

Tumescent Technique for Regional Anesthesia Permits Lidocaine Doses of 35 mg/kg for Liposuction

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Abstract. The tumescent technique for local anesthesia permits regional local anesthesia of the skin and subcutaneous tissues by direct infiltration. The tumescent technique uses large columns of a dilute anesthetic solution to produce swelling and firmness of targeted areas. This investigation examines the absorption pharmacokinetics of dilute solutions of lidocaine (0.1% or 0.05%) and epinephrine (1:1,000,000) in physiologic saline following infiltration into subcutaneous fat of liposuction surgery patients. Plasma lidocaine concentrations were measured repeatedly over more than 24 hours following the infiltration. Peak plasma lidocaine levels occurred 12-14 hours after beginning the infiltration. Clinical local anesthesia is apparent for up to 18 hours, obviating the need for postoperative analgesia. Dilution of lidocaine diminishes and delays the peak plasma lidocaine concentrations, thereby reducing potential toxicity. Liposuction reduces the total amount of lidocaine absorbed systemically, but does not dramatically reduce peak plasma lidocaine levels. A safe upper limit for lidocaine dosage using the tumescent technique is estimated to be 35 mg/kg. Infiltrating a large volume of dilute epinephrine assures diffusion throughout the entire targeted area while avoiding tachycardia and hypertension. The associated vasoconstriction is so complete that there is virtually no blood loss with liposuction. The tumescent technique can be used with general anesthesia or IV sedation. However, with appropriate instrumentation and surgical method, the tumescent technique permits liposuction of large volumes of fat totally by local anesthesia, without IV sedation or narcotic analgesia. *J Dermatol Surg Oncol* 1990; 16:248-263.

INTRODUCTION

The rate of systemic absorption and the maximum safe dose of lidocaine following infiltration into subcutaneous fat have never been documented. Traditional dosage limitations for infiltrative local anesthesia are based more on clinical dogma than on scientific data.

For nerve blocks and infiltration local anesthesia, the Physicians' Desk Reference (PDR) and the Xylocaine (lidocaine hydrochloride) (Astra Pharmaceutical Products, Inc. Westboro, MA) package insert state, "For normal healthy adults, the individual maximum recommended dose of lidocaine HCl with epinephrine should not exceed 7 mg/kg (3.5 mg/lb) of body weight and in general it is recommended that the maximum total dose not exceed 500 mg."¹ Neither the initial manufacturer of lidocaine nor the United States Food and Drug Administration (FDA) have data to support this recommended maximal safe dosage.² In its 1948 application to the FDA for permission to market lidocaine, Astra Pharmaceutical Products, Inc. simply stated that the maximum safe dose of lidocaine is "probably the same as for procaine."³

The present clinical investigation examines the absorption pharmacokinetics of lidocaine and epinephrine infiltrated into subcutaneous fat for liposuction surgery. Guidelines are suggested for maximal safe dosages of dilute lidocaine and epinephrine infiltrated into fat.

Infiltrating subcutaneous fat with large volumes of fluid causes the tissue to become swollen and firm, or tumescent. Infiltrating with large volumes of very dilute lidocaine, epinephrine, and sodium bicarbonate for local anesthesia and hemostasis is known as the tumescent technique. Diluting the anesthetic solution slows the absorption of lidocaine, thus reducing its toxicity. Total lidocaine doses five times greater than the limit traditionally regarded as maximal appear to be safe when infiltrated into subcutaneous fat using the tumescent technique.

In addition to minimizing lidocaine toxicity, the tumescent technique produces extensive and prolonged capillary vasoconstriction, permitting liposuction with almost no blood loss. Since infiltrated tissues remain partially anesthetized for many hours, many patients require no postoperative analgesia.

The tumescent technique for liposuction can be used to supplement general anesthesia. However, the anesthesia produced by the tumescent technique is so complete that it permits liposuction of large volumes of fat totally by local anesthesia, without IV sedation or narcotic analgesia.

MATERIALS

The anesthetic solution containing approximately either 0.05% or 0.1% with epinephrine 1:1,000,000 is prepared by adding either 500 mg or 1000 mg lidocaine (50 or 100 ml of 1% lidocaine), 1 mg epinephrine (1 ml of 1:1000), and 12.5 meq of sodium bicarbonate (1 meq/ml) to 1000 ml of normal saline (0.9% NaCl) (Table 1).⁴

The subcutaneous infiltration of large volumes of dilute anesthetic solution is accomplished using two instruments, a handle and a needle, specifically designed for use with the tumescent technique. (address inquiries to PO Box 1629, San Clemente, CA 92672) (Fig 1) – not included in doc Both of these instruments accommodate a plastic 60-cc Luer-Lock syringe (Becton-Dickinson, Rutherford, NJ). The handle is attached to disposable, sharp hypodermic needles. The disposable needles are a 3.5-in 20-gauge spinal needle (Becton-Dickinson) and a 6-in 18-gauge intradiscal therapy needle (Becton-Dickinson). The needle consists of a blunt-tipped 4-mm outside-diameter needle welded to a device that resembles the handle.

