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LOCAL ANESTHESIA AND ITS CONSIDERATIONS IN HAIR TRANSPLANTATION WITH THE F.U.E TECHNIQUE

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ABSTRACT

Introduction. This literature review addresses key aspects of local anesthesia and its application in hair transplantation. *Development*. Local anesthetics work by reversibly interrupting nerve conduction. They are divided into esters and amides, with amides being the most common in clinical practice due to their stability and safety profile. The action of local anesthetics depends on factors such as their lipid solubility, protein binding, pKa, vasodilation activity and tissue diffusion, they can also be combined with vasoconstrictors to improve their safety profile and

reduce bleeding. It is very important to know the properties of lidocaine and bupivacaine, two local anesthetics frequently used in hair transplants, as well as the most common techniques for applying local anesthesia to the scalp, which are ring or field blocks and nerve blocks. *Discussion*. In hair transplantation, the application of local anesthesia is one of the most important steps to take into account, in order to produce minimal pain or discomfort and to ensure that the patient has a good experience. To avoid side effects and complications, it is important to avoid vascular infiltration of local anesthetics with vasoconstrictors and to consider that in the Follicular Unit Excision (F.U.E.) technique, anesthetizing large areas is required, which may exceed the maximum doses of anesthetics. *Conclusion*. It is important to perform a good evaluation of the patient to avoid complications, as well as to know the application technique and the medications used to avoid side effects and complications that may arise.

KEYWORDS: local anesthesia; side effects of local anesthesia; local anesthesia application technique in hair transplantation.

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ANESTESIA LOCAL Y SUS CONSIDERACIONES EN TRASPLANTE CAPILAR CON TÉCNICA F.U.E.

RESUMEN

Introducción. Esta revisión bibliográfica aborda los aspectos clave de la anestesia local y su aplicación en el trasplante capilar. *Desarrollo*. Los anestésicos locales funcionan interrumpiendo la conducción nerviosa de forma reversible. Se dividen en ésteres y amidas, siendo las amidas las más comunes en la práctica clínica debido a su estabilidad y perfil de seguridad. La acción de los anestésicos locales depende de factores como su solubilidad lipídica, unión a proteínas, pKa, actividad de vasodilatación y su difusión en los tejidos, también se pueden combinar con vasoconstrictores para mejora su perfil de seguridad y disminuyen el sangrado. Es muy importante conocer las propiedades de la lidocaína y bupivacaína, dos anestésicos locales de uso frecuente en trasplante capilar, así como las técnicas más comunes de aplicación de anestesia local del cuero cabelludo que son el bloqueo en anillo o de campo y los bloqueos nerviosos. *Discusión*. En trasplante capilar la aplicación de la anestesia local es uno de los pasos más importantes a tener en cuenta, con la finalidad de producir el minino dolor o molestia y que tenga una buena experiencia el paciente. Para evitar efectos secundarios y complicaciones es importante evitar la infiltración vascular de anestésicos locales con vasoconstrictores y considerar que en la técnica de Excisión de Unidades Foliculares (FUE) se requiere anestesiar áreas extensas, lo cual puede superar las dosis máximas de los anestésicos. *Conclusión*. Es importante

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realizar una buena evaluación del paciente para evitar complicaciones, así como, conocer la técnica de aplicación y los medicamentos que se utilizan para evitar efectos secundarios y complicaciones que se pudieran presentar.

PALABRAS CLAVE: anestesia local; efectos secundarios de la anestesia local; técnica de aplicación de anestesia local en el trasplante de cabello.

INTRODUCTION

The objective of this bibliographic review is to highlight the most important aspects of local anesthesia and application technique in hair transplantation, with a perspective on the Follicular Unit Excision (F.U.E.) technique.

There are currently two methods to obtain Follicular Units (FU) and perform hair restoration in areas of alopecia: 1) the Strip technique, also known as F.U.T. (Follicular United Transplantation) or FUSS (Follicular United Strip Surgery) and 2) the F.U.E. technique. Although the latter has grown much more in popularity and demand, it is perceived by the patient, and in reality it is, as a less invasive technique (1). In the F.U.E. technique, the main donor area is the safe area of the scalp since it usually has a sufficient number of follicles to be transplanted (2).

