

Local Anesthetics: Use and Effects in Autologous Fat Grafting

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Abstract

Autologous fat grafting has been used for over a century and is considered as a technique of choice for soft tissue filling in plastic and reconstructive surgery. However, the critical point of this technique is fat graft survival. In order to assure best efficiency of adipose grafts, new techniques and procedures have been optimized in order to avoid graft resorption and thus, to improve graft survival. Among the steps involved in lipofilling process, some researchers and surgeons have *inter alia* focused on the effects of local anaesthetics on adipose graft.

After an overview on the different local anaesthetics commonly used and their mode of action, this review focuses on the effects of these drugs on non-neuronal cells with special emphasis on adipose tissue and adipose-derived stem cells. Moreover, while there is no consensus on the best way how to handle adipose tissue prior to its injection, this review describes how to get rid of the adverse effects of local anaesthetics.

Keywords: Autologous fat grafting; Liposuction; Local anaesthetics; Lidocaine; Adipose-derived stem cells

Abbreviations: AFG: Autologous Fat Grafting; LA: Local Anaesthetic; ADSC: Adipose-Derived Stem Cell

Introduction

Because of its easy access by liposuction and due to the fact that it contains many progenitor cells, subcutaneous adipose tissue is a tissue of choice for soft tissue filling in cosmetic and reconstructive surgery. Autologous Fat Grafting (AFG), or lipofilling, has been used for over a century and represents a safe technique for soft tissue filling [1-3]. However, although the technique has seen marked improvements over time, surgeons are still facing graft resorption that often requires overcorrection of the treated area or other interventions so that the aesthetic result is in line with expectations of the patient [2,4]. Thus, new processes have been developed in order to increase the rate of engraftment by promoting cell survival within the graft [5]. Among the critical points that may impair adipose graft retention and survival, Local Anesthetics (LAs) have been investigated. Even under general anesthesia, LAs are often infiltrated at the fat donor site (generally through a tumescent solution with epinephrine for vasoconstriction) and can also be delivered at the injection site to ensure patient comfort.

Further studies in the context of autologous fat grafting in plastic surgery have allowed to highlight LAs adverse effects but controversies remain regarding their substantial impact on fat graft survival [6-11]. Although this confusion remains among all LAs, lidocaine is the most commonly used LA for liposuction procedure and is thereby the best described in this context. However, this drug has also been so far neglected in terms of recommendations for dosage.

Thus, through the literature, local anesthesia use and effects in AFG are described herein.

From adipose tissue to soft tissue filling

Adipose tissue is first and foremost an organ of lipid storage. It represents the main body's energy reserve, involving lipids as the main fuel for adult humans. Adipose tissue is also considered as a true endocrine organ where the adipocyte lies at the heart of this system by participating in the regulation of energy homeostasis in the body [12].

While mature adipocytes constitute the specialized cells of adipose tissue, stocking triglycerides in a huge lipid droplet inside their cytoplasm, other cell types are included in adipose environment [13]. Beside mature adipocytes surrounded by conjunctive tissue

with collagen fibers, the Stromal Vascular Fraction (SVF) includes preadipocytes, endothelial cells, smooth muscle cells, blood cells (from blood vessels) and Adipose-Derived Stem Cells (ADSCs), that have been discovered not so far ago [14,15]. These ADSCs share similar properties with mesenchymal stem cells: quite similar phenotype, ability to proliferate and to differentiate into mesenchymal cell types such as adipocytes [15-17], chondrocytes [18-22], osteoblasts [15,18,23-26], tenocytes [27,28], myocytes [15,28,29]. But their differentiation potential is not restricted to mesodermal lineage: ADSCs have been shown to trans differentiate into other cell types, including endothelial cells [28,30] and neuronal-type cells [28,31]. Besides differentiation, ADSCs can also secrete numerous paracrine factors (like cytokines, growth factors, anti-apoptotic factors) that would strongly support tissue regeneration [30,32].

Owing to their high potential for tissue regeneration and their easy access by simple liposuction, ADSCs are subject to special attention and are already used in regenerative medicine (many clinical trials ongoing) [33]. Plastic surgeons also pay attention to these cells as they exhibit special functions that may improve fat graft survival and efficiency [34-40]. Indeed, these ADSCs are known to be able to differentiate into mature adipocytes, which may contribute to face fat graft resorption and maintain the desired volume for soft tissue repair or augmentation. Moreover, there is increasing evidence that ADSCs contribute to vascularization of adipose grafts, thus improving cell survival inside the grafts [38,41-43]. For all that considerations, the technique of cell-assisted lipotransfer has emerged: it consists in ADSCs enrichment of autologous fat prior to its injection [37,38]. However regulations regarding the use of stem cells in plastic surgery differ between countries and this practice is not legally approved everywhere. Further clinical studies must be performed to assure patient safety and efficiency of such procedures [39].

