Acute Pain Management in Emergency Medicine

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1. Introduction
For the International Association for the Study of Pain, pain is defined as: « an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage » (IASP 1979). Acute pain is useful and protective because it is an alarm signal and for the safeguarding of bodily integrity, in contrast to chronic pain. However, when the pain is recognised its treatment must begin without delay because at this time it has no more utility. Indeed, it could have deleterious effects.

2. Mechanism of acute pain in emergency medicine
Acute pain in emergency situations is mainly due to excessive nociception which is secondary to an inflammatory reaction, a trauma or a visceral lesion (Fletcher 2004). However, neuropathic pain was present in more than 20% of patients in the ED and necessitated a specific clinical investigation with a DN4 score (Table 1) (Lecomte 2011; Bouhassira 2004). The behaviour of patients in response to pain varies greatly. For example, the intensity expressed for identical lesions can be very different. This is because it depends on the personal history of the patient, his own psychology, the circumstances of the disease’s occurrence etc. This is really personal. This requires that pain management be adapted to each patient.

3. Epidemiology
In the emergency department, 60% to 80% of patients have acute pain. For more than 80% of them, pain is the main ground of appeal and the pain is intense in 54% of cases (Cordell et al 2002, Tcherny-Lessenot et al. 2003). Otherwise, 47% of the patients seen in the ED complain of procedural pains (Tcherny-Lessenot et al. 2003). In out-of-hospital settings, the prevalence of pain was 43% and with intense pain in 53% of cases (Galinski et al. 2010). Neuropathic pain was present in more than 20% of patients in the ED and this necessitated a specific clinical investigation with a DN4 score.

4. Objective of the acute pain management
- Recognition of pain and measurement of its intensity
- Treatment adapted to the intensity, the patient and the pathology
- Systematic and regular reassessment permitting an appreciation of the efficiency of the treatment.
- Take into account any procedural pains (puncture, suture of wound, mobilisation of trauma patients etc.)
The diagnostic and therapeutic approaches must be simultaneous. An early analgesia (with morphine) during acute abdominal pain did not modify the final diagnostic, nor did it delay it (Gallagher et al. 2006; Ranji 2006).

**Question 1: Does the pain have any of the following characteristics?**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Burning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Painful sensation of cold</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Electric shocks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Question 2: Is the pain associated with any of the following symptoms in the same area?**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Tingling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Pins and needles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Numbness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Itching</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Question 3: Is the pain located in an area where examination reveals either of the following?**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Hypoesthesia to touch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Hypoesthesia to prick</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Question 4: Is the pain provoked or increased by the following?**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Brushing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Neuropathic Pain Questionnaire with 4 questions (DN4). A score equal to or above 4 permits the suspicion of neuropathic pain. (Bouhassira D et al. 2004).

**4.1 Assessment of pain intensity**
The modality of pain intensity measurement is adapted to the patient (age and cognitive state). A self-evaluation will be preferred as far as possible. The pain should not only to be evaluated. It must also be documented against every clinical parameter. Given diversity of the possible situations and combinations (pain intensity - patient -pathology), pain
management cannot be improvised. Written protocols must be adapted to the different situations faced, both pathological and local

4.1.1 Assessment in adult patients

4.1.1.1 Self-evaluation

Visual Analogue Scale (VAS)

This tool is a rule with two aspects:

**One side for the patient:** « No pain » and « worst pain imaginable » at each extremity of the scale. No other indication.

**One side for caregiver:** Graduation from 0 to 100 millimetres.

This scale is reliable because numerous answers are possible and there is neither attribution nor memorisation of any precise number. Its use is simple and feasible in more than 80% of cases in emergency situations (Berthier et al. 1998; Ricard-Hibon et al. 1999). However, caregivers must be trained. Bijur et al. evaluated its reproducibility, showing that the mean variation, between two consecutive measures at one-minute intervals of a same patient was not above 2 to 9 mm (Bijur et al. 2001).

The question is what should the clinical interpretation of this scale be? Todd et al. have demonstrated that a mean change in VAS of 13 mm was associated with a significant clinical perception of change in pain intensity (Todd et al. 1996).

<table>
<thead>
<tr>
<th>No Pain</th>
<th>Worst pain imaginable</th>
</tr>
</thead>
</table>

Numeric Rating Scale (NRS)

This is a quantitative scale from 0 to 10. The patient verbally defines his level of pain intensity between 0 and 10: « Zero is the absence of pain and ten is the worst pain imaginable. »

This scale is reliable, does not need material tools and has a very good correlation with VAS, being feasible in more than 85% of cases (Bijur et al. 2003).

Verbal Rating Scale (VRS)

Each of the 5 terms proposed and expressed by patients is associated with a number:
No pain = 0; Weak pain = 1; Moderate = 2; Intense = 3; and Awful = 4.

The advantages of this scale are its simplicity, its ease of comprehension and its reproducibility (feasible in 94% of cases) (Bijur et al. 2003, Berthier et al. 1998). Its disadvantages are its lack of sensitivity and its low response categories.

VRS is indicated if the VAS or NRS cannot be used.

4.1.1.2 Intensity levels and therapeutic objectives

The different intensity levels are defined according to the assessment scales:

- VAS ≤ 30 or NRS ≤ 3 or VRS = 1 – 2: Weak to Moderate pain.
- VAS > 30 or NRS > 3 or VRS = 3: Intense pain.
- VAS ≥ 60 or NRS ≥ 6 or VRS = 4: Severe pain.

The therapeutic objective is a VAS ≤ 30 or a NRS ≤ 3 or else a VRS < 2, any of which could define the relief of the pain.
After the first evaluation, therapeutic modalities will be chosen in response to this evaluation, the pathology and the patient (age, history etc.) and in response to the recommendations and the protocols implemented in the health structure.

4.1.1.3 Behavioural assessment

For older patients who are unable to communicate verbally, there is one validated scale in the ED: ALGOPLUS (Rat et al. 2011) (Table 2). Five groups of items are explored and the indication to treat is given if the final score is above or equal to 2. One of the main instructions required of ALGOPLUS is the recording of all the present signs without any a priori interpretation in relation to the underlying disease. This point is very important. The second point is to assess the patient again after the analgesic treatment.

1. Facial expressions: Frowning, grimacing, wincing, clenched teeth, inexpressive
2. Look: Inattentive, blank stare, distant or imploring, teary-eyed, closed eyes
3. Complaints: « Ouch/ Ouch », « that hurts», groaning, screaming
4. Body position: Withdrawn, guarded, refuses to move, frozen posture
5. Atypical behaviour: Agitation, aggressiveness, grabbing onto
something or someone

| Total Yes |  | / 5 |

Table 2. Criteria for evaluation of ALGOPLUS (Rat et al 2011)

4.1.2 Children's evaluation

4.1.2.1 Self-evaluation

From the age of 3, children are able to differentiate coarse levels of intensity. Younger children have more binary responses to the evaluation of pain intensity: « all or nothing ». Before the age of 8 years old, children favour the extremes. Chambers et al. have shown that between 4 and 7 years old, 35% of responses for pain intensity were extremes, versus 4% between 8 and 12 years old (Chambers & Johnston 2002).

Visual Analogue Scale (VAS)

Its use is possible only from the age of 6, in general, although it can be used from the age of 4 in association with another tool, such as the Face Pain Scale-Revised. The rule must be presented vertically to the child.

Face Pain Scale Revised (FPS-R)

This is a scale presenting 6 faces, from a neutral face to a grimacing face. The child must choose the face corresponding with what he is feeling (Hicks et al. 2001). The instruction is: « there are persons who have pain, show me the face that has as much pain as you ». A variation of one face between two measurements is considered to be a significant difference.

Others tools are possible

Others scales could be used, such as the numeric rating scale (≥ 7 y), the verbal rating scale and the poker chip tool. This last one can be used with children aged between 3 and 4 years old. Four chips are presented to the child with the instruction: « each chip is a piece of pain. Takes as many chips as you have pain. Four chips is the strongest pain you can have » (Treatment threshold = 2).
4.1.2.2 Behavioural evaluation

Without an adapted scale, the caregiver’s evaluation is responsible to the bad estimation of pain intensity. Indeed, in this situation there is an overestimation of occurrences of weak pain and an underestimation of occurrences of strong pain. The result is that the treatment is not adapted (Teske et al. 1983).