In hair transplants, both for extraction and implantation, local anesthesia is most commonly used (2-4), even when the donor and recipient areas are other areas of the body other than the scalp. Local anesthesia

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can be assisted by some oral analgesics to have minimal discomfort from the procedure, as well as some anxiolytic (5). However, some other authors may use oral or intravenous sedation as a resource (3,4), to reduce the pain of the placement of local anesthesia, which paradoxically, may be what bothers the most in the procedure (4), although other methods can also be used, such as: topical local anesthesia (6), cushioning (7), and/or heating of the local anesthetic (8), use of vibration (9), use of smaller gauge needle, needle-free injectors, application of ice (3), with cannula, etc.

LOCAL ANESTHESIA

Local anesthetics are chemical agents that interrupt nerve conduction in a localized area, in a transient and reversible manner. The interruption of neuronal conduction occurs by inhibiting the entry of sodium ions through channels or ionophores within neuronal membranes (10,11), thus producing analgesia.

Chemical structure

Local anesthetics are divided based on their physicochemical structure (intermediate chain) into esters and amides (12). The clinical differences between them are related to their possibility of producing adverse effects and the mechanisms by which they are metabolized. Some of their characteristics are the following (12-15):

- Esters (procaine, tetracaine, chlorprocaine, benzocaine, cocaine). Unstable chemical structure, they are metabolized in plasma by pseudocholinesterase and other plasma

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esterases. The half-life in circulation is short. The product of the degradation of the metabolism is para-aminobenzoic acid (PABA), which gives it a high hypersensitizing power. For this reason, they fell into disuse.

–Amides (lidocaine, mepivacaine, bupivacaine, prilocaine, etidocaine, ropivacaine, articaine). They are stable in plasma and are metabolised in the liver through initial N-dealkylation, followed by hydrolysis. The elimination half-life is approximately 2 to 3 hours. Their development has led to a significant increase in safety in all interventions where local anaesthetics are used.

Properties of local anesthetics

The action of local anesthetics depends on the following factors (11,13-15):

1. Lipid solubility: Determines its potency, allowing concentrations typically ranging from 0.5 to 4%. Greater lipid solubility of a drug not only improves its potency, but also allows for faster diffusion across cell membranes.

2. Protein binding: Determines its duration of action, mainly due to differences in its affinity for proteins. The greater the tendency for protein binding, the longer the anesthetic will maintain neuronal blockade.

3. pKa: Determines the onset time of the local anesthetic; the closer the anesthetic's pKa is to physiological, the faster it will be.

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4. Intrinsic vasodilatory activity of the anesthetic: it can promote systemic absorption, shortening its duration and, therefore, decreasing the time it remains in close proximity to the neural fibers. Lidocaine has a greater vasodilatory effect than others (mepivacaine and bupivacaine).

5. Tissue diffusibility: The area where the anesthetic will be applied determines the speed and potency of the anesthesia. In the case of the scalp or face, which have a high irrigation, it will produce rapid absorption and a rapid onset, unlike other less irrigated areas.

Pathophysiological factors affecting local anesthesia

There are some pathophysiological factors that influence local anesthetics (13):

1. Decreased cardiac output: reduces the volume of distribution and plasma clearance, increases plasma concentration and the possibility of toxicity.

2. Severe liver disease: may prolong the duration of action of amide-type local anesthetics and be more sensitive to adverse reactions.

3. Kidney disease: has a negligible effect.

4. Decreased cholinesterase activity (newborns, pregnant women), and patients with atypical cholinesterase, may have an increased risk of toxicity.

Combinations with local anesthetics

-A lidocaine-bupivacaine mixture has been documented to produce a block with rapid onset and prolonged duration, although this

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is not universally accepted; the systemic toxicity of the combinations appears to be simply additive (13). The potential benefit of drug combinations is unclear (13).

-Vasoconstrictors. They can be added to local anesthetics to improve the safety profile of the anesthetic and also for the better visualization they provide to the work field. The most commonly used are adrenaline and phenylephrine (14). The duration of action of a local anesthetic is proportional to the time during which it is in contact with the nerve (16), for which vasoconstrictors are used to help increase contact time.

