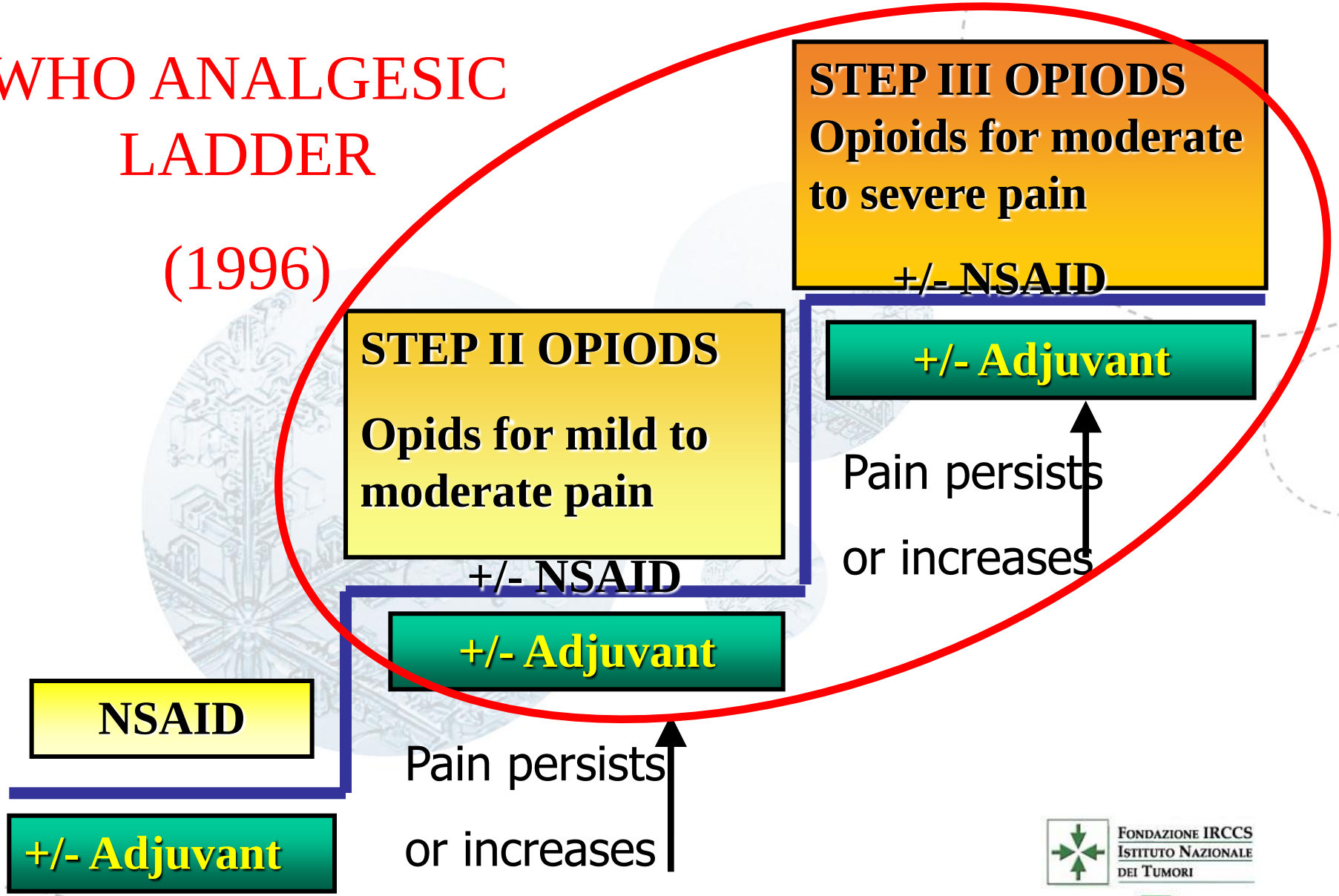
PRC

Europen Association for Palliative Care Opiod recommendation for cancer pain

Research questions and update

WHO ANALGESIC LADDER

(1996)



THE EAPC RECOMMENDATIONS

Morphine in cancer pain: modes of administration

Expert Working Group of the European Association for Palliative Care

BMJ - 1996

Morphine and alternative opioids in cancer pain: the EAPC recommendations

Expert Working Group of the Research Network of the European Association for Palliative Care

BJC - 2001

2012 EAPC RECOMMENDATIONS
distinctive features

- **Evidence based**: 18 systematic reviews (Palliative Medicine 2011)
- **GRADE** system
- Obtained through an **international consensus**
- **Indipendence** warranted by European funding and EAPC endorsement.
- To be **used and adapted to local needs all over the world**

Fondazione IRCCS Istituto Nazionale dei Tumori
Sistema Sanitario Regione Lombardia

The EAPC recommendations

R 1: WHO Step II Opioids

R 2: WHO Step III opioid of first choice

R 3: Opioid titration

R 4: The role of transdermal opioids

R 5: The role of methadone

R 6: Opioid switching

R 7: Opioid relative analgesic potency

R 8: Alternative systemic routes of opioid administration

R 9: Opioids for breakthrough pain

R10: Treatment of opioid-related emesis

R11: Treatment of opioid-related constipation

R12: Treatment of opioid related CNS symptoms

R13: Use of opioids in renal failure

R14: Role of paracetamol and NSAIDs in addition to Step III opioids

R15: Role of adjuvants drugs for neuropathic pain (antidepressants and anticonvulsants)

R16: The spinal route for opioid administration

WHO STEP II OPIOID

For patients with mild to moderate pain or whose pain is not adequately controlled by paracetamol or an NSAID given regularly by mouth, the addition of a Step II opioid (e.g. codeine or tramadol) (table 1) given orally might achieve good pain relief without troublesome adverse effects. Alternatively low doses of a Step III opioid (eg, morphine or oxycodone) may be used instead of codeine or tramadol. The data permit a weak recommendation to start a Step II opioid in these circumstances.

