Benefits, safety and side effects of tumescent local anesthesia in dermatologic surgery in infants

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Summary
Tumescent local anesthesia (TLA) plays an important role in dermatosurgical procedures. TLA has several benefits such as long-lasting anesthesia, reduced bleeding during surgery and the avoidance of general anesthesia-associated complications. Convenience and a favorable risk profile along with a broad spectrum of indications are further reasons why TLA is increasingly applied in infants as well. There are not only a variety of indications for surgical excisions in infancy, such as congenital nevi, but also substantial benefits when performing these excisions at an early age. These include the smaller size of the lesions as well as the unproblematic wound healing and tissue regeneration in infancy. Nevertheless, several aspects need to be considered when applying TLA in infants including dosing, altered plasma protein binding and the need for adequate and long-lasting pain control.

Introduction
Tumescent local anesthesia (TLA) was first described in 1892 by the German surgeon C. Schleich [1]. This technique vanished into oblivion and was reinvented in liposuction surgery in 1987 [2]. Subsequently, its fields of application have expanded considerably, particularly in dermatologic surgery as it allows an extensive regional anesthesia of skin and subcutaneous tissue [2–4]. TLA is nowadays used not only in dermatologic surgery but further in plastic surgery, burn care, and vascular surgery [3, 5, 6], but there is a paucity of data on its use in infancy. Table 1 gives an overview of indications and the use of TLA. When administered via an infusion pump, the injection of local anesthetic agents is well tolerated even in infants [7, 8] and large areas of up to 20 % of the body surface area can be treated [3, 9]. The TLA-solution consists of local anesthetic agents and epinephrine diluted in a carrier solution such as balanced-electrolyte solution [10, 11]. The addition of epinephrine facilitates vasoconstriction, enabling a decreased blood loss and prolonging the anesthetic effect. No evidence for acral necrosis due to epinephrine has been demonstrated, despite concerns being expressed in the past, and it is still used in an off label manner [12–15]. In a short summary several positive aspects of adding epinephrine are presented, such as application in hand surgery without the need for an additional tourniquet [15]. Avoiding general anesthesia with its potential side effects is another main reason why TLA is also increasingly applied in infancy, but special aspects require consideration in this group of patients. We review the use of TLA in dermatologic surgery with an emphasis on its application and special considerations in infancy.

Benefits of TLA
Several studies demonstrated that excellent pain control can be achieved through TLA in infancy. Heister et al. were able to demonstrate that TLA is a suitable treatment option also in infants under the age of six months, enabling an outpatient treatment without major complications [7]. It has been demonstrated that TLA induces long-lasting analgesia in pediatric patients [3, 16]. Breuninger et al. further showed that ropivacaine can prolong anesthesia when added to a prilocaine-based TLA-solution [17]. Long-lasting pain control through TLA reduces the need for additional analgesic drugs postoperatively, thereby reducing the risk of drug-induced side effects. Reduced risk of bleeding is another benefit of TLA, as the vasoconstrictive effect of epinephrine and the increased hydrostatic pressure in the tissue lower the incidence of intra- and postoperative bleeding [2]. The safety of using epinephrine even in acral surgery (applied in a dilution of 1 : 200,000) was demonstrated in a study analyzing surgical...
excisions of polydactyly in infants, where no ischemic complications such as tissue necrosis were observed in 402 procedures [18]. Another benefit associated with the reduced tissue blood flow is the slow absorption of anesthetic agents thereby reducing required dosing and plasma levels. Consequently, the risk for systemic side effects is considerably reduced [7, 19]. A study assessing the plasma level of lignocaine in TLA with or without epinephrine nevertheless found no difference in maximum plasma concentrations [9].