Adrenaline is a potent stimulant of both α- and β-adrenoceptors (16). The maximum dose of adrenaline (as a vasoconstrictor) should probably not exceed 200-250 µg in adults or 10 µg/kg in children; the recommended concentration is a dilution of 1:100,000 or 1:200,000 (optimal) (13,14). Despite the popularity of epinephrine 1:100,000, concentrations greater than 1:200,000 (5 µg/ml) offer little or no advantage (11). Higher concentrations also do not reduce serum concentrations of the local anesthetic (17,18). Injected adrenaline markedly decreases cutaneous blood flow, with constriction of precapillary vessels and small venules (16), prolonging the duration of the anesthetic effect, Increasing the intensity of the block and decreasing the absorption rate, which increases the maximum dose (with decreased systemic toxicity) and reduces bleeding from the work field, however, the risk of necrosis (in areas with low irrigation), delayed wound healing (14) and tissue edema must be considered

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(16). Adrenaline is rapidly inactivated in the body by the liver through two enzymes (catechol-O-methyltransferase and monoamine oxidase) (16). Among the side effects, restlessness, throbbing headache, tremor and palpitation can be observed, which disappear soon with rest, a calm environment, lying down and calming the patient, however, the most serious effects are arrhythmias and with accidental injection of large doses or rapid intravenous injection it can culminate in cerebral hemorrhage (due to severe hypertension) (16). Caution is advised in patients with severe coronary disease, arrhythmias, uncontrolled hypertension, hyperthyroidism and uteroplacental insufficiency (13).

-Sodium bicarbonate. The addition of sodium bicarbonate to local anesthetic solutions increases the pH and increases the concentration of non-ionized free base, which increases the rate of diffusion and the onset of neural blockade (13). With decreased pain on application due to the change in pH.

Adverse effects of local anesthesia

Although it is rare for patients to experience serious adverse effects or complications secondary to the administration of local anesthetics, they can occur (19).

In different studies, the results have been variable with respect to its incidence: the rate ranges from 0.1/1,000 to 6.9/1,000, depending on the anesthetic procedure reviewed, taking into account the use of cocaine and nerve blocks (19). Although in general the incidence is low with all local

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anesthetics, bupivacaine has the highest rate of complications (20).

The toxicity or side effects of local anesthetics can be divided into two categories: 1) local tissue side effects and 2) systemic toxic reactions (21,12,14).

1) Local tissue side effects.

These are mainly caused by the method of application of the local anesthetic and its pH, causing pain, bruising/hematoma, infection, nerve trunk injury and injury to the subcutaneous structure (14).

2) Systemic toxicity.

Side effects may occur when the plasma concentration is high enough to affect organs with membranes that may be irritable, toxic levels may be reached as a result of (12):

- Intravascular injection;

- Overdose, particularly in areas with good blood perfusion and its corresponding high reabsorption;

- Dose mismatch in patients with liver or kidney disease.

Symptoms of the central nervous system (which is more sensitive) are the most common clinical presentation and generally precede evidence of cardiovascular toxicity, which rarely occurs in isolation (22). Similarly, cases of patients with more potent local anesthetics (for example, bupivacaine) have been described in which the first manifestations are cardiovascular (including patients who present with cardiorespiratory arrest) (23). However, they can also occur in smooth muscle.

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a) Central nervous system.

Symptoms appear gradually and can be summarized in phases of toxicity in Table 1 (12). Some authors consider low toxicity symptoms to be prodromal symptoms (22).

Table 1: Symptoms in the Central Nervous System due to local anesthetic toxicity.

Excitement phase, low toxicity.
Tingling of the lips, paresthesias in the tongue, perioral numbness, tinnitus, metallic taste, anxiety, restlessness, muscle tremor and vomiting.
Excitement phase, moderate toxicity.
Language disorders, dazed state, drowsiness, confusion, tremor, choreic movements, tonic-clonic convulsions, mydriasis, vomiting, tachypnea.
Paralytic phase, severe toxicity.
Stupor, coma, irregular breathing, respiratory arrest, flaccidity, vomiting with aspiration, sphincter paralysis, death.

b) Cardiovascular system.

The symptoms that may occur are: hypotension (first sign), palpitation, tachycardia, dry mouth, primary heart failure, arrhythmias, blockages, shock and cardiac arrest in asystole (12,14,19,22,23).

c) Smooth muscle.