**EVENDOL:** Evaluation of Children’s Pain (« EValuation ENfant DOuLeur »)

This is a behavioural scale specifically built to evaluate children between the ages of 0 and 7 in the emergency department (Table 3). Its proper use requires the following of instructions (Fournier-Charrière et al. 2011). One of the main points is that the evaluation must be done several times: at rest (before touching the child), during the examination or else during mobilisation, and after the treatment.

<table>
<thead>
<tr>
<th></th>
<th>Absent</th>
<th>Weak or transient</th>
<th>Moderate or present about half the time</th>
<th>Strong or present almost all the time</th>
<th>Assessment at admission</th>
<th>Following assessments and/or analgesic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At rest (R)</td>
<td>During examination or mobilisation (M)</td>
</tr>
<tr>
<td><strong>Vocal or verbal expression:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cries and/or screams and/or moans and/or complains of pain.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Facial expression:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furrowed forehead and/or brow bulge and/or tense mouth</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Movements:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restlessness, agitation and/or stiffness and/or muscular tenseness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Postures:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unusual and/or antalgic posture and/or protection of the painful area and/or immobility.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Interaction with the environment:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can be comforted and/or interested in playing and/or interacts with people</td>
<td>Normal</td>
<td>Low</td>
<td>Very low</td>
<td>Absent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remarks</td>
<td>Total / 15</td>
<td>Date &amp; Time</td>
<td>Signature</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Criteria for evaluation of EVENDOL scale (Treatment threshold: 4/15) (Fournier-Charrière et al 2011)
4.1.2.3 Assessment of children in practice

Before 4 years old: EVENDOL

4-6 years: Use 2 self-assessment scales: VAS and FPS-R, for example. If the results are discordant, use EVENDOL.

≥ 5-6 years: Use VAS or FPS-R or another self-assessment scale. If there is no response, EVENDOL can be used for children up to the age of 7.

5. Treatment of pain

5.1 General considerations

The treatment should be early.

It must be adapted to:

The intensity of pain.
The patient.
The pathology.
Local particularities.

5.1.1 Pain intensity

The power of the painkillers used and the modalities of their implementation will depend on the pain intensity. For example, the morphine consumption necessary for pain relief is correlated with the importance of initial pain (Aubrun et al. 2003). The World Health Organisation (WHO) has classified painkillers according to 3 levels as a function of the intensity of pain. The painkillers of step 1 are paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and nefopam. The painkillers of step 2 are tramadol, codeine and – perhaps - nitrous oxide and, – of step 3 – strong opioids.

In practice, for weak or moderate pain (VAS ≤ 30 or NRS ≤3), paracetamol, NSAIDs or nefopam could be used. Their doses are fixed (as a function of weight) and the time of assessment of their efficacy should be taken into account from the onset of action. For intense pain (30 < VAS<60 or 3<NRS<6), a combination of drugs at level 1 can be efficient (see below, multi-modality). In general, the combination should be done with a painkiller from level 2. In fact, drugs with tramadol or codeine (which are weak opioids) are frequently associated with paracetamol. The dose of these drugs – particularly tramadol – can be adapted to the pain intensity but there is a maximum dose which must not be exceeded (200mg in adult). In case of a failure with these drugs, a strong opioid – or else morphine in general – must be used.

Severe pain (VAS≥60 or NRS≥6) is an indication of a strong opioid – at step 3 – at first. This drug is frequently associated with another one, such as paracetamol and/or NSAIDs and/or nefopam (level 1) (see below, multi-modality). Morphine does not have a ceiling effect. Its effects on analgesia and on respiratory and digestive systems are dose-related. So, there is no maximum dose. This one is adapted to pain relief and also to tolerance (close monitoring).

5.1.2 Patient

Some physiological and/or pathological conditions determine the nature of painkillers and/or the modalities of their use (contraindications, adaptation of posology etc.).

Elderly patients must receive particular attention. The difficulties of treatment are related to several factors, such as pathophysiological conditions (Hwang & Jagoda 2008). Many elderly
patients have factors of fragility, which are defined with an albumin concentration ≤ 30g/L, 3 or more comorbidities, 5 or more concomitant treatments, an age above 80 years, and renal insufficiency. These conditions could be associated with a modification of the pharmacokinetics of drugs. Another point is the difficulty involved in precisely evaluating the pain intensity of patients with an inability to communicate verbally. In practice, when confronted with the suspicion of intense or severe pain in an elderly patient with factors of fragility and/or an inability to verbally communicate, morphine could be administered under certain conditions. It is not a contraindication. The administration must be very cautious. It is possible to inject 1 to 1.5 mg of morphine intravenously and then to evaluate the evolution of pain or algorplus with very close monitoring.

For pregnant women, there are a lot of contraindicated painkillers (table 4) (CRAT 2021). These contraindications are variable in response to the term of pregnancy. For example, NSAIDs (including aspirin ≥ 500 mg and COX-2 inhibitors) are formally contraindicated from 24 weeks of amenorrhea (w.a). Aspirin is contraindicated during breastfeeding. However, NSAIDs are possible in this case. Paracetamol is the painkiller of choice for pregnant or breastfeeding women. Opioids can be used in cases of indication. However, the risk of withdrawal syndrome or respiratory depression justifies the close monitoring of the newborn. During breastfeeding, their use is possible if necessary but the monitoring of the newborn should be implemented in case of high or prolonged doses.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>0-12 w.a</th>
<th>13-20 w.a</th>
<th>21-36 w.a</th>
<th>&gt; 37 w.a</th>
<th>Breastfeeding</th>
<th>Specialties...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
<td>Withdrawal risk in newborn</td>
<td>YES</td>
</tr>
<tr>
<td>Morphine</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticoids</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Neuropathic pain: Anti-depressive drugs</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>New born impregnation</td>
<td>Clomipramine</td>
<td></td>
</tr>
<tr>
<td>Neuropathic pain: Antiepileptic drugs</td>
<td>NO ?</td>
<td>NO ?</td>
<td>NO</td>
<td>NO</td>
<td>Gabapentine</td>
<td></td>
</tr>
<tr>
<td>Migraine: Triptans</td>
<td>OUI</td>
<td>OUI</td>
<td>OUI</td>
<td>OUI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti spasmodic</td>
<td>OUI</td>
<td>OUI</td>
<td>OUI</td>
<td>OUI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caffeine</td>
<td>OUI</td>
<td>OUI</td>
<td>OUI</td>
<td>OUI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opium powder</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>Stop breastfeeding if prolonged treatment</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>To avoid</td>
<td>To avoid</td>
<td>NO</td>
<td>NO</td>
<td>To avoid</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>To avoid</td>
<td>To avoid</td>
<td>NO</td>
<td>NO</td>
<td>Possible</td>
<td></td>
</tr>
<tr>
<td>Dihydroergotamine</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Floctafenine</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tienonium methylsulphate</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Use of painkillers during the different stages of pregnancy- (CRAT 2011)
5.1.3 Pathology
Some pathologies must receive specific treatment independent of pain intensity. Acute migraine attacks must be treated with NSAIDs in the first instance if they are known to be efficient for the patient. In the second instance, in case of failure, triptans should be used. However, opioids must not be used for this disease, whatever the intensity. Indeed, they are inefficient and are associated with a risk of drug abuse. For the cluster headache, subcutaneous triptans (Sumatriptan) are a first line abortive treatment. Oxygen (6 l/min) can be efficient too.

For ankle sprains, specific treatment is associated with NSAIDs and paracetamol, but also rest, ice, compression and the elevation of the lower limbs (RICE). For trauma patients, with long bone fractures, the strategy consists in systemic analgesia combined with locoregional anaesthesia, if possible, and immobilisation in a splint. Patients with myocardial infarction will have a decrease in chest pain intensity after manoeuvres of coronary recanalisation (thrombolysis or angioplasty). However, a standard analgesic treatment (morphine in general) is necessary initially because the recanalisation is – of course – not immediately possible.