A plastic IV bag containing the anesthetic solution is attached to either the handle or the needle by a 94-in-long IV tubing with an in-line check valve ADDitIV Primary IV Set (Kendall McGraw Laboratories, Sabana Grande, Puerto Rico). This check valve prevents retrograde flow of the anesthetic solution back into the IV bag. The syringes are initially filled directly from the IV bag containing the anesthetic solution via the ADDitIV line using a female-female luer connector. (PO Box 1629, San Clemente, CA 92672)

Preoperative sedation consisted of flurazepam (Dalmane, Roche Laboratories, Nutley, NJ) 30 mg by mouth the night before surgery and midazolam (Versed, Roche Laboratories, Nutley, NJ) 2.5 mg intramuscularly just prior to surgery. Neither general anesthesia nor IV sedation was employed. Surgeries were accomplished totally by local anesthesia using the tumescent technique for liposuction.

Table 1
Recipe for Tumescent Technique Anesthetic Solutions for Liposuction
(Lidocaine 0.05%, Epinephrine 1:1,000,000)

Lidocaine	500 mg (50 ml of 1% lidocaine solution)
Epinephrine	1 mg (1 mg of 1:1,000,000 solution of epinephrine)
Sodium bicarbonate	12.5 meq (12.5 ml of an 8.4% NaH ₂ CO ₃ solution)
Normal saline	1000 ml of 0.9% NaCl solution
The resultant solution is lidocaine (0.047%), epinephrine (1:1063,500), and sodium bicarbonate 11.8 meq/L in 1063.5 ml of saline 0.84%	

METHODS

Each blood sample, obtained by a separate venipuncture, was collected in a heparinized glass container. After separation, plasma was frozen and stored in plastic containers. Lidocaine levels were measured by an enzyme immunoassay.⁵

This study consisted of the following experimental procedures:

1. For each of 8 female volunteer patients, ages 33-44, plasma lidocaine concentrations were measured repeatedly over 24-36 hours following liposuction in order to determine the time and magnitude of peak levels. One of these patients participated as a volunteer on three separate occasions. The time and magnitude of an individual patient's peak lidocaine concentration were determined by plotting sequential plasma levels and connecting the points with a smooth (continuously differentiable) curve. The time of the peak is defined as the length of time between the beginning of the lidocaine infiltration until the occurrence of the peak plasma lidocaine concentration.
2. Four female volunteers were given local anesthesia by the tumescent technique on two separate occasions, each time followed by sequential determination of plasma lidocaine concentrations over more than 24 hours. After the first infiltration there was no liposuction; a week or more later, after second infiltration, liposuction was completed before measuring plasma lidocaine levels. Time and magnitude of peak plasma lidocaine levels, without and with lidocaine, are compared.
3. On two different days, a 70-kg female volunteer received 1 gm, of lidocaine, 1 mg of epinephrine, and 12.5 meq of sodium bicarbonate infiltrated into subcutaneous fat, with the dose divided evenly between the two medial thighs. On the first day the patient received 1000 ml of a dilute anesthetic solution consisting of lidocaine 0.1% (1 gm/L), epinephrine 1:1,100,000 (1 mg/L), and sodium bicarbonate (12.5 meq/L). One week later the patient received 100 ml of a standard, commercially available solution of lidocaine 1% (1 gm/dl) with epinephrine 1:100,000 (1 mg/dl), to which was added 12.4 meq of sodium bicarbonate (1 meq/ml). On both days the solution was infiltrated over a 45-minute interval (22½ for each thigh). The time and magnitude of peak lidocaine levels were compared.
4. An 85-kg male volunteer, age 42, had 900 mg of lidocaine 0.1% with epinephrine 1:1,000,000 infiltrated subcutaneously over 45 minutes into the abdomen and flanks without subsequent liposuction. Sequential plasma lidocaine levels were determined at 5 and 15 minutes after beginning the infiltration and then every 30 minutes over the next 6 hours.

TUMESCENT TECHNIQUE METHOD

The tumescent technique has improved since publication in 1987.⁶ Using an even more dilute lidocaine solution, 0.5% instead of 0.1%, permits greater tumescence with better vasoconstriction and more complete anesthesia. The addition of sodium bicarbonate to the anesthetic solution minimizes the pain of infiltration.⁷⁻⁹ Using a local anesthetic solution without

sodium bicarbonate often necessitates the use of IV sedation and narcotic anesthesia. With the tumescent technique, IV sedation and narcotic analgesia are virtually unnecessary.

When only one body area is treated by liposuction, usually no sedation is needed. When multiple areas are treated, requiring the patients to remain recumbent for more than 1 hour, intramuscular midazolam in 2.5-5-mg increments is given every 2-3 hours. Fewer than 5% of patients, those who are exceptionally anxious, will require 25-50 mg of Demerol (Winthrop-Breon Laboratories, New York, NY) given subcutaneously. None of the patients in the present study required Demerol.