They depress contractions in the intact intestine and in isolated strips of intestine (24). They also relax vascular and bronchial smooth muscle, although low concentrations

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may initially produce contraction of the same (25).

Adverse effects resulting from the psychogenic reaction (vasovagal reaction)

These are the most frequent, the symptoms originate from the state of anxiety prior to and during the intervention, so the most common is that the symptoms appear once the intervention is finished, and consist of a feeling of dizziness when getting up from the stretcher, paleness, sweating, nausea, bradycardia, hyperventilation and syncope, for which the patient has to be put in the Trendelenburg position, calmed down, and preventive measures applied when getting up from the stretcher after the intervention, telling him to do so slowly and after remaining seated for a few seconds (14).

Hypersensitivity to local anesthetics

These are rare with amides, however, if they occur, they may manifest as allergic dermatitis (itching, hives, erythema, etc.) or a characteristic asthma attack (14,24).

Local anesthetics in hair transplantation

The choice of local anesthetic should consider the duration of the procedure, the regional technique used, the needs of each procedure, the possibility of local or systemic toxicity, and any metabolic limitations (13). Note that both liver and kidney function decrease by 50% by age 65 (26).

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In hair transplantation, the most commonly used local anesthetics are lidocaine and bupivacaine (3,5).

1) Lidocaine:

Commercially, it can be found in 1% (100 mg), 2% (200 mg) or 5% (500 mg) formulations (14). It has a rapid onset of action of 2-4 min (27), with a duration of action of 1-2 hrs (14), making it suitable for application in infiltration, regional and superficial, with a moderate vasodilatory effect (28), it is mainly metabolized by the enzyme CYP3A4 in the liver into pharmacologically active metabolites (29), its dose is 3-4 mg/kg with a maximum of 300 mg and while the dose with epinephrine should not exceed 7 mg/kg with a maximum of 500 mg (30).

Lidocaine is eliminated from the body by diethylation in the liver by the cytochrome p450 isoenzyme groups 1A2 and 3A4, so all drugs that inhibit the 3A4 isoenzyme and cytochrome p450 can affect the metabolism of lidocaine, such is the case of midazolam, which is also metabolized by this cytochrome isoenzyme, which can become overworked and decrease the metabolism of lidocaine, in addition to the fact that the effects of midazolam can mask the symptoms of lidocaine toxicity, until the onset of cardiovascular collapse; Other drugs that inhibit the 3A4 subfamily are: propofol, flunitrazepam, diazepam, cimetidine, methylprednisolone, dexamethasone, amiodarone, nifedipine, verapamil, beta-blockers, etc (31). Lidocaine administered in clinical doses rarely causes cardiac toxicity (28), however, it has proconvulsant effects at

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high doses and anticonvulsant effects at low doses (27).

2) Bupivacaine.

It has an onset of action of 5 to 8 min (27), it is considered long-acting, two to three times longer than lidocaine (28), it can last up to approximately 6 hours and this drug is four times more potent than lidocaine (31). It is metabolized in hepatic microsomes with a high metabolic rate (12).

The central nervous system toxicity and cardiac depressant effects are greater than in the case of lidocaine (28). Animal studies indicate that the high lipophilic character of bupivacaine and its high affinity for myocardial sodium channels are associated with cardiotoxicity (32). Therefore, special care is required when using bupivacaine in patients with cardiotoxic conditions due to the use of beta-blockers, calcium channel blockers and cardiac glycoside drugs that cause cardiac function disorders (27). The single dose threshold is 175 mg without adrenaline in adults and with adrenaline 1:100,000 0.25% is 225mg or 90ml (3,13,14).

Table 2 summarizes the characteristics of lidocaine and bupivacaine as local anesthetics (12,13,16).

Table 2: characteristics of lidocaine and bupivacaine as local anesthetics (12,13,16).

