Cancer Pain

The Fifth Vital Sign
Agony Is A Medical Emergency

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Pain (통증, 痛症)

- An unpleasant **sensory** and **emotional** experience associated with actual or potential tissue damage, or described in terms of such damage

- **Pain is what the patient says hurts**
- Pain is whatever the experiencing person says it is, and exists whenever he says it does

- Pain is always subjective
- **Trust him/her !!!**

Cause of pain in cancer patient

- **Direct tumor involvement (65-85%)**
  - Bone pain (most common)
  - Nerve infiltration
  - Hollow viscus infiltration
- Cancer therapy (15-25%)
  - Chemotherapy : mucositis, neuropathy, or phlebitis
  - Radiotherapy : mucositis, enteritis, or cord injury
  - Surgery, etc.
- Non-cancer-related problems (3-10%)
  - Common causes of pain in the general population

Oxford textbook of palliative medicine, 3rd ed.

Epidemiology

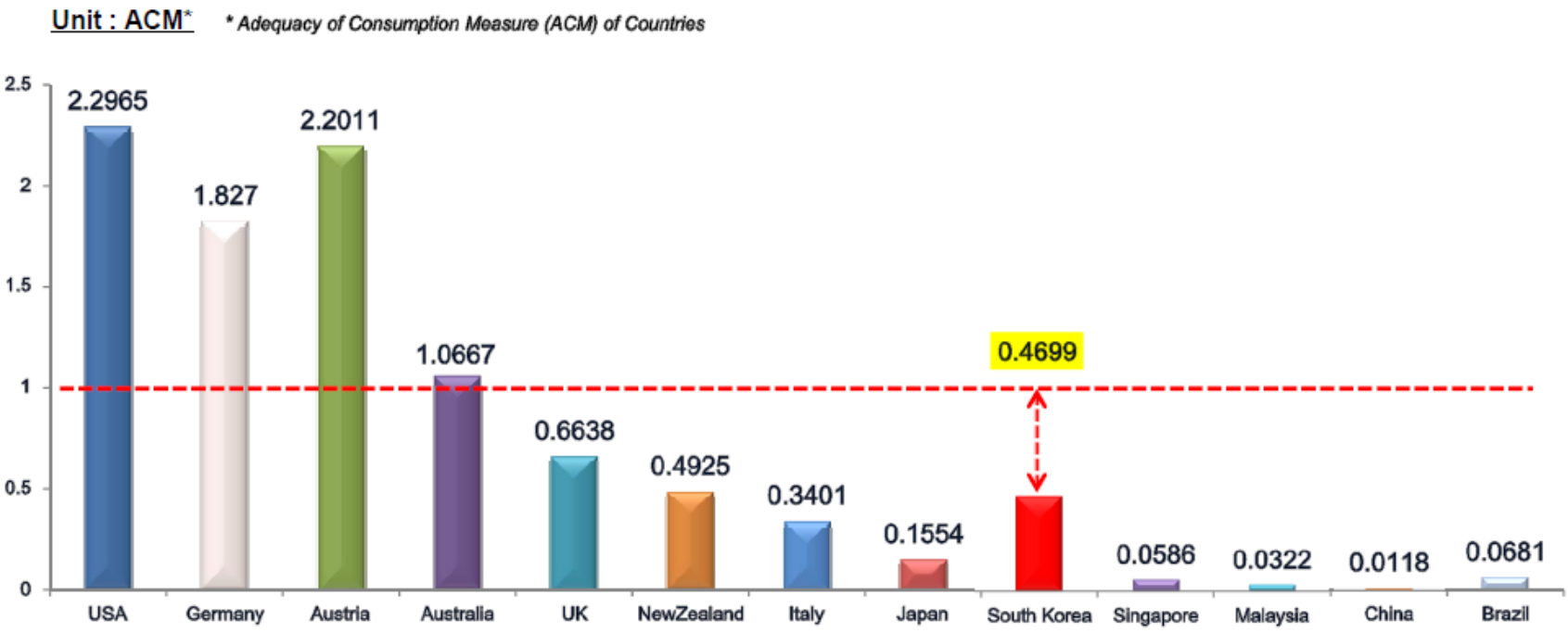
"Moderate to severe pain is experienced by one-third of cancer patients receiving active therapy and by 60% to 90% of patients with advanced disease."

World Health Organization. *Cancer pain relief,* 2nd ed. Geneva: World Health Organization, 1996

Epidemiology

- **One in five patients** with cancer has **uncontrolled pain**
- Pain affects the majority of patients with cancer
  - At diagnosis : 30-40%
  - Advanced disease : 60-80%
- 69% of patients reported they would consider committing suicide if their pain were not adequately treated
- 86 of physicians surveyed reported that the majority of patients with pain were under-medicated

Inadequate Controlled Pain



* Consumption of mEq in kg

Beatrice Duthey, and Willem Scholten, Adequacy of Opioid Analgesic Consumption at Country, Global, and Regional Levels in 2010, Its Relationship With Development Level, and Changes Compared With 2006, Feb;47(2):283-97 J Pain Symptom Manage. 2014.