### Dosing

As there are no general recommendations for the dosing of TLA, different formulations are utilized in different settings and centers. However, recommendations from the European Society of Regional Anesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine [20] for the use of local anesthetics for regional and spinal anesthesia in infants can serve as dosing guidelines. Vittinghoff et al. recommended a maximum dosage for wound infiltration and other settings for bupivacaine (2.5 mg per kg BW), L-bupivacaine (2.5 mg per kg BW) and ropivacaine (3 mg per kg BW) [21]. In the past, the combination of two local anesthetic agents was discussed controversially. On the one hand the combination leads to a faster onset of action and a longer duration of action, while on the other hand toxic effects can be potentiated by increased free agents based on competitive protein binding [22]. It is therefore critical to be aware of each component’s dosing when mixing local anesthetic agents, which is not equivalent to the respective single drug use [23]. Considering the respective pharmacokinetics, several studies demonstrated the safety of mixing these agents [24]. In our department, a formulation of 10 ml lidocaine 2 %, 10 ml ropivacaine 1 % and 0.5 mg epinephrine 1 : 1000 in 500 ml balanced electrolyte solution is used in infants [7] without reported adverse events over the last 20 years. In a retrospective study Heister et al. described the safe use of tumescent local anesthesia in 92 infants with a median age of 4.2 months between 2005 and 2015 without any side effect [7]. Moehrle et al. analyzed 354 surgical procedures in children in the year 1999, in which TLA was used in 204 cases. The median age of these children was 9.0 years. In these procedures no side effects of local anesthesia were observed [11].

### Special aspects of local anesthesia in infants

Infants are at a higher risk for systemic side effects from local anesthesia [25]. Table 2 gives an overview of systemic side effects and emergency measures. Local anesthesia systemic toxicity (LAST) is a severe and potentially life-threatening adverse event which can occur after applying local anesthetic agents, especially if the recommended maximum dose is exceeded or in accidental intravascular injection [19, 25]. Neurologic symptoms such as convulsions, loss of consciousness or agitation are the most common systemic side effects from local anesthesia [26]. Cerebral vulnerability is increased in infants due to the immature blood brain barrier and cerebral toxicity can lead to apnea and grand mal convulsion [27, 28]. However, two large studies of pediatric patients found that the overall incidence of cerebral toxicity is only about 0.01–0.05 % [29, 30]. Further, cardiovascular symptoms including bradycardia, hypotension and cardiac arrhythmias can occur as a result of toxic plasma levels [26]. Similar to neurologic toxicity, cardiac adverse events are very rare. A prospective study analyzing more than 24,000 procedures of regional anesthesia in children reported only four patients (0.017 %) with cardiac toxicity [30]. With regard to risk profiles of different anesthetic agents, a retrospective study in adults showed that bupivacaine was the causative agent in 55 % of all reported adverse events, followed by ropivacaine (30 %), while 15 % of the events were related

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**Table 1** Indications and use of tumescent local anesthesia.

| Indications and use of TLA | Dermatologic surgery | Gynecological surgery | Plastic surgery | General surgery | Cardiac surgery | Hand surgery | Pediatric surgery |
|----------------------------|----------------------|-----------------------|-----------------|----------------|----------------|--------------|-----------------|
| Benign skin lesions, skin cancer, sentinel-node-biopsy, lymph node dissection, phlebectomy | (total) mastectomy | Liposuction, burn surgery | Inguinal hernia repair | Pacemaker implantation | Tendon repair, tenolysis, tendon transfer, carpal tunnel | Dermatologic surgery, pediatric burn patients, genital surgery e.g. circumcision |

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to other local anesthetic agents [26]. Signs of neurological toxicity with symptoms of the central nervous system were reported in 89% of the cases including seizure, loss of consciousness, agitation and other symptoms. In 55% of cases, signs of cardiovascular toxicity were reported with a broad spectrum of clinical presentation [26]. Several specificities of the pediatric metabolism contribute to the higher risk of systemic toxicity. First, plasma levels of the lidocaine and ropivacaine-binding alpha-1-acid glycoprotein and albumin are lower, leading to a higher concentration of unbound molecules, which is directly correlated to the risk of systemic toxicity [31]. Further, hepatic clearance is reduced as local anesthetic agents are predominantly metabolized by the cytochrome P450 system, which is immature and has a reduced capacity particularly in young infants. The relative intrinsic clearance for bupivacaine is about one-third at the age of one month and two-thirds at six months, and toxic effects are directly correlated to the free plasma concentration of anesthetics [31–35]. Consequently, infants and newborns in particular are at an increased risk for adverse events following accidental intravascular injections considering the higher doses per body weight used for surgery [25]. Finally, risk of toxicity is increased if perioperative hypothermia or respiratory problems such as hypercarbia or hypoxemia occur, as the changes in plasma pH increase the dissociation of anesthetics from plasma binding proteins [27]. Another potential side effect that needs to be considered in infancy is the risk of inducing methemoglobinemia. Due to its indirect oxidizing effects, local anesthetics put particularly newborns at risk, especially when combined with other drugs that affect the NADH pathway [36]. Here, reports indicate that lidocaine has the lowest risk of inducing methemoglobinemia [36, 37]. As in adult patients, allergic reactions can occur after the injection of local anesthetic agents, whereas immediate type allergic reactions due to local anesthetic agents are rare [38–40]. These reactions are not dosage-dependent and more often seen in the use of ester-anesthetics (e.g. procaine, tetracaine) than amide-anesthetics (e.g. bupivacaine, lidocaine) [19, 24, 25].