Feature.	**Lidocaine.**	**Bupivacaine.**
Start of action	Fast: 2-4 min	Slow: 5-8 min
Duration.	Moderate: 1-2 hr	Very long: 6 hr
Potency.	Moderate	High
Toxicity.	Moderate (mainly CNS)	High. (Mainly cardiotoxicity)
Characteristics.	Most commonly used local anesthetic.	In local and regional anesthesia requiring long duration
Maximum recommended dose (mg).	300	175
Maximum recommended dose with adrenaline (mg).	500	225
In local infiltration.		
Concentration (%).	0,5-1,0	0,25-0,50
Duration (hr).	0,5-2,0	2-4
Duration with adrenaline (hr).	1-3	4-8
Dose (mg/kg).	4,5	2
Dose range (ml; patient 70 kg).	1-50	1-45
Peripheral nerve block.		
Concentration (%).	1-2	0,25-0,50
Duration (hr).	1,5-3,0	6-12
Duration with adrenaline (hr).	2-4	6-12
Dose range (ml; patient 70 Kg).	40-50	40-50
Approximate potency ratios.		
Anesthetic potency.	2	14
CNS toxicity.	3	12

Note: The potency ratio and equivalent doses depend on the method of anesthesia used.

min: minutes, hr: hours, CNS: Central Nervous System, mg: milligrams, kg: kilograms.

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Treatment of local anesthetic toxicity may include: airway management, seizure suppression (preferably with benzodiazepines), treatment of cardiac dysrhythmias, and in case of significant overdose, lipid emulsion treatment may be necessary (33).

LOCAL ANESTHESIA APPLICATION TECHNIQUE IN HAIR TRANSPLANTATION

The most common techniques for local anesthesia of the scalp are ring or field blocks and nerve blocks.

Donor area

The nerves that innervate the donor area do not have stable reference points to be able to block them in a simple way, which is why the ring or field technique is used more, in addition to being easier to apply.

Field block is produced by subcutaneous injection of a local anesthetic solution, such that the region distal to the injection site is anesthetized (16). The anesthetic is first injected as a ring block at the inferior margin of the occipital donor area to anesthetize the upward-running occipital nerves (2-5), branches of the cervical plexus (34), with 1% lidocaine and 1:100.000 epinephrine (2,4). The safe donor area is then infiltrated with the aforementioned mixture to decrease bleeding or with a tumescent anesthetic solution. Tumescence is achieved with lidocaine, vasoconstrictor, saline solution and sometimes triamcinolone to prevent subsequent edema (35). Infiltration anesthesia involves the direct injection of a

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local anesthetic into the tissues, without taking into consideration the path of the cutaneous nerves; the infiltration may be so superficial that it includes only the skin or it may involve deeper tissues (16).

Due to their simplicity, adequate pain control, and safety, ring blocks are typically used for F.U.E. donor hair harvesting, reserving nerve blocks only for patients who cannot be adequately anesthetized with the ring block (36).

Recipient area

The main recipient area in hair transplantation is the frontal area. The innervation of the area from the forehead to the vertex of the head is via the supraorbital and supratrochlear nerves (37,38). These nerves have fairly reliable reference points and can be easily blocked. To anesthetize the recipient area, a ring block or a combination of ring blocks and supraorbital and supratrochlear nerve blocks can be used (3). In the recipient area, the anesthetic solution is injected as a ring block 1-2 cm below the proposed frontal and/or temporal hairline (5). The anesthetic solutions are similar to those for the donor area. Tumescent solution can also be used.

Some physicians use bupivacaine for post-anesthesia maintenance due to its longer duration of action (39), or for performing nerve blocks together with lidocaine (4), prior to field block anesthesia.

DISCUSSION

The safety, application and maintenance of local anesthesia in hair transplantation is one

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of the most important steps to take into account, especially when it is not used in conjunction with sedation. Local anesthesia is essential for the patient to have a good experience, with minimal pain or discomfort.

When choosing the anesthesia application technique, the use of distractors (vibration, ice, etc.) should be considered in order to reduce the pain of both the needle prick and the burning sensation of the anesthetic due to its pH. The use of smaller gauge needles (30G or smaller caliber) or cannulas and the slow injection of the anesthesia also reduces pain.

To avoid vascular infiltration of significant amounts of local anesthetic, one should either constantly aspirate with each injection or advance the needle and then inject while constantly withdrawing the needle (3). Intravascular infiltration is more likely to occur if the syringe is placed too deep (Figure 1). There are two plexuses of arterial blood vessels in the dermis, one plexus is located between the papillary and reticular dermis, and the other between the reticular dermis and the hypodermis (40), the latter being larger in caliber. It is recommended to apply the anesthetic at a more superficial level, which adds a longer duration of anesthesia, due to less reabsorption. If intravascular injection of the anesthetic is performed with vasoconstrictors, secondary effects may occur. The addition of 10 to 15 mcg of epinephrine has an 80% sensitivity for detecting intravascular injection in adults: if the heart rate increases by at least 10 beats per minute, or there is an increase in systolic blood pressure of 15 mm Hg or more (41).