Barriers to cancer pain management

Cancer Pain

Table 2. Physicians' perceived barriers in the optimisation of cancer pain management (n = 463)

Potential barrier	n (%) of respondents (NRS score > 5)	Median (IQR)
Patient's reluctance to take opioids due to fear of addiction	311 (67)	7.0 (3.0)
Patient's reluctance to take opioids due to fear of adverse effects	301 (65)	7.0 (3.0)
Patient's reluctance to report pain	243 (53)	6.0 (5.0)
Inadequate assessment of pain by physicians and/or nurses	230 (50)	5.0 (5.0)
Lack of available pain or palliative medicine services	226 (49)	5.0 (5.0)
Excessive regulation of opioid drugs	222 (48)	5.0 (5.0)
Physician's reluctance to prescribe opioids	198 (43)	5.0 (4.0)
Patient's inability to pay for interventional analgesics/ pharmacotherapy/opioid analgesics	173 (38)	5.0 (5.0)

IQR, interquartile range; NRS, numeric rating scale

Non-cancer Pain

Table 3. Physicians' perceived barriers for optimal CNCP management (n = 695)

Potential barrier	n (%) of physicians (NRS score > 5)	Median (IQR)
Patient's reluctance to take opioids due to fear of adverse effects	452 (65)	7.0 (3.0)
Patient's reluctance to take opioids due to fear of addiction	451 (65)	6.0 (3.0)
Physicians reluctance to prescribe opioids	443 (64)	6.0 (3.0)
Inadequate assessment of pain by physicians and/or nurses	423 (61)	6.0 (3.0)
Limitations of non-opioid analgesics	401 (58)	6.0 (4.0)
Excessive regulations of opioid drugs	398 (57)	6.0 (3.0)
Lack of pain or palliative medicine services	353 (51)	6.0 (4.0)
Patient's reluctance to report pain	327 (47)	5.0 (5.0)
Patient's inability to pay for medications*	308 (44)	5.0 (4.0)

CNCP, chronic non-cancer pain; IQR, interquartile range; NRS, numeric rating scale
*Medications including inteventional analgesics/pharmacological treatment/opioid analgesics

Poster presented at the IASP 15th World Congress on Pain at 2014 Oct, Buenos Ares in Argentina

- **의료진의 문제점[1-3]**
  - 통증조절 지식부족
  - 통증호소에 대한 평가부족
  - 법적규제에 대한 우려
  - 마약중독에 대한 우려
  - 마약성 진통제의 부작용에 대한 우려
- **제도의 문제점[1-3]**
  - 통증조절의 중요성에 대한 인식부족
  - 건강보험의 삭감
  - 마약성 진통제의 취급규제

- **환자의 문제점[1-3]**
  - 통증을 다른 사람에게 호소하는 것을 기피
  - 마약성 진통제의 중독우려
  - 진통제의 부작용 우려
  - 진통제 사용시 질병치료 방해 우려

1. Young Jin Yuh, MD, Opioid Use in Pain , Journal of Pain and Autonomic Disorders. 2013. Vol 2 No 2
2. Yun YH, Kim CH. J Korean Acad Fam Med 1997;18:591-600.
3. Kim MH et al. Jpn J Clin Oncol 2011;41:783-791.

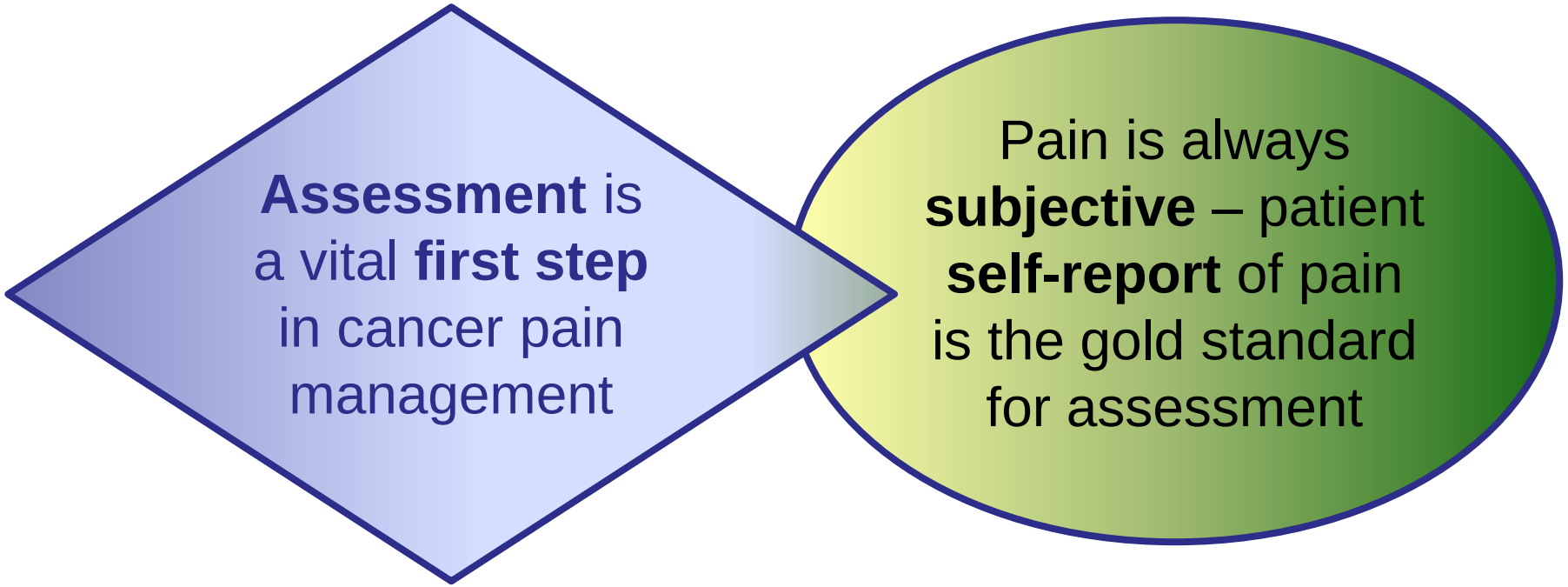
암성 통증이 조절되지 않으면...