The large volume of normal saline infiltrated into fat as part of the tumescent technique is more than sufficient to compensate for insensible fluid losses as well as fluids lost by liposuction. In fact, patients will usually need to urinate during a lengthy procedure. This suggests that there is no significant deficit of intravascular fluids associated with the tumescent technique.

Because there is virtually no blood loss associated with the tumescent technique, routine IV fluid replacement is not necessary. Nevertheless, an IV is routinely established to provide access for resuscitative medications in the unlikely event of an emergency.

The initial infiltration of the anesthetic solution is accomplished using the handle attached first to a 20-gauge 3.5-in-long spinal needle and subsequently to an 18-gauge 6-in-long intradiscal needle. The 20-gauge needle is used initially because it causes less discomfort than an 18-gauge needle when passed through unanesthetized tissue. These needles are inserted at sites around the periphery of the targeted fatty compartment either through intact skin, or the incision sites that will be used to insert the liposuction cannula. The sites of needle insertion are initially anesthetized using a 30-gauge needle on a 6-cc syringe to infiltrate a small bleb of the local anesthetic solution intradermally.

The needle, consisting of a 30-cm-long, 4-mm outside-diameter needle, is the only instrument needed with the tumescent technique is used in conjunction with general anesthesia or deep IV sedation. When used for regional local anesthesia without IV sedation, the needle is used for the last stage of infiltration of the anesthetic solution. Large areas can be completely anesthetized by systemically passing the blunt-tipped needle throughout the targeted fatty compartment along the same pathways that will be used by the liposuction cannula. The anesthetic solution must be infiltrated carefully and methodically to assure that no areas are missed. Uniform infiltration is most easily accomplished by using a grid pattern drawn by a blue felt-tipped pen on the overlying skin pre-operatively (Fig 2) – not included in doc. By infiltrating anesthetic solution as the needle is advanced, large volumes can be instilled quickly and uniformly, producing firm tumescent and extensive vasoconstriction. The blunt tip will cause discomfort when it encounters an area not previously well anesthetized. Upon detecting an area not adequately anesthetized, the surgeon or anesthesiologist can immediately infiltrate additional anesthetic solution exactly where it is needed. Because it is blunt-tipped, the needle can be passed deeply within the fat, with minimal risk of puncturing subjacent structures.

Filling a 60-cc syringe with anesthetic is the first step in using the handle or the needle. An IV line is attached to the IV bag containing the anesthetic solution. Next using the female-female

luer connector, the IV line is connected to a 60-cc syringe, the IV-line flow-regulator clamp is opened, and the syringe plunger is retracted. Once the syringe is full, it is removed from the connector and IV line.

Inserting the 60-cc syringe into the handle, the syringe is turned until it is engaged with the luer-lock attachment. After removing the connector, the IV line is attached directly to the side-port of the handle, and either a 20-gauge 3.5-in-long spinal needle or an 18-gauge 6-in-long intradiscal needle is attached to the end of the handle. Next, the needle is inserted into subcutaneous fat.

In certain areas where the adipose tissue is regularly more sensitive, the infiltration must be done more slowly than other areas. Areas that are always rather sensitive include the distal-lateral and posterior thighs, upper abdomen and waist near the costal margin, the periumbilical areas, and the medial knees. Except in these areas, most patients can barely detect any sensation as the anesthetic solution is injected.

If not used carefully, a sharp spinal or intradiscal needle may inadvertently penetrate the tissue underlying the subcutaneous fat. To minimize the risk of puncturing the peritoneum or causing a pneumothorax, one must continuously pay careful attention to the exact location of the needle tip within the subcutaneous fat. The safe use of the handle requires that the surgeon or anesthesiologist palpate the tip of the needle while it is being gently advanced along its intended path. To anesthetize deep tissue planes, the thumb and finger of one hand gently grasp and elevate the skin and subcutaneous fat while simultaneously palpating the needle tip. At the same time the other hand grips the handle and simultaneously advances the needle and depresses the syringe plunger. Refilling the 60-cc syringe is easily accomplished; without removing the needle from the subcutaneous fat simply open the IV-flow regulator clamp and retract the syringe plunger.

By repeating these maneuvers systemically, and directing the needle radially in many directions, large regions of the skin and subcutaneous tissue are efficiently anesthetized and vasoconstricted. Well-anesthetized areas are easily recognized visually by the pallor, and tactually by the coolness induced by the vasoconstriction.

The tumescent technique minimizes the risks of postoperative irregularities of the skin. With careful and methodical infiltration one can produce uniform tumescence and avoid irregularities and distortions. Enlarging or magnifying the targeted fatty compartments, and using suction cannulas of less than 5-mm outside diameter, permits liposuction to be done more uniformly and more completely. Because of this “magnification” of subcutaneous fat, focal residual collections of fat are easily detected and treated before completion of the surgery. These features of the tumescent technique minimize irregularities of the skin, which are more likely to be seen after liposuction when only general anesthesia is used.

