REVIEW ARTICLE

Analgesia and Sedation for Painful Interventions in Children and Adolescents

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SUMMARY

Background: Painful procedures on children and adolescents often have to be performed with the aid of analgesia and sedation in order to prevent pain and emotional distress. Moreover, many procedures can be performed more rapidly and more effectively in a relaxed patient. Because the combination of analgesia and sedation can cause serious or even life-threatening complications, it must be accompanied by the same safety precautions as a general anesthetic.

Methods: Selective review of the literature.

Results: A high level of safety can be achieved by adherence to the published guidelines of the societies for anesthesiology and pediatrics. The depth of sedation during procedures performed under combined analgesia and sedation is often equivalent to that resulting from general anesthesia. Therefore, in order to avoid serious complications, combined analgesia and sedation should only be administered by physicians trained in pediatric anesthesia or pediatric critical care. This is particularly so when propofol is used, because it has a narrow therapeutic range and can cause cardiorespiratory respiratory problems without warning. As long as the appropriate safety precautions are followed, non-anesthesiologists can also administer propofol in combination with an analgesic, such as ketamine, to children and adolescents.

Conclusion: In children and adolescents, the combination of analgesia and sedation can prevent the emotional trauma that would result from a painful procedure, while often enhancing the quality of the procedure itself. This method should be considered a variant of general anesthesia. Accordingly, any non-anesthesiologist employing this method must be as well versed as an anesthesiologist in the management of its specific side effects and complications.

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Children and adolescents can suffer considerable pain during the smallest interventions, even without an existing tissue injury—especially when they are afraid (e1). The negative consequences of inadequate pain therapy in this age group can be extensive (e.g., traumatization, chronification) (1, e2, e3).

The importance of adequate preventive pain therapy is often underestimated. In addition to thoroughgoing analgesia, the management of painful interventions in children also requires adequate sedation/analgesia, partly in order to keep the intervention stress-free for the child, so that no psychological traumatization results, and partly to ensure adequate toleration of the procedure. Young children in particular lack the ability to understand that they are ill and need treatment to the extent that they can accept the treatment (2); but for older children and adolescents, too, medical interventions usually signify an indefinable threat that carries a considerable psychological burden (e4).

It has long since become reality in clinical routine that sedation/analgesia for brief interventions in children is carried out not only by anesthesiologists, but increasingly also by non-anesthesiologists (e5). This state of affairs can only be supported, however, so long as the care provided by non-anesthesiologists is of the same quality and can guarantee the safety of the patient. In a retrospective study Coté et al. analyzed factors that led to 95 selected adverse sedation events, 51 of which were fatal (3). In all cases they found serious infringements of the safety standards current in anesthesiology. When carrying out sedation/analgesia in children, it must be particularly borne in mind that painful interventions in this age group often require a deeper level of sedation than in adults (4, 5). The basic principle is that the deeper the sedation, the greater the risk of respiratory and cardiovascular complications (5–7). Equally, however, too shallow sedation/analgesia can increase the spectrum of complications (e6). As regards the sedation level attained (*Box 1*), sedation/analgesia must be regarded as a variant of general anesthesia (4, 8, 9). In consequence, the same safety aspects must be required as for general anesthesia. Where the sedation/analgesia is not carried out by anesthesiologists, therefore, "sedation teams" should be created who show similar competence (10, 11). To create a standard of care and limit the risks for the patients, the professional societies for anesthesiology and pediatrics have

BOX 1

Definitions according to the American Society of Anesthesiology (ASA)*[1]