- 불필요한 고통에 시달리게 된다
- 전신상태가 악화된다
- 암치료에 대한 순응도가 저하된다
- 환자의 사회적, 가족적인 역할을 수행하지 못하게 된다
- 삶에 대한 의욕, 희망이 없어진다

Symptoms of chronic cancer pain

- 기분이 우울하다
- 식욕이 저하된다
- 잠을 쉽게 이루지 못하고 자주 깬다
- 종일 침대에서 누워서 지낸다
- 다른 사람과 대화가 적다
- 일상 생활이 어렵다

Assessment of cancer pain : key concepts



(WHO 1996) (APS 1999)
(Portenoy RK. In: *Contemporary Diagnosis and Management of Pain in Oncologic and AIDS Patients*. 2nd ed. Newtown, PA: Handbooks in Health Care Co; 1998)

Assessment

- **Trust patients** assessment of pain
- Tell me **all about** your pain
- The extent of disease doses not exactly tell the extent of pain
- Location, onset, duration, type and intensity

Importance of Listening

Assessment of pain (PQRST)

- Position
- Quality : somatic, visceral, neuropathic
- Relieving or aggravating factor
- Severity
- Timing
  - Acute, chronic, breakthrough pain

Quality (type of pain)

- Nociceptive : nociceptors involved
  - Somatic : bone, soft tissue, muscle, skin
  - Visceral : cardiac, lung, GI tract, GU tract

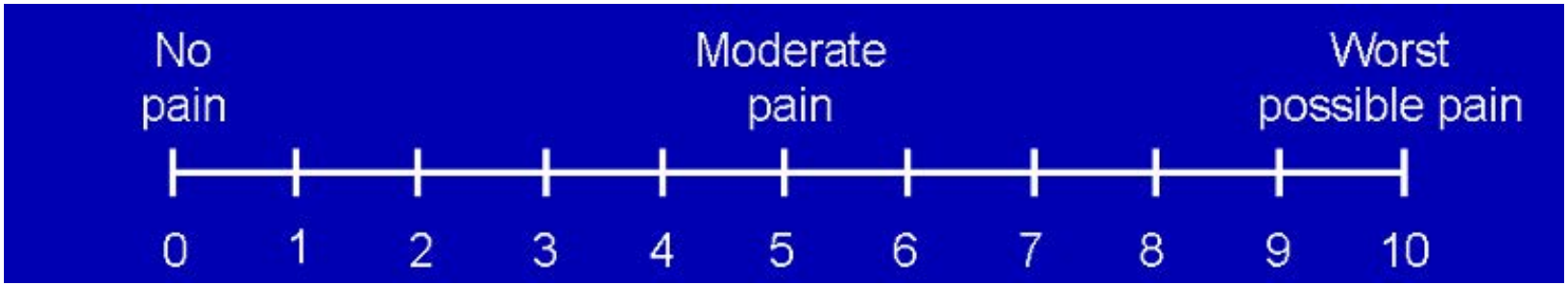
- Neuropathic : direct invasion/ injury to nerve
  - Peripheral : mono- & polyneuropathies
  - Central : spinal cord, brainstem, thalamus
  - Sympathetic : causalgia, brachial or sacral plexus tumor infiltration

Type of pain

Type	Characteristcs	Examples	1° therapy
Somatic	Constant, aching, gnawing, well localized	Bone meta, post surgical pain	Tx of tumor, anti-inflammatory agent, analgesics
Visceral	Deep,squeezing, often associated with nausea, poorly localized	Pancreatic ca	Tx of tumor, analgesics, nerve blocks
Neuropathic	Severe burning-like m/c in the site of sensory loss a/w hypersensitivity to stimuli	Postherpetic neuralgia	Tx of tumor, analgesics, nerve blocks

Severity of Pain

- Numeric Rating Scale (NRS)



  - None (0), Mild (1-3), Moderate (4-6), Severe (7-10)