Thus, containing many different types of cells (voluminous

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adipocytes, stromal cells) and being easily accessible, adipose tissue has been shown to be a great filler and is now commonly used to fill soft tissues and restore volume. Lipofilling has now gained popularity, especially with the development of liposuction technique and also thanks to abundance and availability of subcutaneous fat in the human body. Beside its role as a secretory and endocrine organ, adipose tissue is used to correct soft tissue defects as well as facial rejuvenation, body contouring, or other numerous applications, both for aesthetic and reconstructive purposes [32,34].

Autologous fat grafting and the tumescent technique for liposuction

Autologous fat transfer has been subject to great evolution over the last century. Conceived by Fisher and Fisher, liposuction first appeared as a revolutionary technique in 1974 [44]. Then, Klein invented the tumescent liposuction which consists of infiltrating at the sampling zone a local anesthetic and a vasoconstrictor diluted in a large volume of fluid (saline type) [45]. Usually, the volume of tumescent solution is almost equal to the volume of adipose tissue to be removed. This technique allowed the patients to benefit from liposuction totally by local anesthesia, thus avoiding the risks of general anesthesia and promoting a short recovery time. This also allowed the use of much smaller cannulas and practice of superficial liposuction, only 3-4 mm deep subcutaneous [46]. Patients no longer had to fear excessive bleeding and undesirable skin depressions. In addition, liposuction by cannulation did not seem to damage the adipocytes. Then in the mid-80s, plastic surgeons began to inject the fat obtained by liposuction [47,48].

With invention of the innovative technique of tumescent liposuction by Klein, lidocaine systemic toxicity has been significantly reduced: dilution of lidocaine in a large volume of normal saline significantly decreased systemic absorption rate of the drug [45,49,50].

Tumescent anesthesia finally offers many advantages, among which: decreased LA absorption at the infiltrated donor site, increased patient comfort after surgery due to a longer lasting effect of LA, decreased and delayed systemic absorption and lower peak blood plasma levels (thus, avoiding toxic potential like cardiotoxicity or central nervous system toxicity) [51]. Moreover, even if LA infiltration at the fat donor site can allow avoiding general anesthesia and its related risks, tumescent liposuction with local anesthesia is currently mixed with general anesthesia in order to assure post-operative patient comfort. Despite recorded patient safety with tumescent anesthesia, questions remain about LAs effect in AFG.

Local anesthetics: classes and mode of action

Local anesthetics act by blocking sodium ionic channels involved in neural impulse conduction, thus avoiding peri- and post-operative pain [52,53]. These cocaine-derived substances have been discovered more than a century ago, and are divided in two distinct chemical families: amino esters (tetracaine, procaine...) and amino amides (lidocaine, bupivacaine, ropivacaine) (Table 1). Compared to amino esters, amino amides may cause rare allergies.

Lidocaine was the first amino amide-type LA synthesized by Löfgren [54]. This LA presents a rapid onset and an intermediate duration of action. Through the years, other LAs have been discovered in order to improve duration of action and decrease toxicity risk when possible (Table 1). Although lidocaine is the oldest aminoamide LA, this drug is widely used all over the world and seems to be the most appropriate in the context of liposuction and autologous fat transfer [45].

LA potency is partly due to their lipid solubility: LAs have a lipophilic chemical group (comprising benzene ring or thiophene ring for articaine) that allows them to diffuse across plasma membrane and