- Sedation
  - Condition that allows patients to tolerate uncomfortable procedures while maintaining adequate respiratory and cardiovascular function.
- Deep sedation
  - Drug-induced loss of consciousness in which patients cannot be easily aroused but respond purposefully to repeated and/or painful stimuli.
- General anesthesia
  - Drug-induced loss of consciousness in which patients do not respond purposefully even to painful stimuli.
- Levels of sedation in sedation/analgesia
  - May be in the region of "deep sedation," but frequently a state is reached similar to general anesthesia, especially if the patient must not show any kind of reaction during the procedure (4, 8, 9). Sedation/analgesia therefore represents a variant of general anesthesia.
- Spontaneous ventilation during sedation/analgesia
  - As a rule spontaneous ventilation is adequately maintained, so because of the usually short duration (5 to 45 minutes) intubation is not necessary. The fasting guidelines must be followed. Airway obstruction may be overcome using, e.g., the Esmarch maneuver (jaw thrust maneuver); transient phases of respiratory insufficiency or apnea are managed by mask ventilation.
- Indications for intubation
  - Should be decided on an individual basis (depending on the nature and duration of the procedure, fasting state, and the child's age, previous illnesses, and anatomy. Intubation anesthesia should be carried out by an anesthesiologist.
- Change in level of consciousness
  - The nature, combination, and dosage of the drugs used determine the sedation level. Irrespective of which drugs are used, transitions from one level of consciousness to the next deeper one occur on a continuum, vary between individuals, and can be very rapid (15). In addition, the relationship between stimulating factors (e.g., pain) and depressing factors (e.g., drugs) determines the degree of sedation and may vary during the procedure. Particular care is required at the end of the intervention, because when stimulation ceases, the patient may fall into a deeper level of sedation than desired.
- Influence of sedation level on ventilatory and cardiovascular function
  - Increasing loss of consciousness is accompanied by a loss of tone in the pharyngeal musculature and the tongue, with the risk of airway obstruction and impairment of protective reflexes (coughing and swallowing); hypnea, apnea, and arterial hypotension are also more likely. At the level of general anesthesia, therefore, intervention to secure ventilatory and cardiovascular function become increasingly necessary (6).

*[1] modified from (6, e39)

published guidelines for the practice of sedation by non-anesthesiologists (6, 7, 12). This review will look more closely at the relevant recommendations for the practice of sedation/analgesia. Sedation management for non-painful procedures (e.g., CT, MRI) will not be discussed.

Indications

Any fear-inducing/unpleasant procedure associated with pain, and painful interventions that require maximum toleration or immobility are indications for sedation/analgesia (*Box 2*). Reservations about when sedation is indicated in children (especially young children) are not justifiable (e7). Sedation/analgesia when properly carried out does not traumatize the child or adolescent and helps to improve the quality of medical interventions (9, 13).

Psychological aids and non-medical methods, e.g., a child-friendly environment, age-appropriate distraction strategies, explanations, the presence of the parents until the child is asleep, positive reinforcement through comforting, praise and loving attention, can all reduce fear and stress before the procedure and should be given to all children (e8).

Pain during so-called "minor interventions" on the surface of the body (e.g., venous access, vascular and lumbar puncture) can be reduced with a topical local anesthetic (e9). Infiltration anesthesia, on the other hand (e.g., lidocaine, mepivacaine), can in itself be very unpleasant for children. Fear and agitation (e.g., fear of the needle) can make it necessary to give oral premedication (e.g., midazolam) or additional sedation in these cases. Although local anesthesia has an important role in pain therapy during painful interventions, the emphasis in this review will be on intravenously administered analgesia and sedation.

Special patient groups

Newborns and infants, especially premature infants, require special procedures (an experienced team, intubation narcosis if necessary, hospital admission).

A high incidence of apnea and hypoxia is to be expected (immaturity of the respiratory center, unstable airways, smaller functional residual capacity). A longer monitoring period of up to 72 hours is advisable especially in premature babies up to a postconceptual age of 50 weeks (e10).

Particular care is also required in children with

- Respiratory impairment (severe asthma, upper airway infection in the past 6 weeks, chronic pulmonary disease)
- Cardiovascular disease (heart defect, pulmonary hypertension, cardiomyopathy)
- Gastroesophageal reflux or other disease of the esophagus/stomach
- Restricted hepatic and renal clearance
- Muscular and metabolic disease (be aware of contraindications)
- Neurodegenerative disease (cerebral palsy, latent dysphagia)
- Craniofacial malformations.

