb 26, 2018
- 🧐 66 studies of RCT were included in the study



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 Check for updates

## Conclusion

### Preemptive **anticonvulsants, ketamine and dexmedetomidine**

 **Positive effect** on postoperative pain and opioids use

 **Limited by side effects**

### Preemptive **dexamethasone, acetaminophen and NSAIDS**





 **Modest effect** on postoperative control



# Analgesic Effect of Pre-Emptive Gabapentin on Knee Surgery: A Systematic Review and Meta-Analysis

Eun Jin Ahn; Jeong Wook Lee; Hey Ran Choi; Kyoung Woo Kim; Si Ra Bang ; Hyun Jung Kim

*Int Surg* (2017) 102 (11-12): 552–559.

-  Conducted a systemic review and meta-analysis of RCT
-  Searched MEDLINE, EMBASE and Cochrane Library and Korean Med (Jan 1976 – Apr 2014)
-  225 patients in 4 studies were included in the study
-  The overall pooled results from meta-analysis demonstrated that compared with placebo



# Gapapentin

🧐 Anticonvulsant drug

🧐 Treatment

🧐 neuropathic pain

🧐 diabetic neuropathy

🧐 postherpetic neuralgia

🧐 antihyperanalgesia

🧐 anxiolytic

# Gabapentin

- ☹️ The antinociceptive effects involve central sensitization
- ☹️ The unique **binding to the  $\alpha 2\delta$  calcium subunit** explains the reduction of neurotransmitter release by gabapentin and thus its antinociceptive effect
- ☹️ **Several studies** have shown the **role of preoperative gabapentin on decreases in postoperative pain scores and opioid requirements**

# Gabapentin

- 😊 Gabapentin : mean maximum plasma concentration in 2 hours
- 😊 The administration time of gabapentin is **recommended 2 hours before surgical stimulation**
- 😊 The overall outcome of postoperative pain score appeared to be **reduced until postoperative 4 hours**

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## The subgroup analyses



-  **General analgesia** : Gabapentin significantly reduced the postoperative pain score
-  **Regional analgesia** : Could not clarify the effective of gabapentin on reducing postoperative pain





Table 2 Further data extracted from the included studies

Sources	Gabapentin given time and dose	Regional anesthesia	Type of anesthesia	Postoperative additional analgesics use	Premedication
Clarke H 2009	600 mg, 2 hours preoperatively	femoral and sciatic NB	spinal anesthesia	celecoxib 200 mg every 12 h 4 day and IV PCA	celecoxib 400 mg 2 hours preoperatively
Menigaux 2005	1200 mg, 1–2 hours preoperatively	no	general anesthesia	ketoprofen 150 mg po bid, IV PCA	no
Paul 2013	600 mg, 2 hours preoperatively	no	spinal anesthesia	IV morphine PCA	acetaminophen 100 mg PO, ketorolac 15 mg IV 2 hours preoperatively
Montazeri 2007	300 mg, 2 hours preoperatively	no	general anesthesia	iv morphine	no

🧠 **Spinal anesthesia** : study of Clarke and Paul

🧠 not only regional analgesia, but also multimodal analgesia



🧠 incremental benefit of gabapentin is **negated by the effects of multimodal analgesia or regional anesthesia**

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Eun Jin Ahn; Jeong Wook Lee; Hey Ran Choi; Kyoung Woo Kim; Si Ra Bang ; Hyun Jung Kim

*Int Surg* (2017) 102 (11-12): 552–559.

## Conclusion

-  Preemptive gabapentin reduced early postoperative pain scores
-  Unclear whether gabapentin reduces postoperative pain score in regional analgesia or multimodal analgesia





REVIEW ARTICLE

# Preventive analgesia in hip or knee arthroplasty: A systematic review<sup>☆</sup>

J. Díaz-Heredia<sup>a,\*</sup>, E. Loza<sup>b</sup>, I. Cebreiro<sup>a</sup>, M.Á. Ruiz Iban<sup>a</sup>

<sup>a</sup> *Servicio de Traumatología y Cirugía Ortopédica, Hospital Universitario Ramón y Cajal, Madrid, Spain*

<sup>b</sup> *Instituto de Salud Musculoesquelética, Madrid, Spain*

Received 20 March 2014; accepted 16 September 2014

- ☺ Systemic reviews, meta-analysis, RCT and observational studies were selected
- ☺ Searched MEDLINE, EMBASE and Cochrane Library up to May 2013
- ☺ A total of 36 articles, moderate quality were selected
- ☺ The treatment included NSAIDs, opioids corticosteroids, anticonvulsant, topical





REVIEW ARTICLE

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ELSEVIER

## Conclusion

LE; RG

- Preventive analgesia with NSAIDs seems to decrease both pain and opioid consumption in the postoperative period
  - Results were more consistent and longer-lasting with Cox-2 than with traditional NSAIDs
  - With traditional NSAIDs there were no significant adverse events except for perioperative bleeding, which did not appear with Cox-2
- Preventive analgesia with opioids reduced the consumption of analgesics in the postoperative period. An improvement of analgesia was also observed in the immediate postoperative period, albeit not in the long term
  - Safe strategies, with no significant adverse events