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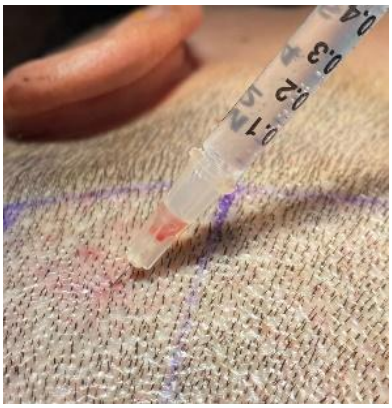
Figure 1. Aspiration of blood when the needle is intravascular.



Because of the "convenience" of epinephrine as an effective hemostatic agent, hair transplant doctors performing large sessions have resorted to using increasingly higher concentrations in increasingly greater volumes, although not proven, it is likely that epinephrine infiltration into the recipient area is a contributing factor in the development of the "central necrosis," which has occasionally been reported during hair transplantation (42). The use of large amounts of epinephrine for the purpose of establishing hemostasis in large hair transplant sessions is neither necessary, nor desirable (42). It is therefore advisable to use proportions of 1:100,000 or 1:200,000 without exceeding the maximum doses.

In the F.U.E. technique, the area to be anesthetized is larger than in the F.U.T. technique. The more units to be extracted, the larger the area to be excised and implanted and therefore the greater the amount of anesthesia to be used. In the F.U.E. technique, the duration of the procedure is usually prolonged, which is

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why it is sometimes necessary to resort to reapplications of anesthesia to maintain analgesia. The above-mentioned factors contribute to exceeding the maximum doses, sometimes producing side effects. It is recommended not to exceed the maximum doses of lidocaine with adrenaline (7 mg/kg or 500 mg) and bupivacaine with adrenaline (225 mg). These maximum recommended doses vary between countries and are not based on clinical studies, but on extrapolation from research in animals (43).

Because F.U.E. is a lengthy procedure, patient relaxation during the procedure is important and can be achieved with oral agents; this is distinct from conscious sedation, which involves intravenous medication and requires continuous monitoring of oxygenation and airway status (33).

Regarding the use of tumescent solutions in other medical areas, preliminary estimates of maximum safe doses of tumescent lidocaine have been published as 28 mg/kg without liposuction (44) and with liposuction the safe range is 35 to 55 mg/kg (31) taking into account the mode of metabolism and excretion in various parts of the body. However, in the tumescent technique for scalp anesthesia, it can be used without exceeding the threshold of 7 mg/kg of total daily dose of lidocaine (33).

Although some physicians may administer higher than the maximum recommended doses of local anesthesia, it is suggested not to exceed the maximum recommended doses. During transplantation, it is important to be alert to the earliest signs of toxicity (excitement phase or low toxicity, table 1) in

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order to act immediately; monitoring vital signs is of great help.

On the other hand, decreased clearance of local anesthetics associated with renal, hepatic and cardiac diseases is the most important reason for reducing the dose for repeated or continuous administration, the magnitude of the reduction should be related to the expected influence of the pharmacodynamic change (43). The use of topical medications such as minoxidil can increase the blood supply to the implantation area, therefore, bleeding and elimination of anesthesia may increase.

CONCLUSION

Before performing the hair transplant, it is very important to explain to the patient what the local anesthesia process consists of, in order to reduce stress during the procedure.

During the patient's medical history, it is important to be able to identify factors that can produce adverse effects of anesthesia, such as illness, taking medications, or any other cause that contraindicates local anesthesia.

It is important to know the technique for applying anesthesia and the medications used, in order to be able to identify side effects prematurely. Although local anesthetics are sometimes used at doses higher than the maximum, it is recommended not to exceed them, in order to avoid complications. The authors prefer the use of lidocaine with adrenaline 1:100,000, since they consider a greater

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safety margin than with the use of bupivacaine.

The main objective is for the patient to have a good experience in their hair transplant, with the least discomfort and that the application of local anesthesia is safe.

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