BOX 2

Examples of interventions for which sedation/analgesia is usually indicated

- Colonoscopy
- Gastroscopy, transesophageal echocardiography
- Bronchoscopy
- Biopsies (e.g., liver, muscle)
- Fracture and wound care
- Change of dressings
- Placement of drains and catheters (e.g., thoracic drain)
- Ultrasound-guided puncture
- Bone marrow aspiration

Recommendations from the professional societies (6, 7, 12)

Preparation

Before sedation/analgesia, the following are to be performed in every case:

- Measurement of biometric data, history, diagnoses (allergies, heart and liver disease), previous medication
- Physical examination, especially of the airways, with a view to identifying potential difficulties with mask ventilation or intubation
- Risk assessment and ASA physical status classification (*Table 1*)
- Laboratory tests depend on the nature of the intervention and any underlying disease
- The patient (or the patient's parent or guardian) must be informed about the nature of the procedure on the day before it is carried out
- Arrange for fasting before elective procedures (*Table 2*). If a fasting state cannot be awaited (emergency procedures), or if gastric emptying is delayed (after trauma, medication, ileus, or intestinal stenosis), the risk of pulmonary aspiration must be taken into account (possibly alternative procedure, delay the procedure, intubation anesthesia carried out by an anesthesiologist).
- Oral premedication for anxiolysis (e.g., midazolam) if necessary, and agree medication for the day of the procedure.

Location for sedation/analgesia

Sedation/analgesia may only be carried out at a location where typical complications can be recognized and treated. A defibrillator (with age-appropriate paddles) should be rapidly available in case of emergency.

Monitoring

Basic monitoring after sedation includes:

- Continuous pulse oximetry (with acoustic signal)
- Electrocardiogram
- Non-invasive blood pressure measurement (before the start of sedation, then at 5-minute intervals).

The level of sedation is monitored clinically. The airways and the position of the child's head should always be checked for airway obstruction; respiration is assessed clinically (precordial stethoscope if necessary). Sidestream capnography, e.g., with a nasal catheter in spontaneously breathing patients, can be helpful in practice. This procedure is practical both for trend analysis and for apnea recognition (e11, e12), although in some circumstances the values shown for end-expiratory CO_2 can vary from the actual values (e13). If clinical assessment is limited, capnography is recommended for additional safety in ventilation monitoring (7).

If the monitoring is being done automatically, the monitor's alarms must be set so that critical events and changes are recognized immediately.

Documentation

Vital signs, the nature and dosage of drugs and how and when they are administered, the amount of oxygen given, and all emergency measures (ventilation, intubation, etc.) must be documented (at the start of analgesic/sedative administration and then at 5-minute intervals during analgesia/sedation and during the recovery period).

Oxygen

Sedation/analgesia should not be carried out without giving supplemetal oxygen. If apnea occurs, the drop in saturation may be delayed, and for this reason the respiration must be closely monitored clinically (capnography may be used).

In premature infants born before the 37th gestational week, and in patients with heart defects, the normal saturation limits for these groups must be maintained.

TABLE 1

ASA physical status classification *1

ASA class	Examples	Suitability for sedation
I A normally healthy patient	Normal history and exam	No restrictions
II A patient with mild systemic disease without restricted function	Child with controlled reactive airway disease	Usually no restrictions
III A patient with severe systemic disease and definitely restricted function	Child with asthma and marked stridor (wheezing)	Some restrictions; a risk–benefit analysis should be carried out
IV A patient with severe systemic disease that is a constant threat to life	Child with status asthmaticus	Massive restrictions; usually benefit is smaller than risk
V A moribund patient who is not expected to survive without the operation	Child in cardiogenic shock, intended to undergo heart transplantation	Not suitable