Classification and name	Date of discovery	pKa (25°C)	Metabolism	Onset (min)	Duration of action (min)	Relative potency	Maximal dose (for adults)	Maximal dose with epinephrine	Dose for tumescent anesthesia	Relative toxicity
Amino esters										
Procaine	1905	9	Plasma esterases	Slow (10-20)	Short (15-60)	1	500 mg (7 mg/kg)	-	-	1
Chlorprocaine	1952	9.3	Plasma esterases	Fast (5)	Short (15-45)	1	600 mg (8 mg/kg)	-	-	9
Tetracaine	1928	8.6	Plasma esterases	Slow (15)	Intermediate (60-200)	> 4	100 mg (1.5 mg/kg)	-	-	4.1
Amino amides										
Lidocaine	1943	7.9	Liver	Fast (2-5)	Intermediate (60-120) Longer with epinephrine	4	200-300 mg (5 mg/kg)	500 mg (7 mg/kg)	30-35 mg/kg	2
Prilocaine	1960	7.9	Lung Kidney Liver	Fast (2-5)	Intermediate (30-90)	4	500 mg (7 mg/kg)	600 mg (8 mg/kg)	15 mg/kg	1.8
Articaine	1969	7.8	Liver Serum esterases	Fast (2-3)	Intermediate (60-180)	5	7 mg/kg	7 mg/kg	35 mg/kg	1.5
Mepivacaine	1956	7.9	Liver	Fast (3-5)	Intermediate (45-90)	4	300 mg (5 mg/kg)	(5 mg/kg)	-	2.2
Bupivacaine	1963	8.1	Liver	Slow (10-15)	Long (200 +) Longer with epinephrine	16	175 mg (2.5 mg/kg)	225 mg (3 mg/kg)	-	8
Levobupivacaine	1960's	8.1	Liver	Slow (10-15)	Long (200 +)	16	175 mg (2.5 mg/kg)	-	-	< 8
Ropivacaine	1950's	8.1	Liver	Slow (5-15)	Long (200 +)	16	188 mg (2.5-3 mg/kg)	-	-	7

Data from [54,83,84]

Table 1: Key pharmacologic properties of principal LAs.

enter neural cells to reach the inner part of voltage-dependent channels and block them [53,54]. Due to their liposolubility potential, LAs are also known to diffuse in adipose tissue, in the case of tumescent anesthesia for liposuction [55].

Moreover, the use of a vasoconstrictor as epinephrine (adrenaline) provides potentialization of LAs, providing increased long-lasting action [56]. Indeed, epinephrine is used to decrease bleeding and also slows the passage of LAs in systemic circulation, thus ensuring prolonged retention in the tissue.

Currently used LAs in AFG

Maximum recommended doses of LAs are confused. For lidocaine injection, they are estimated at 200 mg [57]; for tumescent lidocaine, estimation is 30 mg/kg for the French Society of Anesthesia and Intensive Care ("Société française d'anesthésie et de réanimation", SFAR), and safe limit dose is estimated at 35 mg/kg by Klein [49] who has also reached highest dose of 50 mg/kg in tumescent anesthesia [58]. LA dose for tumescent anesthesia (30-35 mg/kg) is finally much higher than recommended dose for injection (5-7 mg/kg). This is explained by the fact that 1) LAs are lipid soluble so they may preferentially diffuse into fat; 2) adipose tissue is not much vascularized; 3) supplementation with vasoconstrictor delays plasma diffusion [45,51].

For other LAs like ropivacaine, bupivacaine and levo-bupivacaine, and due to their higher relative potency and their potential higher systemic toxicity (Table 1), doses could be 10 fold less compared to lidocaine [59,60]. The use of long-acting LAs as bupivacaine may offer interesting postoperative analgesia [61] but these drugs are poorly referenced in the context of fat grafting, in which appropriate doses and effects are not well known. This is the same lack of knowledge regarding prilocaine, which has also been used for tumescent anesthesia (maximal dose of 15 mg/kg for safe liposuction) [62].

Ultimately, the most currently used LA for liposuction and AFG is lidocaine and that's on this molecule that literature is the most abundant. Indeed, a survey from the American Society for Aesthetic Plastic Surgery concluded that: for adipose tissue harvest, 40% of surgeons use tumescent solution containing 50 mL of 1% xylocaine + 1 mL epinephrine 1:1000 in 1 L normal saline, which corresponds to 0.5 mg/mL of lidocaine. Then, about 30% of them use a mixture of 0.5% xylocaine with epinephrine and 22% use 1% xylocaine epinephrine mixture. The remaining 8% of American physicians use epinephrine alone or other solution [63].

Among other solutions, articaine, which is widely used in dentistry, has also been reported to be an efficient LA for tumescent liposuction [64,65]. With dose of 0.4 mg/mL articaine combined with 1 µg/mL epinephrine, this tumescent solution presents high anesthetic potency (due to high lipid solubility that improves cell membrane diffusion), and also presents low systemic toxicity (because of easy and rapid metabolism by esterases) [64].

Moreover, regarding site of injection of adipose tissue, 80% of plastic surgeons use either 0.5 or 1% xylocaine with epinephrine. Other solutions may be used but finest fat injections in small areas also allow to avoid the use of local anesthesia at the site of injection [63].