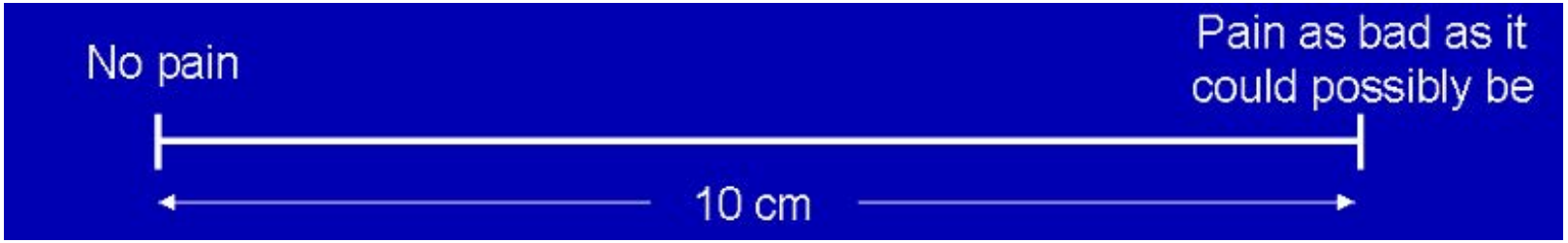
- Pain Affects Faces Scale

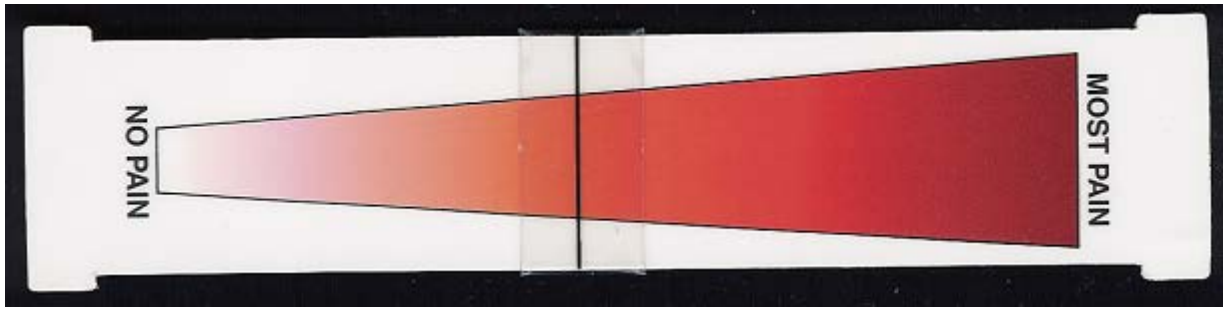
Instructions: "These faces show how much something can hurt. This face (point to the left-most face) shows no pain. Each face shows more and more pain (point to each face from left to right) up to this one (point to the right-most face)--it shows very much pain. Point to the face that shows how much you hurt (right now)."

[1]Hicks CL, von Baeyer CL, Spafford P, et al. The Faces Pain Scale - Revised: Toward a common metric in pediatric pain measurement. Pain 2001;93:173-183.
[2]Ware LJ, Epps CD, Herr K, Packard A. Evaluation of the Revised Faces Pain Scale, Verbal Descriptor Scale, Numeric Rating Scale, and Iowa Pain Thermometer in older minority adults. Pain Manag Nurs 2006;7:117-125.

Severity of pain

Visual Analog Scale (VAS)





Management of cancer pain

- Pharmacological approach
  - Opioid analgesics
  - Non-opioid analgesics
  - Analgesic adjuvants

- Non-pharmacologic approach
  - Psychosocial support
  - Patient and family/caregiver education
  - Physical modalities: massage, physical therapy, TENS, etc
  - Cognitive modalities
  - Spiritual care

진통제 사용의 원칙

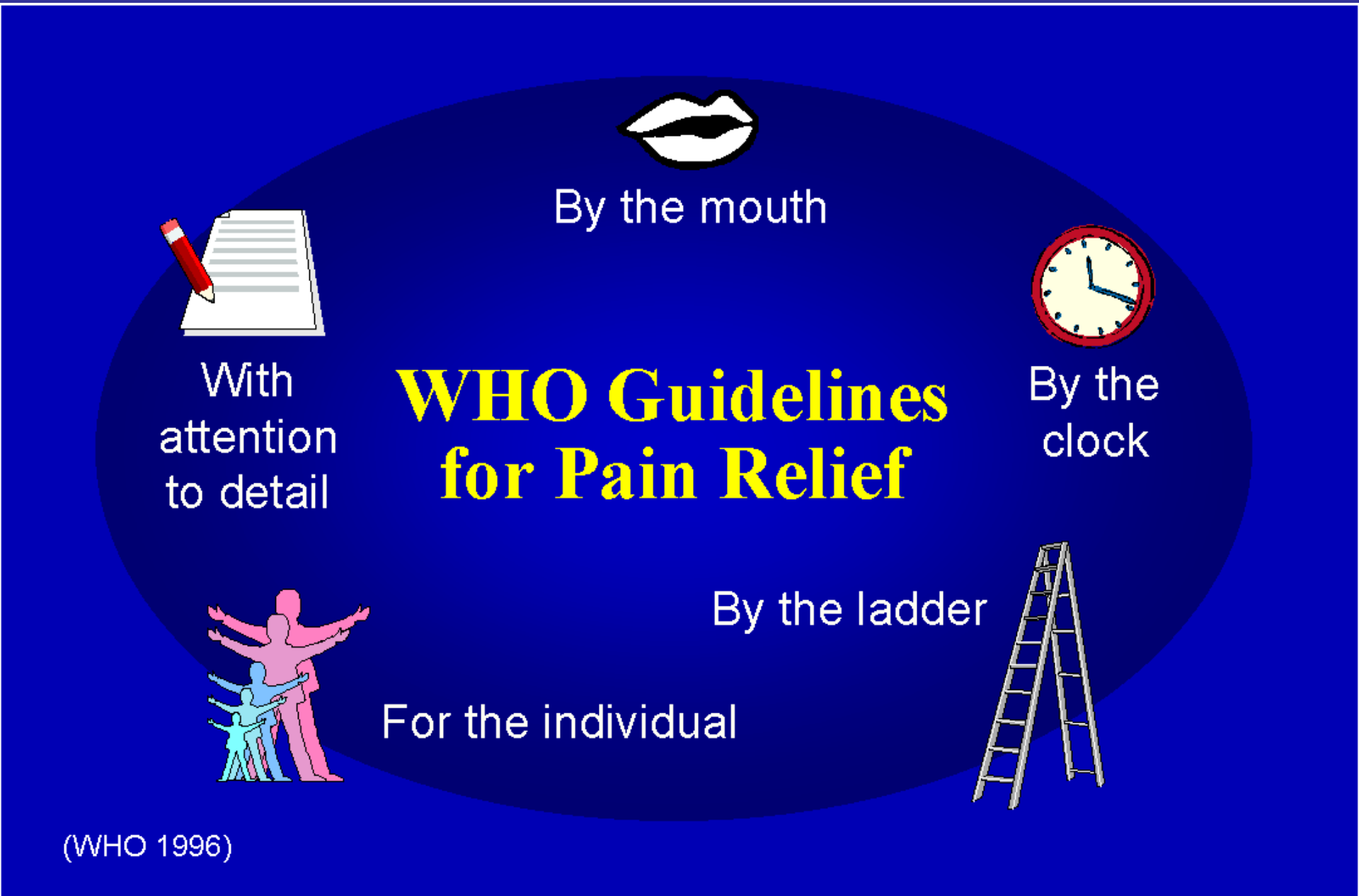
- 환자 개개인에게 적합한 진통제의 종류, 용량 및 투여방법을 선택한다.
- 환자의 상황이 허락하는 한 먹는 진통제를 우선 투여한다.
- WHO 3단계 진통제 사다리에 따라 진통제를 선택 또는 추가한다.
- 진통제를 일정한 시간 간격으로 투여하여 혈중 농도를 항상 일정하게 유지하면 암성 통증의 재발을 예방할 수 있다. 통증이 잘 조절되던 중에 급작스럽게 발생하는 돌발성 통증에 대비하여 속효성 진통제를 미리 처방하여 돌발성 통증 발생시 환자가 사용할 수 있도록 한다.
- 진통제 투여 후 통증조절이 잘 되고 있는지 자주 관찰하고 효과를 평가하고, 통증 조절이 부족하면 진통제 처방을 변경해야 한다.