*1 ASA physical status classification according to (6, 7)

TABLE 2

Minimum fasting periods *1

Fasting periods before elective procedures			
Age	Solid food, breast milk	Infant formula	Clear liquids
<1 year	4 h	4 h	2 h
>1 year	6 h	–	2 h

*1 Modified from (e40)

Sedation team

The sedation team consists of a physician and a nurse who have undergone structured training in carrying out sedation/analgesia (correct use of sedative and analgesics, monitoring of consciousness) and in airway management (mask ventilation, intubation) in children and adolescents and who have adequate experience of the latter. They must both be exclusively tasked with carrying out the sedation:

- The physician's responsibility is to continuously monitor the patient, administer and adjust the drugs, and manage any complications (*Table 3*). At least one physician must be present who has sufficient knowledge and experience of extended cardiopulmonary resuscitation in the relevant age group.
- The nurse must be trained for this task in this age group, and have enough experience to be able to help the physician with the monitoring and all procedures required.
- Help from an anesthesiologist with experience of pediatric anesthesia or a specialist in pediatric intensive medicine (pediatrician with additional specialization in pediatric intensive medicine) should be available within a few minutes (14).
- Patients in ASA classes I and II do not usually suffer any extra problems in sedation/analgesia and can therefore be managed by a sedation team with the qualifications listed above. Patients in ASA classes III and IV, and patients with particular pre-existing diseases (e.g., pulmonary or cardiac problems) or those with anatomically difficult airways, on the other hand, should be cared for primarily by pediatric anesthesiologists or pediatric intensivists.

Intravenous access

Intravenous access (IV access) should be created before the start of sedation, e.g., using an EMLA patch.

Transfer and discharge criteria

After sedation/analgesia, children should be monitored in a suitable child-friendly location. If the patient is not completely awake, oxygen saturation and heart rate should be continuously registered. A long monitoring period may be necessary (drugs with a long half-life, use of antagonists, certain patient groups). Once the child is able to stay awake for 20 minutes in a quiet environment, it is very probably safe to transfer it elsewhere (e14). Neonates, infants, and children with learning difficulties should return to their presedation status.

The following criteria must always be fulfilled:

- Stable and sufficient cardiovascular and respiratory function
- Stable, open airways with adequate protective reflexes (swallowing, coughing)
- Patient awake or easily roused (speaking, sitting up)
- Normothermia and adequate hydration.

We discharge ambulant patients when they are completely awake and have tolerated a meal appropriate for their age.

Intravenous sedation/analgesia

Basic principles

It is difficult to predict how any individual child will react to being given a sedative or analgesic (4, 5, 8). The optimal degree of sedation/analgesia must therefore be determined individually for each patient and in dependence on the procedure being carried out. Although children often need higher doses by body weight than adults, they also react with respiratory depression and airway obstruction more quickly than do adults (5, 16). They change more quickly, usually without warning, from one sedation level to the next deeper one (4).

Midazolam and propofol are suitable sedatives and must be combined with ketamine or an opioid (e.g., fentanyl) (*eTable*). The combination of midazolam and ketamine has the lowest complication rate.

The following principles must be observed:

- No sedative drugs may be given without medical monitoring and an "emergency plan."
- No sedations may be carried out without adequate analgesia or local anesthesia.
- Combinations of more than one sedative with more than one analgesic should be avoided. Complication rates rise with the number of drugs used (15).
- Titrating the drugs used by giving repeated small doses until the desired effect is attained ("titration to effect") is better than giving single doses based on body weight. The cumulative dose may be higher than is recommended in the literature; the pharmacology of the drugs must be taken into account.
- Intramuscular administration should be avoided, as should oral and rectal administration (the exception is oral premedication), as the absorption is often difficult to predict (delayed effect, giving later additional doses can be dangerous).
- Antagonists should be available. The duration of effect of antagonists may be shorter than that of the antagonized drugs.