Quality of evidence is poor we do not know if starting with a step III opioid is an advantage or not, clinical practice in many countries already skips step II

WHO STEP III OPIOID OF FIRST CHOICE

The data show no important differences between morphine, oxycodone and hydromorphone given by the oral route and permit a weak recommendation that any one of these three drugs can be used as the first choice Step III opioid for moderate to severe cancer pain.

THE USE OF TRANSDERMAL OPIOIDS

Transdermal fentanyl and buprenorphine are alternatives to oral opioids. The data permit a weak recommendation that either drug may be the preferred Step III opioid for some patients. For patients unable to swallow they are an effective, non-invasive means of opioid delivery.

Studies comparing different opioids in Step III opiodid naive patients from start in a realistic clinical situation, head to head comparison, are stilll missing

- (see Riley Pall Med 26(4) : 386, 2012. Presented at Trondheim EAPC congres in June 2012)

OPIOID TITRATION

The data permit a weak recommendation that immediate-release and oral slow-release oral formulations of morphine, oxycodone and hydromorphone can be used for dose titration. The titration schedules for both types of formulation should be supplemented with oral immediate-release opioids given as needed.

USE OF METHADONE

Methadone has a complex pharmacokinetic profile with an unpredictably long half-life, but the data permit a weak recommendation that it can be used as a Step III opioid of first or later choice for moderate to severe cancer pain. It should be used only by experienced professionals.

The usefulness of methadone in switching opioid under specific circumstances in clinical practice is not supported by any scientific evidence

OPIOID SWITCHING

The data permit a weak recommendation that patients receiving Step III opioids who do not achieve adequate analgesia and have side effects that are severe, unmanageable, or both, may benefit from switching to an alternative opioid.

RELATIVE OPIOID ANALGESIC POTENCIES

When switching from one opioid drug to another, dose conversion ratios can be recommended with different levels of confidence (Table 2). These conversion ratios are specific for patients in whom analgesia from the first opioid is satisfactory. Therefore, when the opioid is switched because of unsatisfactory analgesia, excessive side effects or both, clinical experience suggests that the starting dose should be lower than that calculated from published equianalgesic ratios. In all cases the dose needs to be titrated in accordance with clinical response.

OPIOID SWITCH	RELATIVE ANALGESIC RATIO	STRENGTH OF THE RECOMMENDATION FOR USING
oral morphine to oral oxycodone	1.5 : 1	strong
oral oxycodone to oral hydromorphone	4 : 1	strong
oral morphine to oral hydromorphone	5 : 1	weak
oral morphine to TD buprenorphine	75 : 1	weak
oral morphine to TD fentanyl	100 : 1	strong

Equipotency and equianalgisic dosing in different circumstances are based on old data and would benefit of new studies (See Hoeben et al Pain 2012).

OPIOIDS FOR BREAKTHROUGH PAIN

The data permit a strong recommendation that pain exacerbations resulting from uncontrolled background pain should be treated with additional doses of immediate release oral opioids and that an appropriate titration of around-the-clock opioid therapy should always precede the recourse to potent rescue opioid analgesics. Breakthrough pain (eg, incident pain) can be effectively managed with oral, immediate release opioids or with buccal or intranasal fentanyl preparations. In some cases buccal or intranasal fentanyl preparations are preferable to the immediate-release oral opioids because of more rapid onset of action and shorter duration of effect.

Additionally, the data permit a weak recommendation that immediate - release formulations of opioids with short half-lives should be used to treat pre-emptively predictable episodes of breakthrough pain in the 20-30 min preceding the provoking manoeuvre .

Use of rapid onset opiods: more evidences ?

- Is the use of PCA methodology applicable to chronic cancer pain with transmucosal fentanyl self administration
- Is the use of transmucosal fentanyls in combination with slow release opioids better than the traditional combination of slow release opioids and immediate release opioids

ROLE OF PARACETAMOL AND NSAIDs IN ADDITION TO STEP III OPIOIDS

The data permit a weak recommendation to add NSAIDs to Step III opioids to improve analgesia or reduce the opioid dose required to achieve analgesia. The use of NSAIDs, however, should be restricted because of risk of serious adverse effects, in particular in elderly patients and those with renal, hepatic or cardiac failure.

The data also permit a weak recommendation that paracetamol should be preferred to NSAIDs in combination with opioids because of a more favourable side-effects profile, but its efficacy is not well documented.

THE ROLE OF ADJUVANT DRUGS FOR NEUROPATHIC PAIN

The data permit **a strong recommendation that amitriptyline or gabapentin should be considered for patients with neuropathic cancer pain that is only partially responsive to opioid analgesia. The combination of an opioid with these drugs is likely to cause more CNS adverse events unless careful titration of both drugs is undertaken.**

- When to combine drugs
- Which other drugs
  - Pregabalin
  - Other AD , duloxetine, venlafaxine ..
  - Clonazepam
- When switching opioid is better than combining another drug

More evidences

- MISSING OR INCOMPLETE EVIDENCE ON RELEVANT TOPICS:

1. NEW DRUGS
    1. TAPENTADOL,
    2. OXYCODONE-NALOXONE COMBINATION
2. KETAMINE
3. CORTICOSTEROIDS
4. INVASIVE PROCEDURE
5. ANTINEOPLASTIC TREATMENTS

WEB VERSION downloadable

- You can know more about it at the next PRC Seminar on cancer pain and cachexia in Milan17-18 October 2013
  - www.ntnu.no/prc
  - www.eapcnet.eu