보건복지부 암성 통증관리지침 권고안

진통제 사용의 원칙

- 모든 통증이 다 진통제에 반응하는 것은 아니다
- 보조 진통제를 사용하는 것이 도움이 된다
- 불면증, 우울증 등을 적극적으로 치료해야 한다

WHO Guidelines

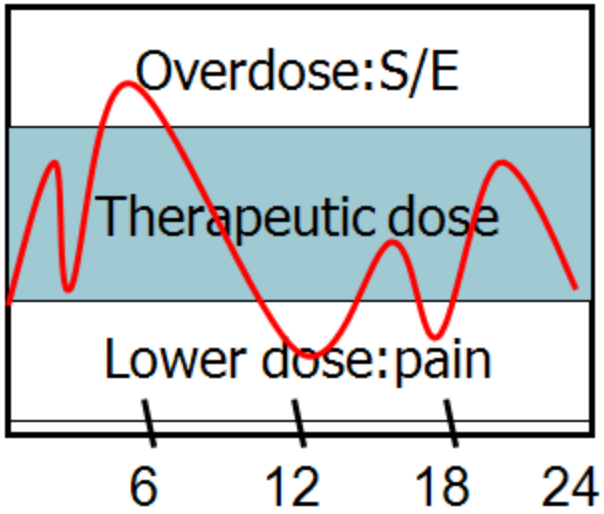


By the ladder

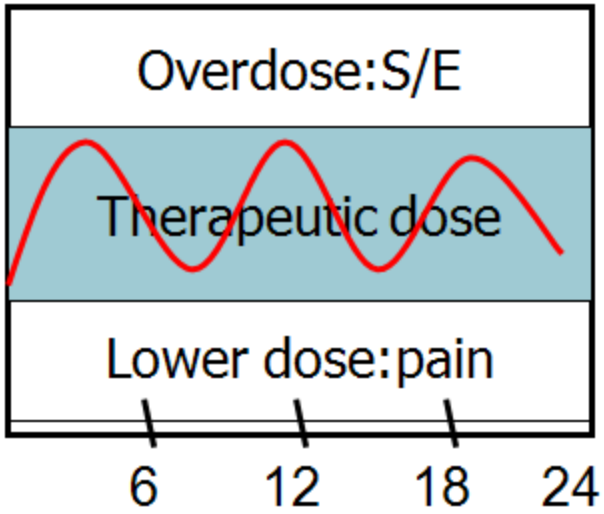
〈그림 2 : WHO 3단계 진통제 사다리〉

By the clock

- Do not use prn orders
- Prevent pain rather than treat pain
- Short acting opioid for breakthrough pain



Drug given in response to pain (prn)



Drug given to prevent pain

By the appropriate route

Route	Advantage	Defect
Oral	Painless Possible self medication	Nausea, vomiting, constipation
Transdermal	Painless Possible self medication Long acting	Slow onset of action Slow elimination Slow dose modification
SC/IV infusion PCA	Rapid onset Rapid dose titration	Invasive, painful Need hospitalization
Epidural, neurolytic block	Control intractable pain	Urinary retention Orthostatic hypotension Low pain control rate

Analgesics

- Non-opioid
  - Acetaminophen, NSAIDs
- Opioid
  - Weak opioid
  - Strong opioid
- Adjuvant drugs
  - Antidepressant, corticosteroid, neuroleptics, anti-convulsant

Non-opioid drug

- Preferentially for mild pain
- Ceiling effect
- Similar efficacy and different toxicity
- Useful for patients with somatic pain from bone metastasis, inflammation,nonobstructive visceral pain
- Careful for adverse effect – nephrotoxicity, skin rash, ototoxicity, aggravating asthma, GI trouble

Opioid drug

- No ceiling effect
- Physical dependence and tolerance vs psychological dependence(addiction)
- Mixed agonist-antagonist drugs have limited utility because of S/E and withdrawal symptoms
- Low propensity for meperidine (Demerol®)