TABLE 3

Typical complications and options for their management

Complication	Management options
Airway obstruction	– Esmarch maneuver (jaw thrust maneuver—upward and anterior displacement of the jaw using both hands) – Oro- or nasopharyngeal tube – Patient in lateral position (pharyngeal space ca. 50% larger than when patient supine)
Apnea, hypopnea	– Mask ventilation with supplemental oxygen – Intubation (if mask ventilation inadequate or not possible)
Laryngospasm	– Mask ventilation with supplemental oxygen – If required, general anesthesia with relaxation and intubation
Vomiting, regurgitation, aspiration	– Patient in lateral recumbent position, apply suction – If aspiration occurs: – Supplemental oxygen if saturation below 95% – Intubation and ventilation (PEEP) if necessary – Bronchoscopy, chest radiograph if necessary – Antibiotics if patient shows signs of infection following the procedure
Arterial hypotension	– Volume replacement: Any of NaCl 0.9%, Ringer lactate, or HAES 6%, 10 to 20 mL/kg IV – In life-threatening cases: vasopressors (epinephrine, norepinephrine, 1 to 10 µg/kg per dose, IV)
Bradycardia	– Atropine 20 µg/kg per dose, IV – In life-threatening cases: epinephrine 1 to 10 µg/kg per dose, IV
Allergic reaction, anaphylaxis	– H_1-blockers (e.g., dimethindene 0.025 to 0.5 mg/kg per dose, IV) and H_2-blockers (e.g., ranitidine 1 to 2 mg/kg per dose, IV – Steroids (e.g., methylprednisolone 5 to 10 mg/kg per dose, IV) – Symptoms of shock: volume therapy and epinephrine 1 to 10 µg/kg per dose, IV

Propofol

Propofol (2,6-di-isopropylphenol) is a hypnotic whose pharmacological properties make it extremely well suited to sedation and anesthesia. Propofol has no analgesic effect and must therefore be combined with ketamine or opioids for sedation/analgesia. Because of its high potency and the respiratory and cardiovascular complications that can result, propofol may only be used when strict precautionary measures are observed (e15). In Germany 1% propofol is licensed for general anesthesia only in children older than 1 month; it is not licensed for sedation under the age of 16 years (e16). While propofol cannot be recommended for long-term sedation of children (e.g., in intensive care), because of the increased risk of propofol infusion syndrome (e17), 1% propofol is suitable for off-label use for short-term sedation of children older than 1 month (ASA class I–II), provided the guidelines described are adhered to (9, 14, 17–19, e18–e20).

The main advantages of propofol are that it takes effect rapidly, achieves a deep state of sleep (hypnosis) quickly and safely, has a relatively short duration of effect, recovery is pleasant, there are few contraindications, barely any hangover, and it has an antiemetic effect (*eTable*). In addition, it can be given to patients with a predisposition to or suspected malignant hyperthermia, and those with acute hepatic porphyria (without lidocaine), epilepsy, and muscular diseases (e21, e22). Nevertheless, a clear advantage of propofol as against, for example, midazolam/ketamine, for sedation/analgesia in children has not been demonstrated in studies (e23, e24). The incidence of airway problems and consequent falls in saturation values is in fact higher with propofol (e12, e23–e25).

Propofol can be administered as boluses (titrate to effect) or by maintenance infusion (*eTable*). The typical pain associated with injection can, for example, be alleviated by giving lidocaine (e26). It should be noted that the therapeutic spectrum in relation to respiratory problems is relatively narrow (20, e27). To achieve 100% toleration during painful procedures in children, Powers et al. needed to give boluses of 2.2 mg/kg followed by infusion of 3 mg/kg per hour (9), corresponding to a drug concentration in the brain (effect side concentration, ESC) of 3.0 to 4.0 µg/mL (e28). the critical ESC, at which airway collapse can occur, is reported to be 4.0 µg/mL (e29). However, pharyngeal dysfunction with dysphagia has been described even at lower ESC (e30). According to current studies, in 2% to 31% of children there was an initial drop in