A substantial volume of anesthetic solution must be injected in order to produce tumescence and complete anesthesia of a fatty compartment (Table 2). Postoperatively there is considerable drainage of slight blood-tinged anesthetic solution. Patients are advised that this typically continues for up to 18 hours. This blood-tinged solution contains approximately 1% packed red blood cells and approximately 2%-3% whole blood. Thus, drainage of 300 ml of this blood-

tinged anesthetic solution represents a loss of less than 10 ml of whole blood. For each liter of pure fat removed by liposuction, patients lose approximately 12 ml of whole blood.¹⁰ One week following the liposuction of 1 L of fat there is virtually no change in the patient's peripheral venous hematocrit.⁶

Table 2
Typical Range of Volumes of Dilute Anesthetic Solutions Used with the Tumescence Technique for Infiltration into Various Areas

Abdomen, upper and lower	(800-2000 ml)
Hip (flank, or love handle), each side	(400-1000 ml)
Lateral thigh, each side	(500-1200 ml)
Anterior thigh, each side	(600-1200 ml)
Proximal medial thigh, each side	(250-700 ml)
Knee	(200-500 ml)
Male breast, each side	(300-800 ml)
Submental chin	(100-200 ml)

MICRO-MACRO 2-STAGE LIPOSUCTION

In order to optimize accuracy and minimize discomfort, liposuction is accomplished using a micro-macro 2-stage liposuction method. Initially a 12-gauge (1.5 mm) micro-cannula (Fig 3) – not included in doc is used. Because a 12-gauge cannula penetrates the fibrous septae in adipose with minimal resistance, the cannula's direction and relative distance from skin are more easily controlled. The tunnel pattern produced by a 12-gauge cannula is more precise and evenly distributed. Subsequently a larger cannula (4.7 mm = 3/16-in outside diameter) (Fig 4) - not included in doc is used to complete the final stage of liposuction. The 4.7-mm cannula follows paths already made by the 12-gauge cannula. Approximately 80% of the extracted fat is removed by the larger cannula during the second stage of liposuction.

Smaller cannulas are most suited for liposuction by local anesthesia. Clinical experience indicates that a cannula with a large inside diameter is more likely to cause discomfort during liposuction by local anesthesia than is a smaller cannula. Larger cannulas exert greater traction on fibrous structures with adipose tissue. This may cause pain in tissues located beyond the effects of the local anesthesia. By reducing the force needed to breach the fibrous septae permeating fatty tissue, the two-stage micro-cannula method minimizes both the discomfort for patients as well as the physical stress on the surgeon's arm.

The use of a 12-gauge cannula is a final test for complete anesthesia. If an incompletely anesthetized area is encountered during liposuction, a 12-gauge cannula causes minimal discomfort compared with the startling sensation that a 4- or 5-mm cannula might cause.

RESULTS

Magnitude and Time of Peak Levels

A typical plasma lidocaine concentration vs. time curve is shown in Figure 5. – not in this doc The time of the peak is defined as the length of time between the beginning of the lidocaine infiltration until the occurrence of the peak plasma lidocaine concentration. Peak levels occurred

between 11 and 15 hours, with most of the peaks occurring at between 12 and 14 hours. The magnitudes of the peak plasma lidocaine concentrations ranged between 0.8 and 2.7 $\mu\text{g/ml}$ over a dosage range of 11.9-34.1 mg/kg (Table 3).

In 8 female volunteers, some participating more than once, a total of 15 separate studies were completed. Each study consisted of an infiltration of dilute lidocaine and epinephrine using the tumescent technique and then obtaining sequential plasma samples for measuring lidocaine concentration over the next 24-36 hours. In 2 of these 8 volunteers more than one area of the body was treated. In these 2 patients, infiltration and liposuction were completed in one area before infiltrating and doing liposuction on the next area.

Table 3.
Experimental Data

PT#	PT-WT* (kg)	Lido Conc (%)	Total Dose (mg)	Dosage (mg/kg)	Fat Out (ml)	Soln Out (ml)	Peak Magnitude ($\mu\text{g/ml}$)	Peak Time (hr)
1	70	0.1	1000	14.3	0	0	1.2	14
1	70	1	1000	14.3	0	0	1.5	10
1	70	0.1	1265	18.1	600	200	0.9	13
2	59.1	0.1	1000	16.9	0	0	1.3	12
2	59.1	0.1	1180	20.0	500	100	1.2	12
3	63	0.05	750	11.9	0	0	1.0	12
3	63	0.05	775	12.3	400	300	0.8	12
4	59	0.05	1411	23.9	0	0	2.5	14
4	59	0.05	1411	23.9	575	200	1.7	15
5†	58.6	0.05	2000	34.1	1450	575	2.3	13
6†	95	0.05	2340	24.6	3050	950	2.7	15
6	92	0.1	2223	24.1	1150	450	2.7	12
6	89	0.05	1646	18.5	2220	700	2.2	12
7	61.4	0.1	1418	23.1	525	200	1.3	12
8	66	0.1	1965	26.9	1550	300	2.4	11

*PT-WT = patient weight (kg). Lido conc = lidocaine concentration in anesthetic solution, % - [(gm of lidocaine)/(100 ml of solution)]. Epinephrine concentration was 1:100,000 except for the only solution in which lidocaine concentration was 1% and epinephrine 1:100,000. Total dose = total dose of lidocaine delivered. Dosage = amount of lidocaine delivered per kg of patient weight. Fat out = the volume of blood-free fat extracted by liposuction, Soln out = the volume of blood-tinged anesthetic solution removed during liposuction procedure. Peak magnitude = peak magnitude of plasma lidocaine. Peak time = the time of the peak is defined as the length of time between the beginning of the lidocaine infiltration until the occurrence of the peak plasma lidocaine concentration.