Classes of opioids

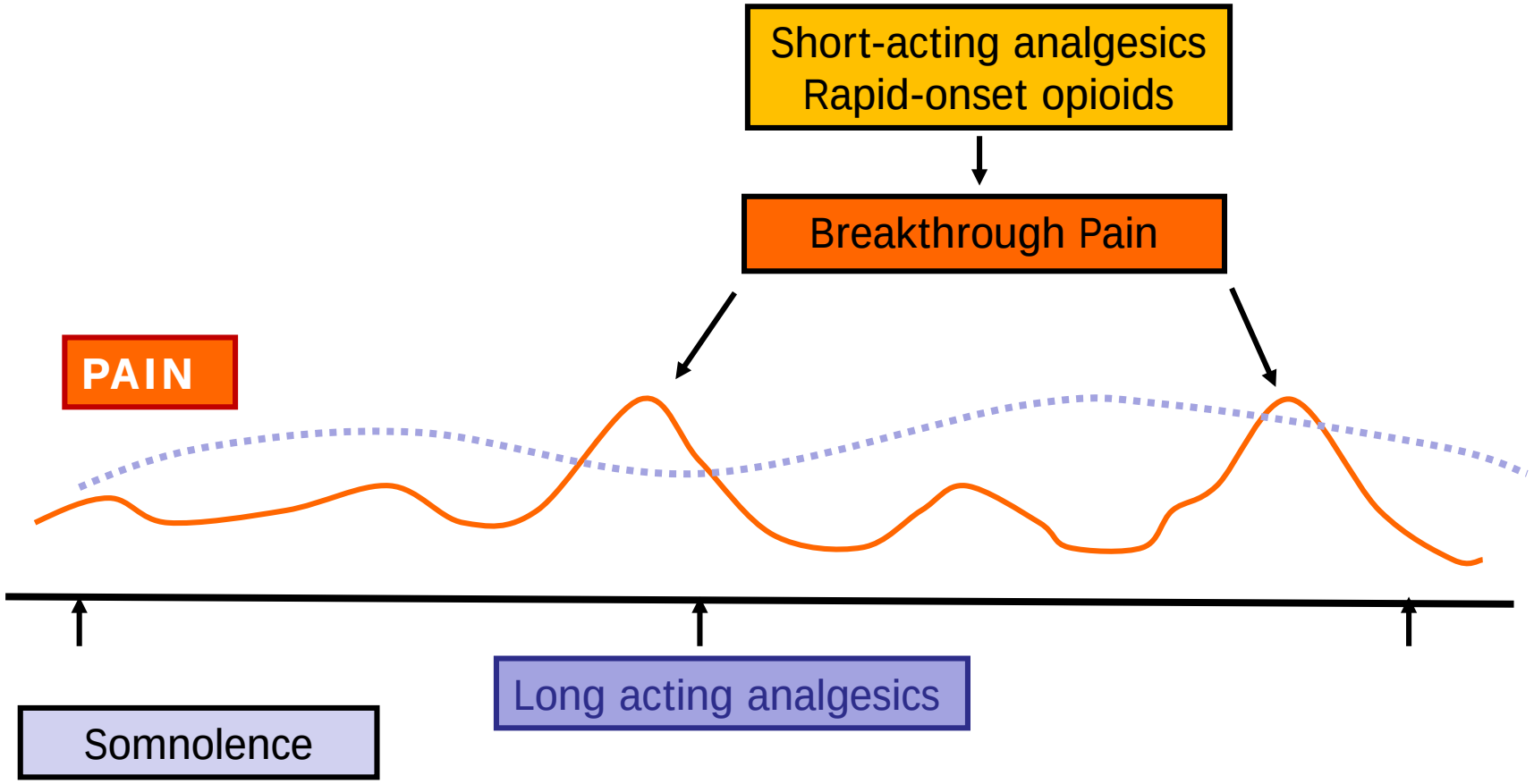
- **Pure (Full) Agonists: Preferred for Chronic Pain**
  - Bind to opioid receptor(s)
  - No antagonist activity
  - No ceiling effect
- Agonist-Antagonists
  - Ceiling effect for analgesia
  - Can reverse effects of pure agonists
  - Mixed agonist-antagonists (butorphanol, nalbuphine, pentazocine, dezocine)
  - Partial agonists (buprenorphine)
- Antagonists
  - Reverse or block agonist effects of pure opioids
  - Naloxone has been used to treat opioid overdose, addiction

Not indicated for the management of cancer pain

- Demerol (Meperidine; Pethidine)
  - Ceiling effect
  - Toxic metabolite nor-meperidine

    (Restlessness, anxiety, hallucianations, delusions, seizures, and death)
  - Short duration of action (2.5-3.5 hours)

- Talwin (Pentazocine)
  - Dose-related ceiling effect
  - May precipitate withdrwal syndrome and increase pain



Around-the-Clock management with "as needed doses."

Tenets of opioid prescribing

- Order an as-needed opioid to treat breakthrough or incident pain (10-15% of daily dose)
- Initiate a prophylatic bowel regimen at the same time
- Treat opioid-induced nausea and vomiting with aggressive anti-emetic management
- Frequent assessment of pain relief is paramount

Routes of administration

- **Oral and transdermal : preferred**
  - **Oral and transdermal: Long-acting**
  - **Oral: short-acting for breakthrough pain**
- **Transmucosal: oral or nasal**
  - **Rapid-onset opioids: for breakthrough pain**
- Rectal route
- Parenteral route
- Intraspinal route

Change to another drug

- Refer to equianalgesic dose tables
- New drug can be started 50-75% doses of previously used drug

  (eg. Morphine 90mg tid ⇒ fentanyl 50μg/hr)
- If previous drug was inadequate, 75-100% of doses are given