Procedural pains concern more than 45% of patients in the ED (Tcherny-Lessenot et al. 2003) and must be anticipated. There are two kinds of procedural pains: 1) frequent acts with moderate pain (various punctures, insertions of a nasogastric tube or a bladder catheter etc.), 2) acts less frequent but very painful (fracture reduction, electrical cardioversion). Specific treatment could be used in each situation. A few therapeutic procedures are proposed in Table 5. In these situations, it is impossible to improvise. Protocols for procedures must be ready and known by caregivers.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous puncture (Blood sample, venous cannulation)</td>
<td>Anaesthetic cream (at least 90 min before) Nitrous oxide in response to the patient and his disease. Distraction</td>
</tr>
<tr>
<td>Puncture pour locoregional anaesthesia</td>
<td>Anaesthetic cream (at least 90 min before) Nitrous oxide in response to the patient and his disease. Subcutaneous lidocaine 1% without epinephrine at the puncture place</td>
</tr>
<tr>
<td>Arterial puncture</td>
<td>In emergency: subcutaneous lidocaine 1% without epinephrine at the puncture place Anaesthetic cream (at least 90 min before)</td>
</tr>
<tr>
<td>Deep venous cannulation</td>
<td>Anaesthetic cream (at least 90 min before) Nitrous oxide in response to the patient and his disease. Subcutaneous lidocaine 1% without epinephrine at the puncture place Localisation of the deep vein with ultrasonography</td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td>Anaesthetic cream (at least 90 min before) Nitrous oxide in response to the patient and his disease. Prevention of post-puncture headache: small-gauge needle (25 or 26 G); atraumatic needle (tip-pen); replacement of the stylet before withdrawing the needle</td>
</tr>
<tr>
<td>Nasogastric tube insertion (NGTI)</td>
<td>Identify the more patent nostril 5 ml of 2% lidocaine gel instilled nasally 5 minutes before NGTI Patient instructed to inhale the gel and to swallow it when it reached the pharynx</td>
</tr>
<tr>
<td>Bladder catheter insertion</td>
<td>5 ml of Specific 2% lidocaine gel instilled in urethra, 5 minutes beforehand</td>
</tr>
</tbody>
</table>
The principles of analgesia

5.2 Implementation of analgesia

5.2.1 Principles of analgesia

The implementation of analgesia is based on 2 phases:

- **Induction:** the objective of this phase is to obtain pain relief as quickly as possible. It continues until the goal is not reached.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobilisation of a fractured limb</td>
<td>Anticipated titration of morphine</td>
</tr>
<tr>
<td></td>
<td>Nitrous oxide beginning 5 minutes before mobilisation</td>
</tr>
<tr>
<td></td>
<td>Locoregional anaesthesia if possible</td>
</tr>
<tr>
<td></td>
<td>Sedation: ketamine 0.5 mg/kg intravenously (in absence of contraindication)</td>
</tr>
<tr>
<td>Exploration and suturing of wounds</td>
<td>Nitrous oxide</td>
</tr>
<tr>
<td></td>
<td>Local or locoregional anaesthesia</td>
</tr>
</tbody>
</table>

Table 5. Possible therapeutics for procedural pain prevention (Galinski 2010 a)

5.1.4 Local particularities

The implementation of analgesic protocols depends on local particularities. Indeed, a protocol which recommends parenteral morphine needs a specific logistic, concerning the modalities of its monitoring. During the administration of morphine, monitoring should include the evaluation of the respiratory rate and the respiratory score (Table 6), the level of sedation (sedation scale (Table 7)), any side effects and, of course, pain intensity. These factors must be recorded every 5 minutes all along the intravenous titration, and when a steady state is obtained, every 15 minutes for 1 or 2 hours. During the maintenance period, the variables must be recorded every 4 hours. Accordingly, this kind of monitoring is only possible if caregivers are trained and available. Caregivers should be able to detect a complication like a sedation score equal to 3 and/or a respiratory score equal to R2, or a respiratory rate of less than 10/min. The response must be quick with an alert for the doctor and the injection of naloxone. This is not possible without specific preparation. Likewise, it is not possible to prescribe morphine in a medicine or surgical ward if there is nobody to monitor the patients regularly.

**Respiratory Score (RS)**

- R0: regular breathing, RR > 10 (> 15 between 1 and 5 years)
- R1: snoring, RR > 10 (> 20 before 1 year)
- R2: irregular breathing, RR > 10
- R3: pauses, apnoeas.

Table 6. Monitoring of Respiration Score during opioids analgesia (Fletcher et al. 2000)

**Sedation Scale (SS)**

- SS 0: arousable.
- SS 1: sleepy but easily arousable
- SS 2: very sleepy, arousable with verbal stimulations
- SS 3: very sleepy, arousable with tactile stimulations

Table 7. Monitoring of sedation during opioids analgesia (Fletcher et al 2000)
- **Maintenance**: once the relief of pain is reached, with a steady state, the maintenance of treatment is planned with the setting up of appropriate prescriptions. Analgesia is based on two principles:
- **Multi-modality**: the combination of some painkillers could improve analgesia (Kelhet & Dahl 1993). A combination of NSAIDs to morphine has a documented 30-50% sparing effect on morphine consumption, reduces some side effects due to the morphine, and improves the relief of pain in some cases (Marret et al. 2005). The combination of ketoprofen and nefopam permits the dramatic reduction of the consumption of both. Indeed, to obtain a decrease of 50% of postoperative pain intensity, the mean dose was 30 mg for ketoprofen and 28 mg for nefopam. After combination, the doses were, respectively, 4.3 and 1.75 mg. This was a synergistic effect (Delage et al. 2005). A study evaluated the effect of the combination of paracetamol (P) and ketoprofen (K) after surgery on a herniated disc of the lumbar spine. The VAS scores throughout the study were lower in the group receiving P, K and morphine (M) than in those groups receiving only morphine, or morphine and paracetamol, or morphine and ketoprofen, both at rest and during movement. The cumulative dose of morphine at 48 hrs was lower in group PKM than in group M, or group PM and similar to that in group KM (Fletcher 1997).
- **Titration**: This principle concerns opioids: the repeated injections of small doses (2 to 3 mg) of morphine every 5 minutes permits the obtaining of pain relief with a final dose adapted to the patient. Otherwise, this permits the reduction of the risk of side effects. Indeed, there is wide inter-individual variability concerning the necessary dose to achieve pain relief. As such, this dose is not predictable. This technique permits the finding of a better dose for each patient.

### 5.2.2 Implementation of a titration of morphine in the ED

For a patient with a severe pain, there is an indication for a strong opioid.  

**Example of a protocol of titration in adult patients:**

Morphine intravenously 3 mg (2 mg if weight <60kg) every 5 minutes.  

**Objective**: VAS ≤ 30/100.  

**Monitoring**: RR, Sedation and VAS.  

The titration will be stopped if: the objective reached; the sedation score is ≥2; the respiratory score ≥R1; or the RR is <10; in the presence of side effects, like vomiting, strong nausea etc.  

When the steady state for relief is reached, close monitoring (every 15 minutes) will last for 1 to 2 hours.  

In a large study in the ED, this protocol has been tested on 650 patients. Each patient with a VAS at admission above or equal to 70 was included. They received morphine intravenously at a dose of 3 mg (2 mg if they weighed under 60 kg) every 5 minutes until the VAS was equal to or under 30. The results showed that more than 80% of patients were relieved. Two factors were associated with a failure of titration: side effects due to morphine (11%) and a lack of respect for the protocol, with either an insufficient dose or the interval between injections being too long (upper than 5 minutes) (Lvovschi et al. 2008).

### 5.3 Different painkillers drugs available in the emergency setting

In the emergency setting, painkillers should have an onset of action as short as possible, and should be administrable by different routes. As seen above, the choice will depend – among other things – on their power and on their possible association with other drugs.
5.3.1 Non opioid drugs

5.3.1.1 Paracetamol - Acetaminophen

This is a level 1 analgesic according to the WHO classification. It can be used alone for weak or moderate pain and in association for intense or severe pain. Orally, its biodisponibility is 80%, its onset of action is between 15 min (intravenously) and 30 min (orally), and its duration of action is 4 to 6 h. Its metabolism is hepatic and its elimination urinary. There are few contraindications, which are – essentially – acute liver disease and decompensated chronic liver disease. The posology is 1 g in adults and 15mg/kg in children, every 6 hours. The therapeutic index of this drug is very wide. Its liver-toxicity is related to an administration over 100 to 150 mg/kg.