† More than one area of the body was treated. Because infiltration and liposuction were completed in one area before infiltrating and doing liposuction on the next area, infiltration occurred over an extended time interval. Consequently, the peak plasma lidocaine concentration occurred later.

Effects of Liposuction on Peak Levels

There were 4 volunteers who received lidocaine infiltrations on 2 separate occasions at least 1 week apart. On the first occasion infiltration was completed without subsequent liposuction, and on the second occasion liposuction followed the infiltration. For each of these 4 subjects the total dose of lidocaine was always infiltrated without interruption over a single time interval. The results of this study are graphically depicted in [Fig 6. – not in this doc](#)

The area under the curve (AUC) of each graph represents the total amount of lidocaine that was absorbed systemically. AUC was calculated using Archimedes method of exhaustion.¹¹

Liposuction reduced both the total amount of lidocaine absorbed systemically and the peak plasma lidocaine concentrations to a similar degree. Liposuction produced an average reduction in the total amount of lidocaine absorbed systemically by 29.9%. Similarly, liposuction produced an average reduction of the magnitude of peak plasma lidocaine concentration by 25.8% (Table 4). The time of the peak plasma lidocaine concentration was not affected by liposuction.

Table 4

Pt#	Dose _o	Dose _L	AUC _o	AUC _{EXP}	AUC _L	ΔAUC	Peak _o	Peak _{EXP}	Peak _L	ΔPeak
1	1000	1265	20.4	25.8	17.1	33.7%	1.2	1.5	0.9	40%
2	1000	1180	20.3	24.0	16.4	31.5%	1.3	1.5	1.2	20%
3	750	775	18.7	19.3	12.5	35.4%	0.9	0.9	0.8	11.1%
4	1411	1411	30.5	30.5	25.5	16.4%	2.5	2.5	1.7	32%

The mean values of Δ AUC and Δ PEAK are 29.8% and 25.8%, respectively. Comparing these two percentages it is apparent that liposuction reduces the total amount of lidocaine absorbed systemically and the peak plasma lidocaine concentrations to a similar degree.

Dose_o and Dose_L represent respective doses of lidocaine in mg/kg associated without and with liposuction.

AUC_o and AUC_L represent the respective observed AUC without and with liposuction.

AUC_{EXP} = [dose_L/dose_o] x AUC_o is the AUC one would expect at dose of dose_L if liposuction had not been done.

Δ AUC = [(AUC_{EXP} - AUC_L/AUC_{EXP}) x 100] is the expected percent reduction of AUC resulting from liposuction.

Peak_o and Peak_L represent the respective peaks observed without and with liposuction.

Peak_{EXP} = [dose_L/dose_o] x peak_o is the peak one would expect at a dose_L if liposuction had not been done.

Δ peak = [(peak_{EXP} - peak_L)/peak_{EXP}] x 100 is the estimated percent reduction of the peak plasma lidocaine concentration resulting from liposuction.

Maximum Safe Dose of 35 mg/kg

The maximum safe dose of lidocaine is estimated by plotting the magnitude of the peak plasma lidocaine concentration versus the dosage (mg/kg) for each study. (Fig 7) – not in the doc Assuming a linear relationship between peak lidocaine levels and dosage, a straight line can be used to predict the maximum safe dosage of lidocaine when using the tumescent technique.

Ideally, a safe maximal dose should yield a peak plasma lidocaine concentration below the toxicity threshold (5 µg/ml) for at least 99% of patients. Using linear regression analysis to define a least-squares estimate for a straight line that best fits our data would yield an inappropriately high estimate of approximately 50 mg/kg. With such an estimate, one would expect a dose of 50 mg/kg to produce peak plasma lidocaine levels greater than 5 µg/ml in approximately 50% of patients.

A more conservative choice is the line for which a peak lidocaine concentration of 5 µg/ml corresponds to a dosage of 35 mg/kg. With appropriate assumptions about linearity, we can expect that a dosage of 35 mg/kg would yield a peak plasma lidocaine concentration of less than 5 µg/ml in every patient who participated in the present study (Fig 7). – not in this doc

Thus a conservative estimate of the maximal safe dose of dilute lidocaine infiltrated into subcutaneous fat is 35 mg/kg, with or without liposuction (Table 5).