transcutaneous oxygen saturation to below 95% and respiratory support was needed in from 1% to 19% of cases (18, 21, e18, e19, e23, e25). Thus, airway obstruction and a need for respiratory support should always be anticipated during propofol sedation (typically after the initial bolus). Arterial hypotension (especially in patients with hypovolemia), relative bradycardia, and flushing are also frequent but seldom require treatment (21, e18, e19, e23, e25). Propofol infusion syndrome (PRIS), on the other hand, although carrying a high mortality, is very rare worldwide given the millions of times the drug is employed (22, 23, e31, e32).

Despite the risk potential of propofol, studies indicate that it can be used very safely for sedation/analgesia in children even by non-anesthesiologists given the correct training and so long as they observe the guidelines (9, 14, 17–19, 24, 25).

Anesthesia/analgesia

Whenever possible, local anesthesia to prevent pain (e.g., by subcutaneous injection) is to be preferred. The injection should not be carried out until the child has gone to sleep (children do not like needles). If local anesthesia is not possible, adequate analgesia can be ensured by intravenous administration of ketamine or fentanyl. Ketamine is a derivative of phencyclidine (dissociative anesthesia) with analgesic effect (antagonist of NMDA and agonist of μ-opiate receptors), available as a racemate or as the more potent *S*(+)-enantiomer (*eTable*). Because of its slight respiratory depressive and cardiovascular stimulatory effects, it is well suited to combination with hypnotics and sedatives (especially propofol) (21, e33–e35). Disadvantages are the possibility of psychotropic side effects and drooling (*eTable*). Fentanyl is a potent opioid that can be used against strong pain (*eTable*). Like all opioids, however, fentanyl increases the tendency to respiratory depression, hypotension, and bradycardia (21, e36–e38).

Conclusion

Children and adolescents need adequate sedation/analgesia for many painful diagnostic and therapeutic procedures. If these are to be carried out safely, the guidelines of the professional societies for anesthesiology and pediatrics must be followed (24). An approach to sedation is required that is adapted both to the needs of children and adolescents and to the intervention to be performed; it must be carried out correctly, professionally, and in a routine manner by a team consisting of a physician and a nurse who have received structured training and are experienced in working with this age group (11, 19).

Conflict of interest statement
Dr. Weigand has received lecture fees from Glaxo SmithKline, Pfizer, and Braun. Dr. Neuhäuser, Prof. Zimmer, Dr. Heckmann and Dr. Wagner declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

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KEY MESSAGES

- During painful procedures and interventions, children need adequate sedation/analgesia to prevent psychological and physical injury.
- Following the guidelines on sedation and analgesia in children and adolescents published by the professional societies for anesthesiology and pediatrics increases patient safety.
- Creating a "sedation team" consisting of a physician and a nurse, both specially trained for the task, reduces complication rates, increases patient safety, and contributes to the success of the interventions.
- Non-anesthesiologists specially trained for the task (the sedation team) can provide patient safety during sedation/analgesia of ASA class I and II patients that is comparable to that provided by anesthesiologists (including when propofol is used).
- In terms of the safety and comfort of the patient, and the success rate of the interventions, deep sedation correctly carried out is preferable to inadequate, overshallow sedation.
- In terms of the success of sedation/analgesia, no drug combination (e.g., propofol+ketamine, midazolam+ketamine, propofol+fentanyl, midazolam+fentanyl) has been shown to be superior to any other.