To some extent, regarding systemic toxicity and duration of action in the context of liposuction and fat grafting, there is no reason to use another anesthetic as lidocaine [45,66]. Indeed, for this kind of procedure, a tumescent solution containing lidocaine plus epinephrine (at recommended doses) is sufficient, efficient, and present almost no risk of local anesthesia complication.

Cytotoxicity of LAs in non-neuronal cells

LA toxicity in neuronal cells has already been reported [67]. Furthermore, as described above and aside from patient allergies, systemic toxicity of LAs is quite rare, particularly in the context of tumescent liposuction. Even for face surgery, where areas are well vascularized and highly innervated, this toxicity can be easily managed by respecting the recommended doses for LA injection.

However, to a lesser extent in terms of serious medical risk, LAs have been shown to exert cytotoxic effects in many non-neuronal cells, including fibroblasts [68], chondrocytes [69] and myoblast cells [70]. Considering LAs adverse effects in many cell types, their use is therefore more cautious in some clinical applications. This is the case of intra-articular injections following joint surgery, where LAs (mostly lidocaine, bupivacaine or ropivacaine) exert cytotoxic effects on chondrocytes and thus, may contribute to cartilage degeneration [69,71]. Some studies now recommend to avoid intra-articular administration of LA or to find alternatives [72]. Publication of several case reports about postoperative chondrolysis have finally alerted orthopedic surgeons and anesthetists who now pay more attention on these severe and disabling complications that can be partly due to LAs [73].

By the same, it is now time to consider LAs effects in the context of lipofilling. Concerning LAs effects in adipose tissue cells, the debate is still relevant. Overall related studies are reported in Table 2.

Finally, only few studies exist on LA effects in AFG and the methods used are all different, which may explain the different and so-called "controversial" results. Indeed, most of the studies are made *in vitro* and include sometimes high doses, and other times minor doses of LA. Moreover, as there is no standardized protocols, adipose tissue harvest and processing are also involved in these differences between studies, as well as type of cells studied, in culture or not (Table 2). Thus, it is difficult to really compare all these studies.

From our own studies, we have shown that clinical doses of lidocaine (ranging from 0.4 to 1.6 mg/mL) could affect cultured ADSC viability in a dose and time dependent manner [10]. However, this cytotoxicity could be partially prevented by washing the cells after lidocaine incubation. Thus, depending on the dose, duration of action, and also procedure of adipose tissue handling (like centrifugation and washing that may remove LAs and avoid their deleterious effects) LAs can cause more or less harmful effects on the cells within the graft. Similarly, Keck et al. have shown that LAs impair preadipocyte viability and their differentiation into mature adipocyte [7,8]. Finally, our results were confirmed in an *in vivo* study of fat transfer into immunodeficient mice (Table 2) [74,75].

Actually, the different conclusions made in all these studies are dependent on the method used for adipose tissue handling prior to injection, insofar as centrifuging and washing adipose tissue must allow removing most of the drugs present from liposuction.

Moreover, regarding the use of epinephrine for vasoconstriction, the low doses that are currently used (usually 1 µg/mL) seem to be safe for the patient and do not influence adipose-derived stem cell viability [10]. Therefore, epinephrine can be used in liposuction procedure for AFG.

Knowing the importance of ADSCs for fat graft survival [38-40,42,43], the potential impact of LAs on these cells has to be considered in the context of AFG. Indeed, as mentioned here above, ADSCs properties may be of great interest for fat graft retention and efficiency,