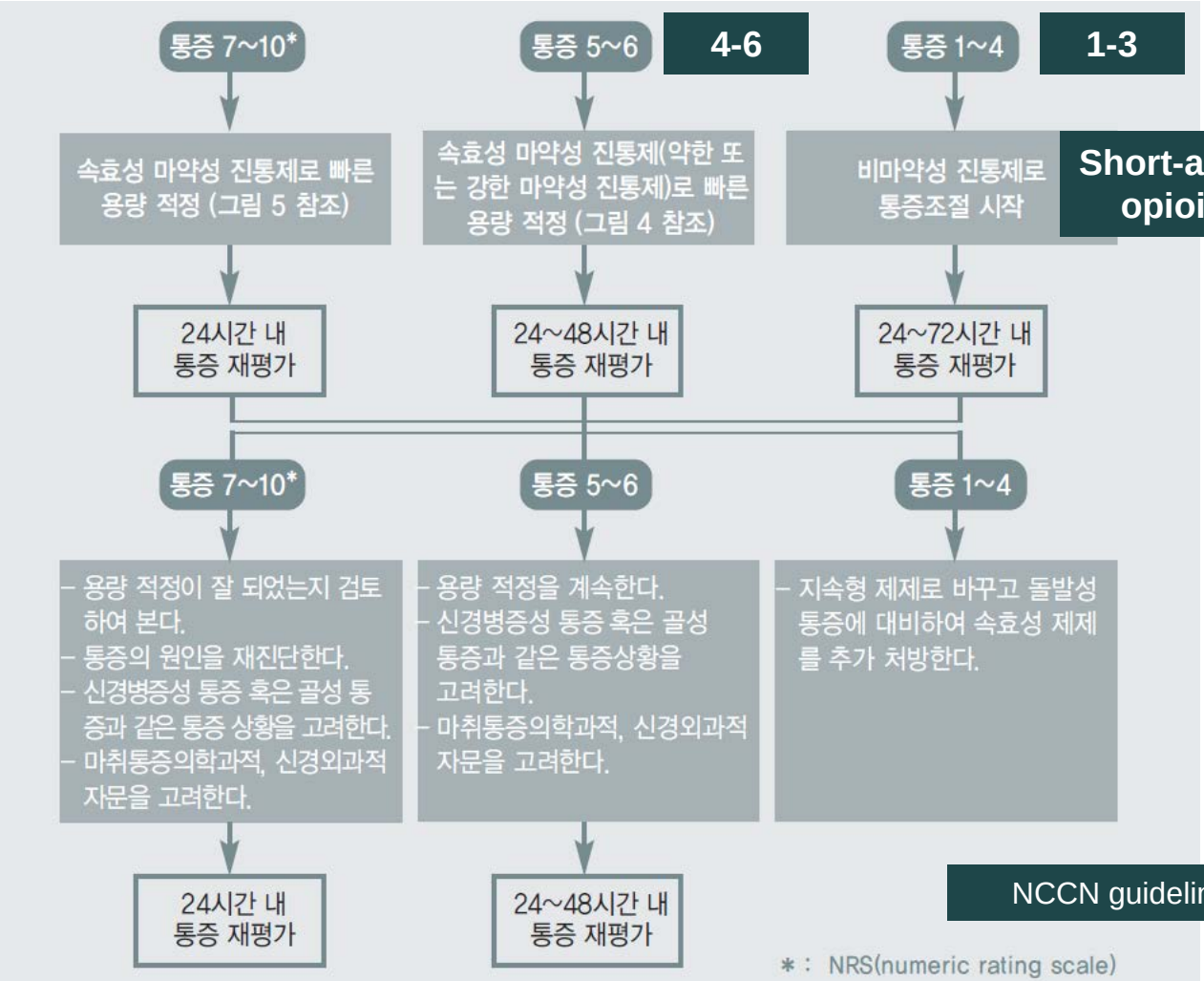
Equianalgesic doses of opioids

Drug	Dose equianalgesic to 10 mg IV/SC morphine		PO : IV/SC potency ratio	Half-life (hr)	Duration of action (hr)
	PO	IV/SC			
Morphine	30	10	1:3	2~3.5	3~6
Codeine	200	-	-	2~3	2~4
Oxycodone	**20**	**10**	**1:2**	**3-4**	**2-4**
Tramadol	120	100	1:1.2	6	4-6
Hydromorphone	7.5	1.5	1:2-1:5	2.5	4-5
Hydrocodone	30-45	-	-	-	3-5