1b; A

1b; A



REVIEW ARTICLE

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- Preventive analgesia with corticoids seems to reduce both pain and opioid consumption in the postoperative period at 48 h, but not after 6 months or 1 year 2a; B
- Preventive analgesia with pregabalin seemed to reduce neuropathic pain in the short and long term 2b; B
  - There is insufficient evidence to determine the effect on postoperative nociceptive pain and consumption of opioids
  - Preventive analgesia with gabapentin did not influence postoperative pain
- The use of ketamine and magnesium sulfate during analgesic induction seemed to have a beneficial effect on pain control and opioid consumption in the immediate postoperative period 1b; A



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- There is insufficient evidence to determine the effect of preventive analgesia with nimodipine, duloxetine and clonidine 2b; B
- Preventive analgesia with combinations of various analgesics reduced pain and the need for analgesics after surgery 2b; B
- There is insufficient evidence to recommend a specific strategy for preventive analgesia or administration protocol. However, it seems that administration of one or more analgesics at some point during the preoperative process reduces postoperative pain and consumption of analgesics 2b; B



REVIEW ARTICLE

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## ☺ Conclusion

- ☺ The use one or more pre-surgical analgesics decrease the use of post surgical drugs, at least for short term pain





Original Contribution

**Effect of preemptive and preventive acetaminophen on postoperative pain score: a randomized, double-blind trial of patients undergoing lower extremity surgery<sup>☆</sup>**

Gholamreza Khalili MD (Associate Professor)<sup>a</sup>, Mohsen Janghorbani PhD (Professor)<sup>b,\*</sup>,  
Hamid Saryazdi MD (Assistant Professor)<sup>a</sup>, Abbas Emaminejad MD<sup>a</sup>

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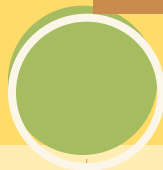
☺ 75 adults, ASA 1 and 2 in 3 groups

☺ Group 1 : NSS 100 ml as placebo

☺ Group 2 : preemptive acetaminophen 15 mg/kg half an hour preoperatively

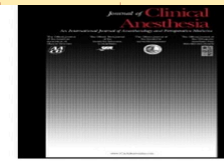
☺ Group 3 : preventive acetaminophen 15 mg/kg prior to skin closure

Pain scores assessed at 5 min before spinal analgesia and 6, 12, 18  
and 24 hours after surgery





	Treatment groups			<i>P</i> -value*
	Preemptive acetamin mean (SD)	Preventive acetamin mean (SD)	Normal saline mean (SD)	
Patients (n)	25	25	25	-
VRS at 6 hrs	2.72 (1.27)	2.87 (1.96)	4.48 (1.04)	0.001
VRS at 12 hrs	4.08 (1.66)	4.42 (1.82)	4.24 (1.45)	0.775
VRS at 18 hrs	2.92 (1.06)	2.96 (1.34)	3.17 (1.05)	0.727
VRS 24 hrs	2.00 (1.48)	1.83 (0.83)	1.77 (1.41)	0.821
Postop meperidine (mg)	23.0 (20.3)	30.0 (22.8)	42.0 (15.7)	0.003
Time to first postop request for analgesic (min)	10.8 (4.4)	10.7 (4.3)	7.0 (3.3)	0.008



Original Contribution

Effect of preemptive and preventive acetaminophen on postoperative pain score: a randomized, double-blind trial of patients undergoing lower extremity surgery<sup>☆</sup>

Gholamreza Khalili MD (Associate Professor)<sup>a</sup>, Mohsen Janghorbani PhD (Professor)<sup>b,\*</sup>,  
Hamid Saryazdi MD (Assistant Professor)<sup>a</sup>, Abbas Emaminejad MD<sup>a</sup>

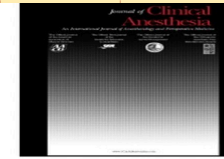
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🕒 Results

- 🕒 Pain scores were lower in both preemptive and preventive acetaminophen group at 6 hours after surgery
- 🕒 Total analgesic consumption 24 hour after surgery was lowest in the preemptive acetaminophen group
- 🕒 Average time to initial analgesic requirement was slightly longer in the preemptive and preventive acetaminophen group





Original Contribution

Effect of preemptive and preventive acetaminophen on postoperative pain score: a randomized, double-blind trial of patients undergoing lower extremity surgery<sup>☆</sup>

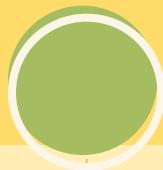
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😊 Conclusion

- 😊 Both preemptive and preventive acetaminophen may enhance analgesia and decrease postoperative analgesic consumption



# Take Home Messages

Preemptive		
Before surgical incision	During surgery	After surgery
Preventive		

- ☺ Preemptive analgesia was based on the inhibition of the central sensitization
- ☺ Management : multimodal analgesia
- ☺ Goals : decreasing postoperative pain, decreasing the consumption of analgesics after surgery and reducing of long-term pain sensitization



Thank you

Do you have any questions?