5.3.1.2 Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

This is a level 1 analgesic according to the WHO classification. It can be used alone for weak or moderate pain and in association for intense or severe pain. However, during renal colic with intense to severe pain, NSAIDs alone could be efficient. There are many NSAIDs (Table 8). As such, the onset and duration of action are very variable (Table 8). The main points are that NSAIDs are associated with some serious side effects, namely gastro-intestinal bleeding and renal insufficiency. Accordingly, the selection of patients and the duration of treatment are 2 very important points. The main precautions are to avoid patients with chronic or acute renal insufficiency, patients at risk of hypovolemia, very elderly patients (with a high prevalence of chronic renal insufficiency), high doses, a duration above 5 days, a history of peptic ulcers (this is a non-exhaustive list). The contraindications must be checked very closely (White & Thomas 2008).

<table>
<thead>
<tr>
<th>Molecules</th>
<th>Administration routes</th>
<th>Onset of action (min)</th>
<th>Duration of action (h)</th>
<th>Posology (mg)</th>
<th>Posology per day (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Niflumic acid</td>
<td>PO</td>
<td>60 to 120</td>
<td>8</td>
<td>250</td>
<td>750</td>
</tr>
<tr>
<td></td>
<td>IR</td>
<td>30 to 60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aceclofenac</td>
<td>PO</td>
<td>60 to 120</td>
<td>8 to 12</td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>Tiaprofenic acid</td>
<td>PO</td>
<td>60 to 120</td>
<td>8</td>
<td>100 to 200</td>
<td>300 to 600</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>PO</td>
<td>60 to 120</td>
<td>8 to 12</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Injectable IM</td>
<td>20 to 30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurbiprofene</td>
<td>PO IR&lt;sup&gt;2&lt;/sup&gt;</td>
<td>60 to 120</td>
<td>6 to 8</td>
<td>50 to 100</td>
<td>150 to 300</td>
</tr>
<tr>
<td></td>
<td>PO PR</td>
<td></td>
<td>12</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>PO</td>
<td>60 to 120</td>
<td>6 to 8</td>
<td>400</td>
<td>1200</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(w&lt; 40 kg)</td>
<td>10 mg/kg x 3</td>
</tr>
<tr>
<td>Indometacin</td>
<td>PO</td>
<td>60 to 120</td>
<td>8 to 12</td>
<td>25 to 50</td>
<td>50 to 150</td>
</tr>
<tr>
<td></td>
<td>IR</td>
<td>30 to 90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>20 to 60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>PO IR&lt;sup&gt;2&lt;/sup&gt;</td>
<td>60 to 90</td>
<td>8 to 12</td>
<td>50 to 100</td>
<td>150 to 300</td>
</tr>
<tr>
<td></td>
<td>PO PR</td>
<td>60 to 90</td>
<td></td>
<td>150</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Injectable IV/IM</td>
<td>20 to 30</td>
<td></td>
<td>100</td>
<td>100 to 300</td>
</tr>
<tr>
<td>Lodine</td>
<td>PO</td>
<td></td>
<td></td>
<td>200 to 300</td>
<td>200 to 600</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>PO</td>
<td>90</td>
<td>24</td>
<td>7.5 to 15</td>
<td>7.5 to 15</td>
</tr>
<tr>
<td></td>
<td>IR Injectable</td>
<td>60 to 90</td>
<td></td>
<td>7.5 to 15</td>
<td>7.5 to 15</td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>30 to 60</td>
<td></td>
<td>7.5 to 15</td>
<td>7.5 to 15</td>
</tr>
</tbody>
</table>
Table 8. Pharmacokinetic and doses of some NSAIDs (PO: Per os; IR: intra-rectal; IM: intramuscular; IV: intravenous; IR}: immediate-release; PR: prolonged release) (Galinski 2010 b)

5.3.1.3 Nefopam

This is a level 1 analgesic according to the WHO classification. It can be use alone for weak or moderate pain and in association for intense or severe pain.

Orally, its biodisponibility is 36%, its onset of action is between 15 and 20 minutes (intravenously), and its duration of action is 4 to 6 h. Its metabolism is hepatic and its elimination urinary. The particular points are its contraindications with coronary insufficiency, epilepsy, glaucoma and benign prostatic hyperplasia, and its side effects with nausea, vomiting, tachycardia, sweat and acute urinary retention. Most of the side effects can be avoided with a very slow intravenous injection in 20 minutes. Its association with tramadol is not recommended because of a similar mechanism of action on the inhibition of serotonin and noradrenaline reuptake.

The induction posology is 20 mg intravenously in 20 min, and the maintenance posology is 20 mg every 4 or 6 hours. It could be administrated continuously (80 to 120mg) over 24 hours.

5.3.1.4 Equimolar mixture of oxygen and Nitrous oxide

This is a colourless, odourless and non-flammable gas (at room temperature). Its action is analgesic, sedative and anxiolytic. It can be used alone for weak or moderate procedural pains and venous cannulation (Gerhardt et al. 2001, Hee et al. 2003). It was demonstrated that in this situation EMLA and nitrous oxide were equally efficient for pain reduction, however the combination of both provided superior analgesia (multi-modal analgesia) (Hee et al. 2003). Nonetheless, it can be use also in association to other painkillers (multi-modal analgesia) for intense or severe pains. During care of bedsores and painful ulcers in the elderly, a nitrous oxide-oxygen mixture alone or associated with morphine is better than morphine alone for analgesia (Paris et al. 2008). In the emergency department, children having received oxycodeone per os, and were then treated either with the association of a nitrous oxide-oxygen mixture plus a haematoma block (with lidocaine) or with intravenous ketamine plus midazolam, for the reduction of a forearm fracture. There was no difference in pain during the procedure between the 2 groups although the reduction of pain was significant with ketamine but not with the nitrous oxide-oxygen mixture. However, the group with the nitrous oxide-oxygen mixture was associated with fewer side effects and to a more rapid awakening (Luhmann et al. 2006). This can be useful for spontaneous pains, such as sickle cell crisis in association with morphine (Carbajal et al. 1996) or in labour pain,
although it was demonstrated that it was not a potent analgesic in this situation (Rosen 2002). Its onset of action is 5 minutes and its duration of action is 5 minutes after the withdrawing of the mask. Contraindications are presented in Table 9.

<table>
<thead>
<tr>
<th>Emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal occlusion</td>
</tr>
<tr>
<td>Inflammatory sinus and middle ear</td>
</tr>
<tr>
<td>Undrained pneumothorax</td>
</tr>
<tr>
<td>Serious chest trauma</td>
</tr>
<tr>
<td>Altered consciousness</td>
</tr>
<tr>
<td>Head trauma non-evaluated with a suspicion of intracranial hypertension</td>
</tr>
<tr>
<td>Intracranial hypertension</td>
</tr>
<tr>
<td>Suspicions of air embolism</td>
</tr>
<tr>
<td>Diving accident</td>
</tr>
<tr>
<td>Serious facial trauma</td>
</tr>
<tr>
<td>Refusal of the patient</td>
</tr>
<tr>
<td>Intraocular gas for surgery less than 3 months</td>
</tr>
<tr>
<td>Neurological abnormalities recent and non-explained</td>
</tr>
<tr>
<td>Deficiency in B12 vitamin and non-compensated</td>
</tr>
<tr>
<td>Temperature less than - 5°C</td>
</tr>
</tbody>
</table>

Table 9. Contraindications of the Equimolar Mixture of Oxygen – Nitrous oxide

The use of this gas was met with several precautions, although there are few side effects and they are rarely serious. The risk of deep sedation increases with the association of other sedative drugs. This risk is particularly high with young children. The principle of use is self-inhalation so that when the patient falls asleep his tonus falls down and the mask as well. As such, the inhalation is stopped automatically. In a young child (younger than 3 or 4 years) self-inhalation is impossible. Caregivers maintain the mask. They must closely monitor the patient so as to anticipate all events. Accordingly, caregivers must be trained. The posology is the flow of the gas to adapt to the patient’s respiratory volume. The monitoring of the flow-inflating bag permits the adaptation of the flow. The duration of inhalation depends on the duration of the act. The patient must receive an explanation as to what will happen because without his cooperation the technique cannot succeed. Close monitoring is necessary with regard to the level of sedation (maintaining verbal contact) and the efficacy of analgesia. The criteria of efficacy and safety are the absence of pain and side effects. However, in case of inefficacy (after an exposition above 5 minutes) the modalities must change.

5.3.2 Opioids

5.3.2.1 General considerations

This is a level 3 analgesic according to the WHO classification. It can be used alone or in association, for intense or severe pains. There are many opioids with variable onsets and durations of action (Table 10). The common feature shared by all of these opioids is the lack of a ceiling effect, either for the analgesia or for the respiratory depression or other side effects. The other important point is the existence of an effective antidote: naloxone. With close monitoring, naloxone provides the other fundamental pillar in the use of opioids.
Various opioids differ from each other by their power of action, their onset of action and their duration of action. Opioids must be compared in response to their equianalgesic doses. Between the 2 opioids, the more powerful was identical to a smaller dose (Table 10).