Table 5

Estimated Maximal Safe Dosage of Lidocaine

Using the Tumescent Technique is 35 mg/kg

Weight	Maximal Safe Dosage (mg)
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125 lb = 57 kg	2000
160 lb = 73 kg	2500
190 lb = 86 kg	3000

Dilute Delays Absorption

Following the infiltration of 1 gm of lidocaine as a 1% solution with 1 mg of epinephrine at 1:100,000, the peak plasma level occurred at approximately 9 hours, with a magnitude 1.5 $\mu\text{g/ml}$; the maximum pulse rate during this infiltration was 118. In comparison, following the infiltration of 1 gm of lidocaine as a 0.1% solution with 1 mg of epinephrine at 1:1,000,000, the peak plasma lidocaine level occurred at 14 hours, with a magnitude 1.2 $\mu\text{g/ml}$; the maximum pulse rate during this infiltration was 78, essentially unchanged from preoperative values. On each occasion infiltration of the entire dose was accomplished over a 45-min interval. As a consequence of this study we see that diluting an anesthetic solution results in a clinically significant delay in occurrence of the peak plasma lidocaine concentration as well as a diminution of its magnitude after infiltration into subcutaneous fat (Fig. 8). – not in this doc

Slow Infiltration Delays Absorption

Slow infiltration prevents the rapid lidocaine absorption that can occur immediately after rapid infiltration. After a subcutaneous dose of 900 mg of lidocaine 0.1% with epinephrine 1:1,000,000 infiltrated into subcutaneous fat of an 85-kg male over 45 minutes, the plasma lidocaine levels were less than 0.1 $\mu\text{g/ml}$ at 5 and 15 minutes after beginning the infiltration. Subsequent plasma concentrations determined every 30 minutes over the next 7 hours were no greater than 0.5 $\mu\text{g/ml}$ (Fig. 9). – not in this doc

DISCUSSION

The tumescent technique uses large volumes of a dilute anesthetic solution to produce swelling and firmness of targeted areas of subcutaneous fat. The prolonged and profound anesthesia of skin and subcutaneous tissues that is provided by the tumescent technique is a result of exposing sufficient lengths of sensory axons to marginal blocking concentrations of lidocaine¹². The tumescent technique achieves regional anesthesia by direct subcutaneous infiltration rather than by a proximal nerve block. The technique, which allows liposuction of more than 3 L of fat totally by local anesthesia with negligible bleeding, was first presented in 1986 in Philadelphia at the Second World Congress on Liposuction, and first published in 1987.⁶

Clinical experience with liposuction by local anesthesia has shown that exceeding the traditional recommended maximum dose of lidocaine with epinephrine of 7 mg/kg is safe. The facile pharmacologic explanation for the safety of using very large doses of lidocaine during liposuction is that a significant amount of lidocaine is removed along with the aspirated fat.^{13,14} However, this assertion has never been documented scientifically.

An important result of the present study is an estimate of 35 mg/kg as the maximal safe dose of lidocaine using the tumescent technique for liposuction by local anesthesia. This is five times the traditional maximal safe dose of 7 mg/kg of lidocaine for local anesthesia.¹³

Important factors in determining the fate, efficacy, and toxicity of a drug in the human body include rates of absorption, distribution, metabolism, and elimination. Elegant studies of lidocaine given intravenously (IV) have elucidated its distribution, metabolism, and elimination.¹⁵ The few published studies of lidocaine absorption after infiltration into subcutaneous fat have used elementary pharmacologic analyses.^{4,6,14,16,17} The present study of the clinical pharmacokinetics of the tumescent technique is aimed at a more comprehensive understanding of lidocaine absorption and elimination after infiltration into subcutaneous fat.

Pharmacokinetics of IV Lidocaine

Since lidocaine is relatively lipophilic, tissue membranes are not a significant barrier to lidocaine distribution. The rate of lidocaine distribution into or out of a tissue is perfusion rate-limited.

Immediately after an IV bolus dose, there is a rapid distribution-related fall in plasma lidocaine.¹⁸ This occurs as a result of lidocaine diffusing from plasma into highly perfused organs such as the brain, heart, and liver. Once an equilibrium is achieved between lidocaine concentrations in plasma and all well-perfused tissues, plasma levels decline more slowly. This later decline of plasma drug levels depends on uptake into less well-perfused tissues and on hepatic lidocaine metabolism.

Lidocaine is metabolized by the liver. Hepatic metabolism is so rapid that 70% of lidocaine is extracted from any given volume of blood as it passes through the liver. Following an intravenous bolus injection of lidocaine in a healthy volunteer, half of the drug will have been eliminated after approximately 100 minutes.^{19,20} In a healthy person, lidocaine clearance is 10 mg/min/kg. Thus, when plasma lidocaine concentration is 2.5 µg/ml in an 80-kg person, the liver will metabolize 2000 µg/min or 120 mg/hr of lidocaine.

Hepatic metabolism of lidocaine is so complete that the rate of lidocaine clearance is a direct function of the rate of hepatic blood flow. Any decrease in hepatic blood flow will decrease the rate of lidocaine metabolism, and consequently increase the risk of lidocaine toxicity.