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REVIEW ARTICLE

Analgesia and sedation for painful interventions in children and adolescents

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eTABLE

Drug preparation*[1]

Preparation	Pediatric dosage	Effect onset (minutes)	Effect duration (minutes)	Analgesia/Remarks
Midazolam	Intravenously (0.5 to 5 years): initially 0.05 to 0.1 mg/kg, then titrate to effect up to a maximum of 0.6 mg/kg Intravenous (6 to 12 years): initially 0.025 to 0.05 mg/kg, then titrate to effect up to a maximum of 0.4 mg/kg; Orally: 0.5 to 0.75 mg/kg Intranasally: 0.2 to 0.5 mg/kg	IV: 2 to 3 PO: 15 to 30 IN: 10 to 15	IV: 45 to 60 PO: 60 to 90 IN: 60	– Effects: anxiolytic, amnestic, anticonvulsant, sedative, central muscle relaxation – Wide therapeutic spectrum (as single substance) – Reduced dose when combined with opioids – Paradoxical reactions possible (avoid underdosing) – Respiratory depression possible with rapid IV administration or in combination with opioids – Intranasal use unpleasant – ANTAGONIST: flumazenil 0.005 to 0.01 mg/kg IV
Propofol	Intravenously: initially 1.0 to 2.0 mg/kg, then 0.5 to 1.0 mg/kg titrated to effect Via a perfusor: 3 to 6 mg/kg/h	IV:<1	IV: 5 to 15	No – Narrow therapeutic spectrum – License: general anesthesia > 1 month of age – Typical: injection pain [avoid: e.g., 1 mL lidocaine 1% per 20 mL propofol 1% or lower concentration 5 mg/mL (0.5%) instead of 10 mg/mL (1 %)] – Absolute contraindications: allergy (egg, soya, and peanut allergy), sedation of pediatric intensive care patients < 16 years (risk of PRIS) – Relative contraindications: children < 3 years with acute airway infection (risk of PRIS) – Frequent side effects: airway obstruction, apnea, hypotension, bradycardia, flushing – Rare side effects: rhabdomyolysis, pancreatitis, myoclonia, hyperlipidemia (1 mL propofol 1% contains 0.1 g/mL fat; max. rate: 2 mL/kg per hour)
Fentanyl	Intravenously: 0.5 to 1.0 ìg/kg (up to 50 ìg/dose), may be repeated every 3 to 5 minutes until effective	IV: 3 to 5	IV: 15 to 30	Yes – Narrow therapeutic spectrum – Side effects: respiratory depression, bradycardia, thorax rigidity, low histamine liberation – ANTAGONIST: naloxone 0.01–0.04 mg/kg IV
Ketamine Racemate	Intravenously: 1.0 to 2.0 mg/kg slowly over 30 to 60 seconds, may be repeated every 10 minutes according to effect	IV: 1 to 2	IV: 30 to 60	Yes – Not hypnosis but “dissociative anesthesia” – Wide therapeutic spectrum – Relative contraindications: raised ICP, perforating eye injury, pulmonary and arterial hypertonia, aortic and mitral stenosis, hyperthyreosis, epilepsy and psychiatric illness
S(+)-Ketamine	Intravenously: 0.5 to 2.0 mg/kg slowly over 30 to 60 seconds, may be repeated every 10 minutes according to effect	IV: 1 to 2	IV: 30 to 60	– Side effects: nightmares (therefore: combine with benzodiazepines), hypersalivation (atropine or glycopyrrolate), nausea and vomiting – almost no respiratory depression (as single substance), protective reflexes are generally preserved – Cardiovascular stimulation, bronchodilation
EMLA	Neonates/infants: 0.5 g (max. 1 to (2) g) Young children: 1 g (max. 10 g) School-age children: 1 g (max. 20 g) Adolescents: 1.5 to 2 g	45 to 90	60 to 120	– 1 g cream contains 25 mg lidocaine and 25 g prilocaine – Relative contraindications: neonates and premature infants < 3 months old (risk of methemoglobinemia) – Application time: 30–45 minutes (risk of vein maceration)

*[1] Modified from (5); IV, intravenously; PO, orally; IN, intranasally; ICP, intracranial pressure; PRIS, propofol infusion syndrome.