5.3.2.1 Side effects

Side effects concern all opioids. They are dose-dependent and they justify specific monitoring.

Side effects include sedation, which always precedes respiratory depression. This one is very rare but very serious because it can lead to a ventilatory stop. Nausea and vomiting are very frequent. They are the main cause of the treatment’s interruption. Constipation is constant and must be systematically prevented. The others side effects are less frequent, and concern urinary retention and pruritus. During pregnancy, opioids cross the placental barrier. So there is a risk of respiratory depression in the newborn if the morphine is administered shortly before birth. In this case the baby should be closely monitored.

<table>
<thead>
<tr>
<th>Molecules</th>
<th>Administration route</th>
<th>Onset of action (min)</th>
<th>Duration of action (h)</th>
<th>Equianalgesia versus morphine</th>
<th>Posology (mg/kg)</th>
<th>Posology Per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>PO IR&lt;sup&gt;a&lt;/sup&gt; PO PR SC IV</td>
<td>30 60 to 180 5 to 60 5 - 15</td>
<td>4 to 6 12 to 24 4 to 6 4 to 6</td>
<td>1</td>
<td>0,15 to 0,25 0,5 in 1 0,1 0,05 to 0,1 + titration</td>
<td>To determine</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>IV</td>
<td>2 20 to 30 min</td>
<td>0,01 to 0,02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sufentanil</td>
<td>IV</td>
<td>3 20 to 40 min</td>
<td>0,0015</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>PO IR&lt;sup&gt;a&lt;/sup&gt; PO PR</td>
<td>30 to 60 60 to 180</td>
<td>4 to 6 12</td>
<td>1/2</td>
<td>0,07 à 0,12 0,25</td>
<td>To determine</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>PO PR</td>
<td>120 to 180</td>
<td>12</td>
<td>1/7,5</td>
<td>0,07</td>
<td>To determine</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>IR IV SC-IM</td>
<td>2 to 3 15 to 30</td>
<td>3 to 6</td>
<td>2</td>
<td>0,3 Adults: 20 mg Children: 0,2</td>
<td>Max: 160mg</td>
</tr>
</tbody>
</table>

Table 10: General characteristics of the different opioids (PO: Per os; IR<sup>a</sup>: immediate-release; PR: prolonged release; SC: subcutaneous; IV: intravenous; IR: intra-rectal; IM: intra-muscular) (Galinski 2010 b)

5.3.2.2 Treatment and prevention of side effects

Naloxone is the antidote of reference. Its indications are respiratory depression, severe pruritus and urinary retention. Droperidol (1,25mg IV) is used to prevent or treat nausea, vomiting and pruritus. Ondansetron is also used to treat nausea and vomiting when a droperidol is contraindicated or inefficient. Nalbuphine could be used to treat urinary retention and pruritus. Lactulose (systematically prescribed) is prescribed to prevent constipation and oxygen is desirable for fragile patients, the elderly or those with coronary disease.

In the ED, the prevalence of side effects due to morphine was 11%, the main ones being nausea and vomiting, and without severe adverse events (Lvovshi et al. 2008). There is no contraindication to opioids except allergy. However, doses must be adapted for some diseases and situations. Doses must be reduced and/or the time interval between administrations must be increased during renal insufficiency, liver insufficiency, some respiratory diseases, and elderly patients with factors such as fragility etc.
5.3.2.1.3 Precautions

More than any other painkillers, opioids require the implementation of precise care protocols with modalities of administration and monitoring. Through this, the risk of serious complication (respiratory depression) becomes exceptional. This is demonstrated by experience acquired in postoperative analgesia (Rawal & Berggren 1994). Opioids used for acute pain necessitate the training of caregivers and the provision of information on the protocols concerning treatment and monitoring modalities. The efficacy of the treatment depends upon protocol compliance, like the time between two administrations or doses (Lyovschi et al 2008). The monitoring must be adapted to the opioid and to the modalities of the treatment used. The main objective of the monitoring is to prevent side effects, particularly respiratory depression (Tables 6 & 7). The aim is also to treat other side effects early, such as strong nausea or vomiting which are source of failure because they stop the treatment.

5.3.2.1.4 Which opioid should be used for acute pain in emergency medicine?

Morphine is the opioid of reference. Some studies evaluated others opioids, like alfentanil, fentanyl or sufentanil, which are more powerful than morphine with a shorter onset of action (Table 10). However, their duration of action is largely smaller than that of morphine (Table 10). Alfentanil has been compared to morphine in a controlled randomised trial during acute coronary syndrome. Patients treated with alfentanil obtained a VAS significantly lower than those patients treated with morphine between the 2nd and the 10th minutes. The VAS was not different at the 15th minute (Silfvast & Saarnivaara 2001). Fentanyl has also been titrated in an equianalgesic fashion. At 15 or 30 minutes, there was no difference between the two groups concerning the VAS (Galinski et al. 2005). With a similar study design, but only in trauma patients, sufentanil has been compared to morphine. The results were similar and showed no significant difference between the two groups concerning pain relief (Bounes et al. 2010).

Among opioids which have a relatively long duration of action (4 to 6 hours) with an onset of action compatible with the management of acute pain (a few minutes), intravenous morphine is the drug of choice. Indeed, it has been the object of numerous studies in emergency medicine, in both the ED and the out-of-hospital setting, when compared with oxycodone, hydromorphone or pethidine, which give it (in 2011) a genuine advantage in terms of knowledge. An observational prospective multi-centre study has assessed 691 patients who received intravenous opioids in the ED for severe pain, and looking for factors associated with the failure of analgesia. In this study, two opioids have been used intravenously, namely morphine and hydromorphone, but neither one nor the other was a factor of failure (O’Connor et al. 2009). A study compared IV morphine and oral oxycodone in patients with acute musculoskeletal pain. If the variation of pain was in favour of morphine during the first 20 minutes of recording, it was not the case at the 30th and 40th minutes. However, in this study, only 38% to 44% of patients achieved a decrease of 50% of their initial pain score (Miner et al. 2008). A comparison of oxycodone (5 mg orally) to hydrocodone (5mg orally) has been done in a controlled randomised trial for the treatment of acute pain associated with fractures in ED patients. There was no difference in pain between the patients treated with oxycodone and hydrocodone at 30 minutes or at 60 minutes (Marco et al. 2005).
Nalbuphine is an agonist-antagonist opioid half as powerful as morphine (Table 10). Its action is limited because of its ceiling effect for analgesia but not for its side effects (Mazoit 1998). As such, titration is not possible with nalbuphine. Its antagonist effect is 25 times less powerful than that of naloxone, and it does not contraindicate the use of morphine in case of the failure of nalbuphine. Its indication is intense to severe pain, alone or in association with level 1 painkillers. However, nalbuphine must be replaced with morphine in case of failure.

### 5.3.2.2 Morphine

Morphine is an alkaloid, which has been extracted from opium since the beginning of the 19th Century and used in surgery from the second half of the 19th Century. Handling (enteral or parenteral administration) and high a therapeutic index makes it the leader in central analgesics. Morphine is the opioid of reference in emergency medicine. Morphine is a μ opioid receptor agonist located in the spinal cord and in the over spinal cord. Its fixation to the μ opioid receptor stops nociceptive message transmission. The action of morphine is antagonised by naloxone. Orally, the biodisponibility of morphine is 30%. Its onset of action and its duration of action depend on the route of administration (Table 11).

The route of administration depends on the desired time for the relief of pain (Table 11). For severe pains, in the ED or in out-of-hospital settings, the intravenous route is very quickly efficient with a very high rate of success (more than 80%) (Llovschi et al. 2008). However, the oral route is very useful and easy, and it should be used when it is possible.