An oral dose of lidocaine is absorbed into the portal circulation and rapidly metabolized by the liver, with relatively little lidocaine reaching the systemic circulation. Thus, lidocaine must be given parenterally when treating life-threatening cardiac arrhythmias.

Absorption Rate of Subcutaneous Lidocaine

The 12-14-hour delay of the peak lidocaine plasma levels following infiltration into subcutaneous fat using the tumescent technique is unprecedented. Dilution of lidocaine and rate of subcutaneous infiltration are important determinants of rate of absorption. The present study has shown that dilution delays and diminishes the magnitude of peak plasma lidocaine levels following subcutaneous infiltration. This is contrary to the observation that lidocaine absorption rates are independent of lidocaine concentration for intramuscular and peridural injections over a range of 1% or 10% lidocaine.²¹

Rapid subcutaneous infiltration of a standard anesthetic solution of lidocaine and epinephrine may produce toxicity. The more rapidly a local anesthetic is injected, the more rapidly it is absorbed systemically.²² This is true for both intravenous infusion,²³ as well as for infiltration into subcutaneous fat.

Peak plasma lidocaine levels in healthy persons are generally assumed to occur within 60 minutes of giving the drug, whether it is given by bolus intravenous infusion; intravenous regional anesthesia;²⁴ intramuscular injection,^{25,26} caudal, epidural, intercostals, and peripheral nerve blocks,²⁷⁻³² paracervical infiltration;³³ or oral administration.³⁴

An unexpected result of the present study is that 1 gm of a 1% lidocaine solution with epinephrine 1:100,000 slowly infiltrated into subcutaneous fat over 45 minutes is absorbed so slowly. In fact, the peak plasma level occurred 9 hours after beginning the infiltration.

There are few detailed studies of absorption kinetics of lidocaine infiltrated subcutaneously. For subcutaneous infiltration the peak plasma lidocaine level is usually less than 60 minutes.³⁵⁻³⁸ An average peak plasma lidocaine level occurring at 62 minutes (range 30-120 minutes) is one of the longest delays documented in the literature.³⁹ When 2% lidocaine with epinephrine 1:200,000 is infiltrated into the scalp for hair transplantation, peak plasma lidocaine concentration occurred 45 minutes after the initial infiltration in 6 of 6 patients.⁴⁰

Regional Anesthesia Without Nerve Block

There are two reasons why infiltrative local anesthesia has traditionally been limited to relatively small areas of skin: (1) the stinging pain associated with infiltrating the local anesthesia is not easily tolerated, and (2) published dosage limitations have precluded anesthetizing large areas of skin. These limitations have now been overcome with the recognition that (1) adding sodium bicarbonate in order to neutralize the acidity of commercially available local anesthetic solutions of lidocaine and epinephrine dramatically reduces the usual burning-stinging pain of infiltration,⁸ and (2) using dilute solutions of lidocaine with the tumescent technique permits profound anesthesia of very large areas with minimal risk of lidocaine toxicity. The tumescent technique permits regional local anesthesia of skin and subcutaneous tissue by direct infiltration rather than by proximal nerve block.

Prolonged Local Anesthesia

A remarkable aspect of the tumescent technique is that there is so little postoperative discomfort. Treated areas remain at least partially anesthetized for up to 18 hours after surgery. Thus for liposuction, it is not necessary to use local anesthetics that are longer acting and more cardiotoxic than lidocaine.⁴¹⁻⁴⁴

Following liposuction with the tumescent technique, patients do not require analgesia postoperatively. Although some patients do take acetaminophen for mild to moderate soreness, narcotic analgesics are not prescribed.

There are at least two aspects of lidocaine pharmacology that explain the persistence of analgesia with the tumescent technique. First, the occurrence of peak plasma lidocaine levels more than 12 hours after beginning the infiltration and detectable blood levels well beyond 18 hours indicates that the anesthetic persists in the locally treated areas for up to 18 hours. This is consistent with the clinical observation that slightly blood-tinged anesthetic solution continues to drain from the 5-mm incision sites for approximately 18 hours after the surgery. Second, it has been asserted that a continuous low dose infusion of lidocaine, yielding plasma lidocaine concentration of 1 µg/ml, reduces the severity of postoperative pain and minimizes the necessity for narcotic analgesics.^{45,46} Lidocaine plasma concentrations of 3-6 µg/ml lidocaine decrease the anesthetic requirements of nitrous oxide and halothane by 10%-28%.⁴⁷

Lidocaine Toxicity

Lidocaine toxicity is closely correlated with plasma lidocaine levels. Because toxicity becomes apparent at different levels in different patients, the clinical threshold for lidocaine toxicity is not well defined. It is clinically useful to think of a threshold level for toxicity as being described by a curve similar to that of the bell-shaped curve of a Gaussian (normal) distribution. The point at which 50% of patients can be expected to first manifest toxicity is the median threshold toxic blood level. By definition, 50% of the patients will experience toxicity below this toxic threshold. A corollary statement is that any estimate of a “maximal safe dosage” of lidocaine should account for clinical variation between patients, and the statistical variation between pharmacologic studies.