Oral morphine 60mg = Fentanyl patch 25μg/hr

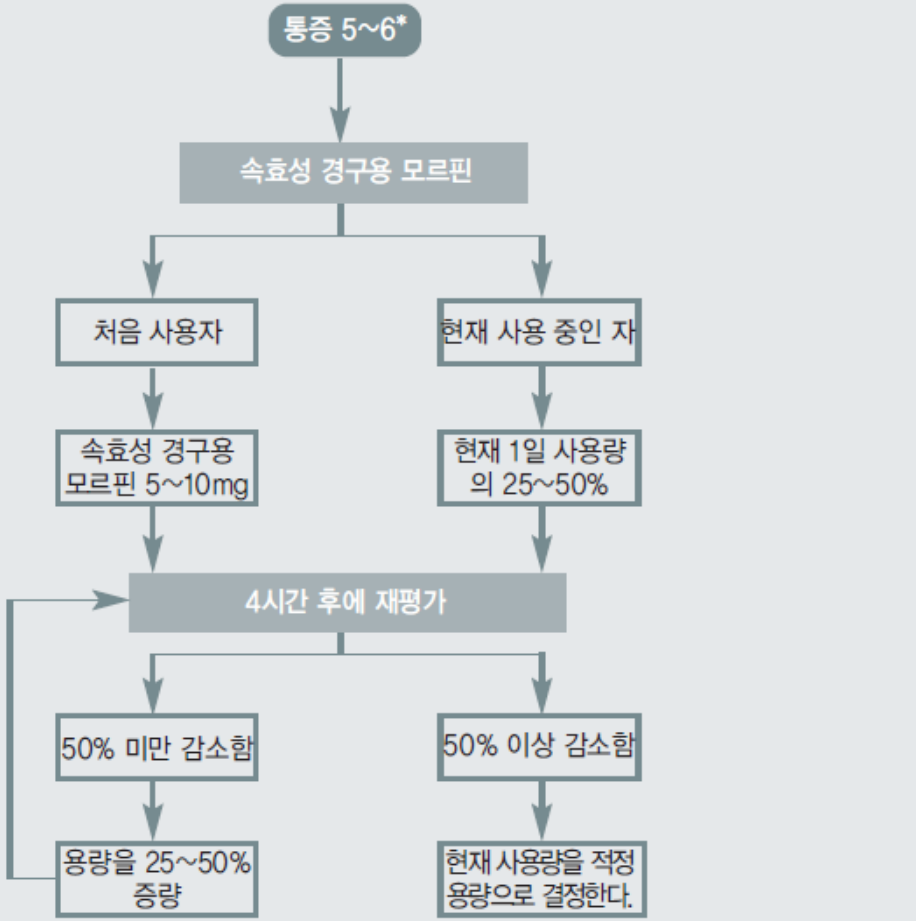
Opioid : side effects

- No evidence of major organ dysfunction
- Minimal risk of respiratory depression with chronic opioid use
- Common
  - Constipation : most common side effect
  - Somnolence
  - Mental clouding
- Less common
  - Nausea
  - Myoclonus
  - Itching
  - Urinary retension
  - Sweating
  - Amenorrhea
  - Sexual dysfunction
  - Headache



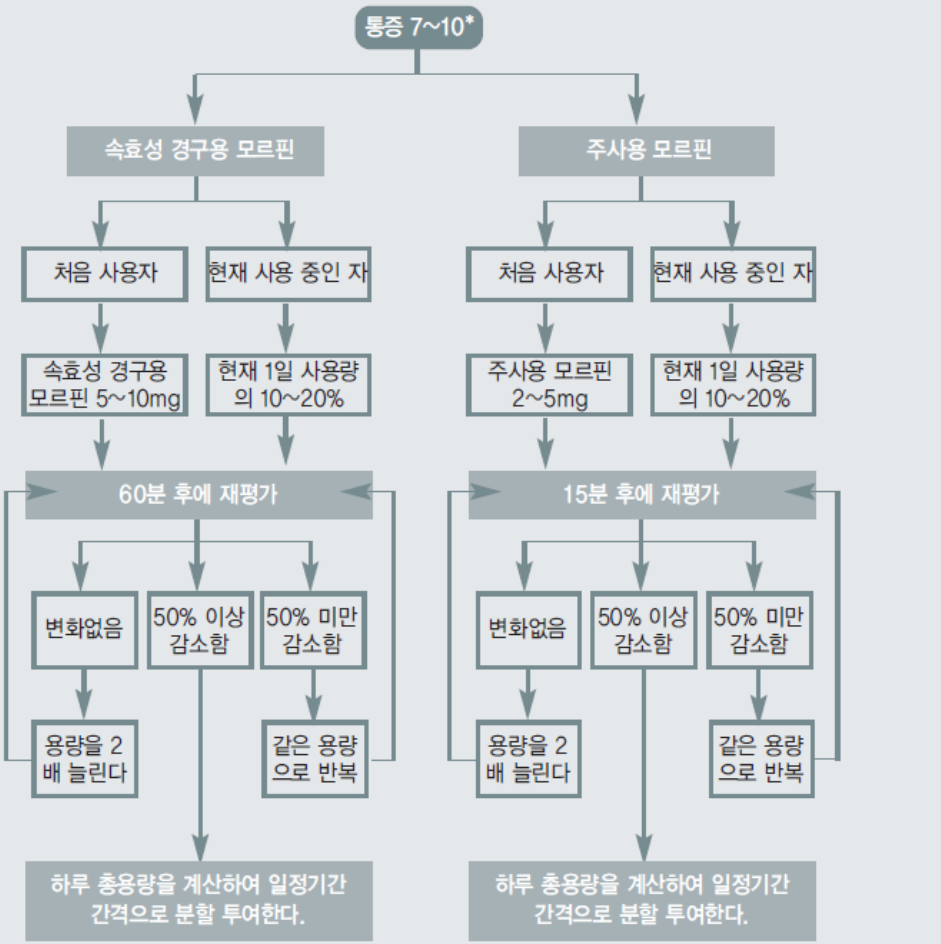
〈그림 3 : 통증조절〉

NCCN guideline v 2.2015



* : NRS(numeric rating scale)

〈그림 4 : 중등도 통증의 조절 예〉



〈그림 5 : 심한 통증의 조절 예〉

통증조절이 잘 안되는 이유?

- 부적절한 용량 : 가장 중요한 이유
- 모르핀에 반응하지 않는 통증
- 적절한 보조 진통제를 사용하지 않은 경우

Listen to patients
Trust what patients say
Reassess pain and titrate medication

- Anger, anxiety, fear 등이 조절되지 않는 경우
- 약을 복용 후 1-2시간에 토하는 경우