<table>
<thead>
<tr>
<th>Molecules</th>
<th>Route</th>
<th>Onset of action (min)</th>
<th>Duration of action (h)</th>
<th>Equivalence (mg)</th>
<th>Posology for titration</th>
<th>Initial Period: Administration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorhydrate of morphine</td>
<td>IV</td>
<td>5</td>
<td>4 to 6</td>
<td>10</td>
<td>Titration: 3 mg (2 if w &lt; 60 kg)</td>
<td>5 min</td>
</tr>
<tr>
<td>Chlorhydrate of morphine</td>
<td>SC</td>
<td>5-60</td>
<td>4 to 6</td>
<td>15</td>
<td>After titration IV: 5 to 10 mg</td>
<td></td>
</tr>
<tr>
<td>Chlorhydrate of morphine</td>
<td>PO-IR</td>
<td>30</td>
<td>4 to 6</td>
<td>30</td>
<td>Titration: 0.2mg/kg Interdose: 1/6 of day dose</td>
<td>60 min for interdoses</td>
</tr>
<tr>
<td>Sulphate of morphine</td>
<td>PO-IR</td>
<td>30</td>
<td>4 to 6</td>
<td>30</td>
<td>Titration: 0.2mg/kg Interdose: 1/6 of day dose</td>
<td>60 min for interdoses</td>
</tr>
<tr>
<td>Sulphate of morphine</td>
<td>PO-PR</td>
<td>120-180</td>
<td>12</td>
<td>30</td>
<td>After IR form - Equivalence 1 for 1</td>
<td></td>
</tr>
</tbody>
</table>

Table 11. The different forms of morphine and its different routes of administration (PO: per os; SC: subcutaneous; IV: intravenous; IR: immediate release PR: prolonged release) (Galinski 2010 b)

**Morphine is metabolised by the liver in two forms:** morphine-3 glucuronid (M₃G) (90 %), which is inactive, and morphine-6-glucuronid (M₆G) (10 %) which is active. The elimination of morphine’s metabolites is urinary.

Side effects and the contraindications of morphine are that of all opioids. However, histamine release is a specific risk associated with morphine when the dose is above 1 mg/kg (the risk of hypotension). The indications of morphine are intense to severe acute pains. However, there are some non-indications, such as idiopathic pains, fibromyalgia, glossodynia or psychogenic pains (depression). Morphine is not recommended for migraines.
The use of morphine should be preceded by the establishment of protocols of care and monitoring, whatever the route of administration. Prescriptions of morphine for outpatients should follow the national legislation. Special monitoring should be established for patients with renal insufficiency, with respiratory disease or with liver dysfunction, as with very elderly patients. The main point is that the posology must be adapted to the disease, case by case. Naloxone should always be available, as the material for resuscitation (oxygen, mask, self-inflating valve-bag). Nurses must know how to use naloxone.

However, what is the good posology? Confronted with acute pain with the indication of morphine, there is no a priori defined posology. The adequate dose will be the one which will achieve pain relief without side effects. There is no maximal dose. This is in the interest of titration, which permits the adaptation of the dose case by case. In the post-operative setting, it has been demonstrated that there was a correlation between initial pain intensity - in the post-anaesthesia ward - and the total morphine dose permitted for reaching a VAS equal to or lower than 30 (Aubrun et al 2003). Bijur et al. demonstrated in emergency medicine that after one bolus of 0.1mg/kg of morphine, 67% of patients had a decrease in pain intensity by 50% at the 30th minute (Bijur et al. 2005). This result had been estimated insufficient. The increase of the bolus to 0.15mg/kg did not significantly improve this result (Birnbaum et al. 2007).

A randomised controlled trial compared two doses of intravenous morphine in out-of-hospital emergency medicine. One group received a first bolus of 0.05mg/kg and then 0.025 mg/kg every 5 minutes, and the other group received 0.1 mg/kg and then 0.05 mg/kg every 5 minutes. The objective was a NRS equal to or lower than 3/10 (Bournes et al. 2008). At the 10th minute, 17% of the first group’s patients reached the objective versus 47% for the 2nd group (p=0.01); however, at the 30th minute, there was no more difference (67% and 77% respectively). Furthermore, there was also no difference in side effects. Lvovschi et al. demonstrated that intravenous titration (3 or 2 mg every 5 minutes) in the ED was performing good performance. Indeed, this study showed that titration was interrupted before pain relief had been obtained in 107 (17%) patients. In the remaining 514 patients, pain relief was obtained in 507 (99%) patients. Two variables were significantly associated with no pain relief: major protocol deviation (odds ratio, 17.3; 95% confidence interval, 10.0-30.1) and morphine-induced adverse effects (odds ratio, 13.0; 95% confidence interval, 6.7-25.3) (Lvovschi et al 2008). Morphine could be used alone but also in association with other level 1 painkillers (multi-modal analgesia). These associations could reduce the total dose of morphine and the rate of its side effects. Different routes of administration could be used for morphine. The interest in the parenteral route lies in the rapidity of its action and its indications are patients with difficulty in swallowing, anxiety, agitation because of the pain, nausea and vomiting. The intravenous route is the best route to reaching rapid pain relief. However, this is possible only if the means for monitoring and managing its complications exist.

5.3.2.3 Example of treatment with parenteral morphine in cases of severe pain in adults.

5.3.2.3.1 Induction of analgesia

The first step is the induction of analgesia. A load dose of 0.05 to 0.1 mg/Kg (particularly in trauma patients, but not systematically) can be done, followed by bolus of 3 mg (2mg if
weight < 60kg) every 5 minutes. The titration will be stopped when the therapeutic objective is reached or if there are SS ≥2 (Table 6) and/or a respiratory rate (RR) <10 c/min or and RS ≥ R1 (Table 7), or strong nausea or vomiting. Respect of the administration times and the posology is the corner stone of the titration’s success.

5.3.2.3.2 Maintenance of analgesia

The second step is the maintenance of analgesia with morphine. This begins when the relief of pain is stable, i.e. there was no new injection of morphine or any side effects for 2 hours after the end of the titration.

There are three possibilities for maintenance with the intravenous route, the subcutaneous route and the oral route. The intravenous route must use a patient-controlled analgesia system (PCA). The patient self-administers morphine when he needs it, with a specific electrical pump operated by a computer. Children from 5 years old and above can use this system. The computer is programmed by the physician and the system is locked, i.e. it cannot be modified without authorisation. In general, the dose of each administration is 1mg (or 0.015mg/Kg for children) with a refractory period of 7 minutes. The monitoring of patients should be programmed and regular, every 4 hours, by trained caregivers and – furthermore – there is a specific monitoring sheet for PCA. The subcutaneous route is not very reliable because of the wide inter-individual variation of morphine absorption. However, this route is often necessary. The first injection is done at least 2 hours after the end of the titration. The following injections have to be given with a minimum of 4 hour intervals and only if patient is in pain. The administrations should not be systematic and the dose should be adapted to the pain’s intensity. For example, if the pain is severe, the dose could be 10 mg SC (7.5 mg if weight< 60Kg) and, if the pain is intense, the dose could be 7.5mg (5mg if w<60Kg). Concerning the enteral route, the first administration should be done 3 hours after the end of the titration, and the dose should be 10 to 20 mg (immediate release morphine). The starting dose is 1mg/Kg divided every 4 hours. This dose has to be adjusted according to the efficacy of the previous doses, after 2 half-lives (8 hours for morphine). The therapeutic readjustment is based on a variation – up or down - of 25% to 50% of the previous dose.

The induction of analgesia could be done by the subcutaneous route. In this case, the initial dose is adapted to the pain’s intensity. For example, if the pain is severe the first dose will be 10 mg (7.5 mg is weight < 60Kg). The maintenance of analgesia will follow the schema described above. The enteral route is possible in an emergency setting when there is no difficulty in swallowing, no anxiety, no agitation, and no nausea or vomiting. However, the onset of action is of course longer than that of the intravenous route (Table 10). This means that the pain relief will be longer to obtain.

5.3.2.4 Example of treatment with enteral morphine in cases of severe pain in adults.

5.3.2.4.1 Induction of analgesia

The first step is the induction of analgesia. An initial bolus of immediate release (IR) morphine sulphate of 0.2 mg/kg could be administered initially, followed by 0.1 mg/kg one hour later if the pain is persistent. The titration will be stopped when the therapeutic objective is reached or if there are SS ≥2 (table 6) and/or a respiratory rate (RR) <10 c/min and/or RS ≥ R1 (Table 7), or strong nausea or vomiting.
5.3.2.4.2 Maintenance of analgesia

The second step is the maintenance of analgesia with morphine. The schema is the same as that described above. The treatment must be re-evaluated according to the evolution of the disease for which the morphine was administered.