Reference	LAs	Type of study	Tissue or cell type and origin	LA effects on adipose tissue, adipose-derived stem cells and fat grafting	Comments
Moore et al. 1995 [85]	Lidocaine	<i>In vitro</i>	Adipocytes from human suction lipectomy, after collagenase digestion	Lidocaine potently inhibits glucose transport and lipolysis in adipocytes and their growth in culture But adipocytes regain their function after washing	This study introduces the impact of LAs in AFG and proposes washing as an interesting method to erase LA adverse effects
Large et al. 1997 [86]	Lidocaine	<i>In vitro</i>	Subcutaneous fat cells from obese patients	Compared to general anesthesia, local anesthesia does not influence adrenergic regulation of lipolysis	This study is more related to obesity (adipose tissue harvest during clinical studies)
Sommer and Sattler (2000) [11]	-	Review	<i>Comparative studies (human, animal and in vitro studies) on graft survival and longevity</i>	Review of literature shows similar survival rates of fat grafts after either general or local anesthesia	This review does not focus on LA effects in AFG and authors draw conclusions from studies that do not focus on the use and effects of LAs
Shoshani et al. 2005 [6]	Lidocaine Adrenaline	<i>In vivo</i> (nude mice)	Adipose tissue from a healthy human patient undergoing elective surgery, and grafted into nude mice	Lidocaine and adrenaline do not have any influence on the take of fat grafts or adipocyte viability after lipotransfer in nude mice	This is the first <i>in vivo</i> study related to lidocaine and adrenaline effects However, this interesting study includes a centrifugation step that may be essential to preserve the cells
Keck et al. 2009 [7]	- Lidocaine 1% - Articaine 1% + epinephrine 1:200,000 - Ropivacaine 0.75% - Prilocaine 1% - Tumescence solution (sodium chloride 0.9% + 25 mL Articaine 1% + epinephrine 1:200,000 + 25 mL bicarbonate)	<i>In vitro</i>	Human preadipocytes in culture (obtained after collagenase digestion of adipose tissue, from abdominoplasties)	All the tested LAs exert cytotoxic effects The tumescence solution used (with diluted articaine) appears to be safe	Incubation time of 30 min is less but very high doses of LAs are directly applied on the isolated cells, which explains the terrible cytotoxic effect
Keck et al. 2010 [8]	- Bupivacaine 1% - Mepivacaine 1% - Ropivacaine 0.5% - Articaine 4% + epinephrine 1:100,000 - Lidocaine 2%	<i>In vitro</i>	Human preadipocytes in culture	All LAs exert cytotoxic effects, to various degrees (articaine + epinephrine is the worst) All LAs significantly impaired the ability of preadipocytes to differentiate into adipocytes	Cells have been let in culture for 24 or 48 h before being trypsinized, centrifuged and resuspended directly in the different high concentrated LAs. This explains the high level of cytotoxicity
Keck et al. 2012 [87]	Lidocaine 2%	<i>In vitro</i>	Human preadipocytes in culture	Lidocaine induces necrosis but not apoptosis on preadipocytes. Necrotic effect of lidocaine cannot be prevented by coenzyme Q10.	The dose of lidocaine used is still very high
Sazaki 2011 [88]	Tumescence lidocaine (10.5 – 20 mg/kg)	Case report	Human adipocytes	The amount of instilled tumescence fluid and lidocaine dosage seem to be safe for water-assisted liposuction	This study focuses on water-assisted liposuction and does not compare with and without LA
Livaoglu et al. 2012 [9]	Lidocaine + epinephrine Prilocaine	<i>In vivo</i> (rat model of AFG with fat from rat)	Adipose tissue from rat grafted for 30 and 180 days	Lidocaine plus epinephrine or prilocaine have no negative effect on microangiogenesis and fat graft survival	Fat was not from human lipoaspirates but was excised from rats (from inguinal region) Histologic findings are questionable
Girard et al. 2013 [10]	Lidocaine (0.4 to 1.6 mg/mL) ± adrenaline (1:1000000)	<i>In vitro</i>	Human adipose-derived stem cells (ADSCs) in primary culture for few days (4 days without any passage)	Lidocaine affects ADSC viability (but no apoptosis) Adrenaline has no effect Lidocaine cytotoxicity can be partly avoided by washing Lidocaine may have anti-inflammatory properties	First authors <i>in vitro</i> study regarding lidocaine effects <i>In vivo</i> effects have to be confirmed Clinical doses of lidocaine have been used
Atlan et al. (2012) [74]	Lidocaine (0.4 to 1.6 mg/mL) Ropivacaine (0.4 to 1.6 mg/mL) ± adrenaline (1:1000000)	<i>In vitro</i>	Human adipose-derived stem cells (ADSCs) in primary culture for 4 days (no passage)	Ropivacaine is more cytotoxic than lidocaine	Ropivacaine and lidocaine have been tested at equal doses, which represent high dose for ropivacaine
Girard et al. 2013 [75]	Tumescence lidocaine (0.8 mg/mL) + adrenaline (1:1000000)	<i>In vivo</i> (mouse model with fat from human patient)	Adipose tissue from human patient (injected into immunodeficient mice)	After 1 month of fat grafting, histologic studies reveal that lidocaine infiltrated at the fat harvest site gives worst results compared to tumescence solution without lidocaine Prior to adipose tissue injection, at least 2 washes with soft and short centrifugations allow to improve graft quality (better organization, more stromal cells)	This <i>in vivo</i> study completes the previous <i>in vitro</i> studies from authors. Comparison is done from a same patient: adipose tissue was harvested on one side without lidocaine (tumescence adrenaline), and on the other side with a currently used tumescence solution with lidocaine + adrenaline

Table 2: Studies reporting LA effects in AFG.

by enabling vascularization of the graft (thus assuring cell survival) and enabling adipose tissue regeneration within the graft (thus assuring graft volume retention). ADSCs are also known to secrete growth factors and exert trophic effects that may contribute to surrounding tissue regeneration [34,38,43].