### Pain in early childhood and psychosocial development

Adequate pain control is of particular importance when utilizing local anesthesia in infants, not only to achieve optimal conditions for surgery. An increased vulnerability to
negative long-term effects following painful experiences is based on anatomy and neurophysiology in infancy and early childhood [25], and several reports have demonstrated an association between pain and stress responses in infancy and long-term effects [41, 42]. Pain exposure in infancy has been shown to result in a prolonged hypersensitivity syndrome [43–45]. Increased pain sensitivity was shown by Taddio et al. in infants who underwent circumcision, which could be reduced through the preoperative use of EMLA (eutectic mixture of local anesthetics) patches [45]. Another study demonstrated a prolonged pain hypersensitivity in children who underwent surgery in early infancy, especially in the area of the previous injury compared to children who had not undergone surgery in the past [46]. To allow for a protective infiltration of TLA, an infusion pump can be used as described by Breuninger et al. in 1998 [8]. An example of a mobile TLA rack used in our hospital equipped with a commonly available infusion pump (Infusomat P, B. Braun, Melsungen, Germany), various needles, drop container, disinfectant and gloves can be seen in Figure 1. Furthermore, a slow subcutaneous infiltration is associated with less pain than intradermal application of local anesthetics [7, 19, 25]. Improving the aspect of preemptive analgesia, a topical anesthesia can be administered before insertion of the infiltration needle. Here, EMLA cream is often used, which consists of a 1:1 mixture of 2.5 % lidocaine and 2.5 % prilocaine. While the use of EMLA is safe due to its negligible absorption, a maximum dosage of 1 g is recommended in newborns and should be applied up to one hour before the procedure starts [27, 47]. Dosage of EMLA can be increased depending on age (age-dependent dosing recommendations are listed in

**Figure 1** Example of a mobile TLA rack with infusion pump (Infusomat P, B. Braun, Melsungen, Germany), various needles, drop container, disinfectant and gloves.

**Figure 2** Application of TLA in infants in the face(a) and occipital area (b). While the local anesthetic solution is being administered, the infant can also be breastfed for comfort. Surgical setting (c): a 6-months-old infant undergoes surgery in TLA while the mother is comforting him with a dummy.
the respective manufacturers instructions). In order to create calming effects, the light in the operating room can be dimmed – with the exception of the surgical lamp. Furthermore, infants should be placed close to a parent’s body for comfort [7]. It is also possible to calm infants by breastfeeding during surgery. Figure 2a, b illustrate the application of TLA in infants, while Figure 2c shows the surgical setting.

Discussion and Conclusion

A broad spectrum of indications, convenience and a favorable risk profile have made TLA an indispensable and popular tool for pediatric dermatologic surgery. Although existing data suggests that TLA is generally safe for use in infants and there are substantial benefits when compared to general anesthetics, potential side effects and systemic toxicity have to be kept in mind. While very rare, these include potentially life-threatening toxicities, for which infants are at increased risk. Non-pediatric physicians in particular therefore need to be aware of potential adverse events and of their clinical symptoms in infancy when working with local anesthetic agents [19, 25, 26]. Another critical aspect in pediatric surgery is adequate pain management as several studies on pain physiology after surgery in infancy highlight the need for adequate pain control in this patient group [43–45]. While there is a paucity of trials, existing literature demonstrates that TLA induces long-lasting anesthesia and frequently abolishes the need for further analgesic drugs [3, 16].

In summary, TLA is a safe and convenient tool for pediatric surgery associated with numerous benefits. Despite the differences in infant physiology and the potentially increased risk for systemic side effects, studies show that TLA can safely be administered in infants [3, 7, 9]. With the increasing use of TLA, further studies are needed to identify patients at risk of complications and to establish guidelines for its use in a pediatric setting.

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