5.3.2.5 Children

In children, the prescription of morphine follows the same rules of administration and monitoring as that for adult patients. For severe pain, the initial bolus is 0.1 mg/kg IV and then 0.025 mg/Kg every 5 minutes. The therapeutic objective is an Evendol lower than 4/15 for babies and young children, and a VAS equal to or lower than 30 for older children. The monitoring should be done every 5 minutes and then every 15 minutes for 2 hours after the end of titration. However, it must be continuous for younger children (babies and young children). The parameters of this monitoring are the same as that with adult patients.

For the maintenance of analgesia with morphine, there are particularities due to age. Babies under 3 months receive a continuous flow of 0.005 to 0.01 mgkg⁻¹h⁻¹ of morphine and children older than 3 months up to 4/5 years receive continuous flow of 0.01 to 0.02 mgkg⁻¹h⁻¹. This means specific monitoring in an intensive care unit for the younger children. From 5 years, children can use a PCA. The subcutaneous or enteral routes are also possible means for the maintenance of analgesia in all children. The monitoring is adapted according to age (Table 6 and 7).

5.3.2.6 Side effects

The treatment of side effects must be provided in the protocol. The prevention of constipation should be systematic with, for example, lactulose at 10 to 30 g/d in adults and 0.25 mg/Kg/d in children. The treatment of nausea or vomiting is provided by droperidol (1.25 mg IV) or ondansetron (4 mg IV). The treatment of pruritus and urinary retention is by naloxone, titrated (1μg/kg IV) and then 1μg/kg/h.

5.3.2.7 Hydromorphone and oxycodone

Hydromorphone is derived from morphine (Table 10). One of its main interests is in its liver metabolism to an inactive metabolite eliminated by the kidneys.

Oxycodone has a similar action to that of morphine (Table 10). This opioid could be efficient in cases of both nociceptive and neuropathic pain.

5.3.2.8 Naloxone

Naloxone is the indispensable antagonist during the use of opioids. Its onset of action is 30 to 180 seconds. However, its duration of action is lower than the duration of action of morphine. During a respiratory depression due to an opioid, the induction dose is 1 to 2 μg/kg intravenously. The objective is a normal respiratory rate (adapted according to the age). The maintenance is a continuous flow of 1 to 2 μg/kg/h.

5.3.2.9 Codeine and tramadol

The indication of weak opioids - level 2 according to the WHO classification - could be for moderate to intense pain in first line, or when pain is partially or unrelieved with level 1
painkillers. Codeine must be metabolised in morphine by the liver (2% to 10% of the dose), which is active on pain. Because of the absence of this means of metabolism, codeine has almost no effect in 7% of Caucasians and at least 15% of Asia’s population (Mazoit 1998). The administration of codeine is only oral and most of time is in association with paracetamol. The onset of action is 1 hour and its duration of action is 4 to 6 hours. Its dose is 25 to 60 mg every 6 hours and for children, 0.5 to 1 mg/Kg every 6 hours. Tramadol is both a serotonin and noradrenaline reuptake inhibitor and an opioid agonist. Its administration is oral or intravenous. The dose per os is 50 to 100 mg and, if the first dose is insufficient, it can be renewed 1 hour later. Afterwards, the administration is done every 4 to 6 hours. Intravenously, the dose is the same and can be renewed 20 minutes later. This drug can be associated with some side effects like sedation, confusion, dizziness and hallucination. Nausea and vomiting are the most common adverse effects. The contraindications of tramadol and its precautions of use must be known.

5.3.3 Local anaesthetics - Local and regional anaesthesia
In emergency medicine there are many situations which could benefit from local or locoregional anaesthesia, from venous puncture to the mobilisation of a trauma patient with a fractured bone (Table 5) as well as in many spontaneous painful situations (dental pains, ear pains etc.).

5.3.3.1 Local anaesthetic
All local anaesthetics (LAs) have a potential toxicity - neurological and cardiac - in cases involving a sudden rise in their plasma concentration, as in an accidental intravascular injection (Jeng et al. 2010). Whatever the LA, the early signs of toxicity must be perfectly known. They are the same for all LAs, the difference being the chronology and plasma concentration of their apparition. Local anaesthetics block the sodium channels of axons, reversibly so. Thus, local anaesthetics stop axonal nervous conduction.

5.3.3.1.1 Lidocaine
Lidocaine offers the best efficacy/safety ratio as compared with ropivacaine and bupivacaine. Its duration of action is relatively short but probably well-adapted to emergency medicine with effects which rarely last very long. Its onset of action is 5 to 10 minutes and its duration is 60 to 120 minutes. Its complications are neurological (convulsion, coma), and cardiac (ventricular dysrhythmia) due to an intravascular passage associated with a high plasma concentration (accidental intravascular injection, too strong a dose, the accumulation of doses) (Jeng et al. 2010). Therefore, doses must be respected and the different contraindications must be known. Lidocaine exists in several forms, topical (local anaesthesia of mucosa like mouth, nose, throat, oesophagus), injectable, cream for the skin, eye or eardrops. Thus, its indications vary widely from procedural pain (Table 3) to analgesia for spontaneous pain (dental pain, mouth ulcers, post herpetic pain) (Galinski 2010b).

5.3.3.1.2 Locoregional anaesthesia
The major interest in locoregional anaesthesia is in the absence of a general impact (neurological, cardiac or respiratory). These techniques must be governed by recommendations and guidelines. Two points must be underlined concerning the choice of a LRA technique. The first point is the benefit/risk ratio of the technique proposed. The
second point is the necessity to minimize the risk of interference with a LRA technique later on, which always possible for an eventual surgical act.

5.3.3.1.3 Conditions of the realization of a LRA in the emergency setting

For a simple local anaesthesia, the injection of 2 to 3 ml of LA does not require the implementation of sophisticated monitoring. In response, the realization of a locoregional anaesthesia with the same volume as that during a LRA for surgery necessitates precautions to ensure safety of the patient, i.e. a venous route and the monitoring adapted before the block (SFAR-Samu de France-SFMU 2004). Before the realisation of the block, it is fundamental to make a precise neurological examination and to make the point about potential nervous lesions. This examination must be precisely consigned in the patient’s medical file. The classical contraindications to these techniques will be respected (allergy, local infection, major haemostasis disease).

5.3.3.1.4 Which LRAs are indicated in emergency medicine?

At the lower limb level, the femoral nerve block and the blocks of the ankle and foot are easily accessible. The femoral block is adapted for femoral fracture and knee lesions. This allows mobilisation, transport and various acts with are very good conditions of analgesia. The fascial iliac compartment block seems to be the better way – in this context – to do this anaesthesia because of its simplicity, its efficacy and its lack of serious complications (Lopez et al 2003). Blocks at the foot level are realised for the management of wounds (exploration, suturing) or the extraction of foreign material. At this level, there are 5 branches to potentially block, and some of them necessitate a neurostimulator (Ferrera et al. 1994). At the upper limb level, the blocks concern 5 nerves at the elbow or forearm levels. The main objectives are the exploration and suturing of the wounds of the forearms, hands and fingers. The neurostimulation is particularly useful for the median and ulnar nerves. Adrenaline in association with LA is strictly forbidden for anaesthesia at the extremities. The anaesthesia of fingers 1, 2, 3 and 4 is obtained by injection in the flexor tendon sheath. For the face and the scalp, LRA is also a good alternative for the suturing of multiple wounds (Pascal et al. 2005). In the face, 4 blocks can be realised in unilateral or bilateral manner: a supra-orbital block and a supra-trochlear block (forehead and upper eyelid), an infra-orbital block (cheek and upper lip) and a mental block (chin and lower lip). All these blocks are easy to do without any risk of serious complication. However, there are some precautions to be taken. The use of epinephrine - associated with lidocaine - must be prohibited. For blocks near the eye, an antiseptic - without alcohol and non-irritative - must be used. The risk of haematoma or an eye wound must be taken into account during the puncture. It is clear that those physicians who make LRA must be trained.