Therefore, ADSC survival inside adipose grafts may improve considerably the quality of the graft, so it is of great importance to limit LA adverse effects during AFG.

How to limit LA effects in AFG: Recommendations

First of all, when fat is used for lipofilling, it is better not to use local anesthesia for liposuction if the surgery is performed under general anesthesia. Indeed, the use of a tumescent solution containing diluted epinephrine is recommended but there is no need of LA administration under general anesthesia. However, in order to ensure post-operative patient comfort, tumescent LA infiltration can be performed after adipose tissue harvest for AFG.

Then, under local anesthesia alone, simple techniques as centrifugation and washing have been tested in order to get rid of LA deleterious effect. But alike controversies about LA effects in AFG, controversies also exist on centrifugation and washing effects.

Smith et al. did not find any advantages using centrifugation and washing and advised minimal manipulation of adipose tissue [76]. While positive aspect of washing have been highlighted in [77], the same authors found that decantation was better than strong centrifugation which could lead to loss of ADSCs, falling to the bottom of the tube as a cell pellet [78].

From our own studies, concerning centrifugation, adipose cell death is correlated to centrifugation speed and time, but cell death remains low below 400 g [79]. Liquid removal (containing LA and epinephrine) is also correlated to centrifugation speed and time, but there is no statistical difference between 400 g and 900 g. Thus, knowing that strong centrifugation has already been reported as a cause of adipose tissue and ADSC damage [78,80,81], soft centrifugation at 400 g (1 min maximum) represents a good compromise.

About washing, Alexander described its effect on adipose tissue by measuring lidocaine remnants [82]. He draws the conclusion that washing allows to remove a part of lidocaine infiltrated in adipose tissue, and he advised at least 2 wash in order to remove most of the drug. But washing steps alone are not sufficient as he could still observe some remnants of the drug. Thus, our combined studies [10,79] allow to define a protocol combining washing (at least 2) and soft centrifugations which clearly improve extraction of remnant liquids, thus removing LA.

In addition, this protocol encourages the presence of stromal cells and a large network of conjunctive tissue inside the graft. These cells are indeed capable of synthesizing collagen fibers and could be involved in neo vascularization of the graft, and therefore in its survival. Finally, this procedure of adipose tissue/lipoaspirate handling enhances graft survival by elimination of deleterious elements, among which local anesthetics, by a non-traumatic protocol involving washings and soft centrifugations (100 g/1 sec, to 400 g/1 min) [74,75].

Actually, it is difficult to compare methods if they have not been made in the same way. This can explain differences observed between studies. Results are mostly from *in vitro* studies in which too high speed centrifugation is used. Moreover, we have to keep in mind that adipose stem cells are essential for the survival of adipose tissue, and that LAs have a negative effect on these stem cells. Thus, our results, combined

with those of other teams, tend to prove that it is necessary to wash the tissue at least two times, with short centrifugation at low speed, in order to obtain better results in fat grafting.

Conclusion

Before imagining overly complex methods to improve AFG (such as the use of bioscaffolds, growth factors...), it is first better to focus on simple ways to maximize cell survival upstream. Since there is so far no consensus on adipose tissue handling, it is still interesting to refine the protocol for adipose tissue harvest and handling.

To summarize, here are the principle recommendations regarding LA use in AFG:

- The use of LA should be avoided under general anesthesia (tumescent solution with diluted epinephrine but without LA is recommended)
- Under local anesthesia, infiltration of a tumescent solution containing diluted lidocaine and epinephrine is preferred
- Maximal dose of tumescent lidocaine is 35 mg/kg (or 30 mg/kg in France) to avoid systemic toxicity
- But lidocaine concentration should be as low as possible (below 0.8 mg/mL and even less) to avoid excessive cytotoxicity inside adipose graft
- Soft and short centrifugations with short washing steps should be included in adipose tissue handling prior to its injection, in order to get rid of infiltrated drugs.

Obviously, these recommendations should also be considered in the context of regenerative medicine when using ADSCs extracted from lipoaspirates.

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