5.3.3.1.5 Topical anaesthetic cream - EMLA (Eutectic Mixture of Local Anaesthetics)

This cream contains lidocaine and prilocaine (50/50). Its main indication is the prevention of procedural pains such as punctures. However, its onset of action necessitates anticipating the act. Indeed, the cutaneous depth of action depends on the contact time: 60 min = 3 mm, 90 min = 4 mm and 120 min = 5 mm. Some indications are presented in Table 3. In the emergency department, for children, there are criteria for anticipating venipuncture and for proposing the installation of anaesthetic cream. (Table 12). EMLA has the same efficacy as the N2O-Oxygen mixture during venous cannulation (Hee et al. 2003). In Babies, there is a risk of methemoglobinemia with anaesthetic cream.
1. Total digestive intolerance for more than 24 h.
2. Fever for more than 3 days in a child less than 2 years old
3. Fever for more than 5 days in a child older than 2 years old
4. Fever and acute abdominal pain
5. Fever and burning on urination
6. Sickle cell crisis
7. Non-traumatic lameness
8. Abnormal behaviour
9. Hemorrhagic syndrome, except in vital emergencies
10. Purpura without fever
11. Hypothermia
12. Hypotonia
13. Convulsion
14. Serious asthma crisis without vital risks
15. Malaise < 1 y.
16. Children sent by the general practitioner for assessment.

Table 12. Criteria permitting the anticipation of procedural pain (venous puncture) and an early application of anaesthetic cream by the nurse, on children in ED (Fournier-Charrière 2005)

5.3.4 Sedation
Sedation is often used in emergency situations. There are two kinds of indications: anxiety and procedural pains. Anxiolysis is probably necessary when anxiety is persistent despite an effective analgesia. However, they increase the sedation due to opioids, and so the use of this association must be cautious. A study showed that midazolam (0.05mg/kg) associated with fentanyl increases the incidence of apneas and hypoxemia (Bailey et al. 1990). In another study on emergency medicine, a respiratory depression was present in 0.5% of patients receiving an association of fentanyl and midazolam (Wright et al. 1990).

To perform painful procedures - including fractures and dislocation reduction, incisions and the drainage of abscesses, electric shock for cardioversion - a deep sedation is required. In emergency situations, 2 drugs are essentially used, namely ketamine and propofol.

5.3.4.1 Ketamine
This drug was synthesised in the 1960s and was defined as a dissociative anaesthetic. Its use was limited because of its psychodyseptic effects with a risk of hallucination and agitation. However, its main advantage was the respect of the hemodynamic tonus and of the spontaneous ventilation during anaesthesia. Furthermore, through its action as a N-Methyl-D-Aspartate (NMDA) receptor antagonist in the nervous system, ketamine alters nociceptive transmission (Dickenson 1997). As such, in addition to its anaesthetic effects, 2 actions of ketamine are interesting for emergency medicine. The first one is its action as an adjuvant in analgesia. It has been demonstrated that weak doses of ketamine (0.2 mg/kg IV) could significantly decrease morphine consumption, in an out-of-hospital emergency setting, in patients with severe pain (Galinski et al. 2007). In the post-operative setting, weak doses of ketamine (0.1 to 0.25 mg/kg) are associated with a decrease in morphine consumption, a reduction of pain intensity and a reduction of side effects due to morphine (Suzuki et al. 1999; Weinbroum 2003; Kapfer et al. 2005). In this case, ketamine is an
adjuvant of analgesia in a multi-modal frame. Its main indication would be probably the failure of a morphine titration being well-conducted. The second interesting action of ketamine concerns its sedative effect. With doses of 0.5 to 1 mgKg⁻¹, a sufficient sedation can be reached, permitting the realisation of very painful but very short procedures (from the reduction of fractures to electric shock for cardioversion). Indeed, intravenously, the onset of action of ketamine is less than one minute, and its duration of action is 5 to 10 minutes. It has been associated with respiratory compromise in 6% of adult patients undergoing moderate sedation (Chudnoffsky et al. 2000). A respiratory depression could occur immediately after an intravenous bolus. (Newton & Fitton 2008; Strayer & Nelson 2008; Green et al. 2009 a). Ketamine has been associated to side effects during recovery, from episodes of agitation to hallucinations, occurring in 5% to 25% of patients, which has limited its use (Newton & Fitton 2008; Chudnoffsky et al. 2000; Strayer & Nelson 2008; Green et al. 2009 b). The frequency and intensity of side effects increase with the dose. The relationship between plasmatic concentration and psychodysleptic effects is linear, between 50 and 200 mg/ml (Bowdle et al. 1998). Contraindications and side effects must be known. This sedative drug must be used with available resuscitation material and probably with a systematic pre-oxygenation.

5.3.4.2 Propofol

Propofol is an anaesthetic drug. Its use must be very delicate because of its hemodynamic effects (hypotension pressure), respiratory effects (apnea) and the loss of upper airways protection. The rate of adverse effects for propofol in the ED has been reported to be 5%, with hypoxemia present in 5% to 30% of cases (Miner & Burton 2007). Its main advantages are the onset of action, at 45 to 60 seconds, and the duration of action, 5 minutes (Burton et al. 2006; Knape et al. 2007; Miner & Burton 2007). These characteristics permit it for the performance of very painful but very short procedures. In emergency medicine, the doses are lower than those used to induce general anaesthesia. The most common doses studied in the ED setting are an initial bolus of 1mgKg⁻¹ followed by 0.5 mgKg⁻¹ every 3 minutes as needed to achieve or maintain sedation (Miner & Burton 2007). This sedative drug must be used with available resuscitation material and with a systematic pre-oxygenation.

The benefit/risk ratio must be measured for each patient, particularly the evaluation of the aspiration risk. Indeed, the other strategy could be a general anaesthesia with endotracheal intubation.

Nonetheless, physicians must be trained to use these two drugs, namely ketamine and propofol. A study demonstrated that the rate of subclinical respiratory depression (essentially a change of ETCO₂) was significantly different between patients receiving ketamine (N=47) and those receiving propofol (N=50), at 64% and 40% respectively (Miner et al. 2010). However, clinical interventions related to respiratory depression were no different between the two groups. Furthermore, no serious adverse events were detected during this study. The median doses (IQR) were 1 mg/kg (1-1.07) in the ketamine group and 1.46 (1.13 –2.50) in the propofol group. A mixture composed of propofol (10mg/ml) and ketamine (10mg/ml), called ketofol, was evaluated in a few studies. Willman and Andolfatto assessed 114 patients who had procedural sedation with ketofol: 7% had minor adverse events, and there were no cases of vomiting or aspiration; three patients became hypoxic and 1 patient
developed agitation. The median dose of ketofol administered was 0.75mg/kg each of propofol and ketamine (Willman & Andolfatto 2007).

5.3.5 Non-drug treatment

5.3.5.1 Physical means

The physical means are represented by immobilisation (splints, collars, traction etc.), cold (which has a local anti-inflammatory effect – trauma and visceral pains, burns etc.) (Bleckley et al. 2006; Nadler et al. 2004), and heat (muscle spasms, destruction of thermolabile venom) (Nadler et al 2004; Evans 1996).

5.3.5.2 Psychological approach

A professional attitude, empathy and an explanation of the actions and examinations prescribed facilitates patient adherence to its support and mobilises the placebo effect (Benedetti 2006). Thus, the efficacy of prescribed painkillers could be increased from 30 to 40% (Kong et al. 2006; De Pascalis et al. 2002). Furthermore, distraction is another route to reduce pain, particularly for procedural pains (Johnson 2005; Murphy 2009).

Table 13. Management of acute pain in emergency medicine: evaluation and treatment (From SFAR-SFMU 2010)
5.3.6 Failure of analgesia
When there is a failure of analgesia a number of factors must be researched:
Is the analgesia adapted to the intensity level?
Is the posology of used painkillers in accordance with recommendations and needs?
Are the time intervals between two administrations in accordance with recommendations?
Example: the failure to respect the 5 minutes intervals between injections of morphine
during titration is a factor of failure.
Is there a multi-modal analgesia?
The mechanism of the majority of acute pains in emergency medicine is due to excessive
nociception. However, Neuropathic pains could be present in more than 20% of cases in the
ED (Table 1)
The relational dimension, if it is not taken into account, can be a source of failure. Did
the patient receive an explanation, about his pathology and his treatment?

6. Conclusion
The management of acute pain in emergency medicine is based on 3 principles: the
evaluation of pain intensity with a scale adapted to the patient, a treatment adapted to the
intensity, the patient, their pathology and the protocols. The objective is to relieve pain and
avoid the side effects due to painkillers. In this way, training and the knowledge of
caregivers are fundamental, particularly in relation to the use of opioids. Each structure
must develop its own protocols of care and monitoring. These protocols must be adapted
not only to patients and their pathology but also to the knowledge of caregivers themselves.

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