Therapeutic plasma lidocaine levels for suppressing ventricular ectopy in the clinical setting of acute myocardial ischemia range between 1 and 5 µg/ml. Subjective side effects can probably be recorded at between 3 and 6 µg/ml with objective undesirable side effects, or toxicity, becoming apparent at plasma levels above 5-9 µg/ml.⁴⁸ Potentially fatal lidocaine toxicity may occur at plasma lidocaine concentrations as low as 9 µg/ml (Table 6).

The following classification of lidocaine toxicity is intended to provide insight into clinical situations where infiltrating lidocaine subcutaneously can result in an unexpected toxic reaction. Toxicity may result from (1) an overdose, (2) an excessively rapid systemic uptake of an otherwise safe dose, (3) impaired hepatic metabolism, or (4) drug interactions.

Table 6

Lidocaine Levels and Toxicity

3-6 µg/ml	Subjective toxicity Lightheadedness, euphoria Digital and circumoral paresthesias Restlessness, drowsiness
5-9 µg/ml	Objective toxicity Nausea, vomiting, tremors Blurred vision, tinnitus Confusion, excitement, psychosis Muscular fasciculations
8-12 µg/ml	Seizures Cardiorespiratory depression
12 µg/ml	Coma
20 µg/ml	Respiratory arrest
26 µg/ml	Cardiac standstill

These are approximate values abstracted from multiple previously published reports including: Binnion PF et al. Br Med J 3:390-393,1969; Benowitz NL, Meister W. Clinical pharmacokinetics of lidocaine. Clinical Pharmacokinetics 3:177-201, 1978; Mather LE, Cousins MJ. Local anaesthetics and their current clinical use. Drugs 18:185-205, 1979.

OVERDOSE

The following definitions of “overdose” give a perspective on the problem of defining dose-limits for lidocaine in local anesthesia.

A *mistaken overdose* occurs when too much drug (more than a safe amount) is given as a result of either carelessness or ignorance. A mistaken overdose may or may not cause a toxic reaction.

A *retrospective overdose* is a dose that retrospectively actually caused a toxic reaction in a specific patient. In some patients a retrospective overdose may occur despite an administered dose that is well below the recommended safe upper dose limit.

A *prospective overdose* is defined as a dose above which a toxic reaction can be expected in an arbitrary but significant number of patients. Such an overdose is defined prospectively based on (1) route of administration and (2) concepts of population pharmacokinetics and (2) concepts of population pharmacokinetics that take into account inpatient and outpatient variability. Factors that affect rates of drug absorption and elimination are the variables that define important subpopulations of patients.

A *dogmatic overdose* is any dose that exceeds a “standard recommended maximum safe dose” that has no scientific basis in fact. A dogmatic overdose may be quite safe. This is obviously true in the case of the tumescent technique where the maximum safe dose of lidocaine when infiltrated into fat, 35 mg/kg, is five times the “standard recommended maximum safe dose” for local anesthesia, 7 mg/kg, as listed in the Xylocaine (lidocaine) package insert. Unfortunately many published dosage limitations for lidocaine in local anesthesia are based more on clinical dogma than on scientific data.

Following an IV bolus dose the initial distribution-related fall in plasma lidocaine concentration is rapid. The half-life of this early distribution-related phase is 8.3 minutes.¹⁵ As a consequence,

the duration of a toxic reaction following an inadvertent IV injection should be relatively brief.⁴⁹ Even a massive IV bolus dose is not necessarily fatal.⁵⁰

On the other hand, toxic reactions to lidocaine that occur after an excessive cumulative dose, such as with a prolonged IV infusion or repeated injections, are more dangerous. The half-life of lidocaine blood levels after a prolonged infusion is approximately 100 minutes in healthy adults and depends on liver metabolism. In this clinical setting toxic plasma concentrations may persist for hours and may be associated with refractory cardiac arrest.

RAPID SYSTEMIC UPTAKE

Inadvertent intravascular injection of an otherwise safe dose of local anesthetic is a relatively common cause of toxicity.^{51,52} In a 10-year study that includes 9287 regional nerve blocks, there were 8 systemic toxic reactions, and all were attributed to an inadvertent intravascular bolus injection.⁵³

Injection of a lipophilic drug, such as lidocaine, into highly vascular tissue promotes rapid diffusion out of the tissue into the vascular space. Intercostal nerve blocks, which involve injections into very vascular tissue, are particularly likely to result in rapid systemic absorption and toxicity.⁵⁴ Similarly, cutaneous infiltration of lidocaine prior to laser treatment of a hemangioma can easily produce transiently toxic plasma levels. The potential toxicity of a local anesthetic is less when infiltrated into relatively avascular subcutaneous tissue than when it is injected into the highly vascular intraperitoneal space.⁵⁵

A highly concentrated lidocaine solution will produce rapid diffusion into the vascular compartment because the rate of drug diffusion across a membrane is proportional to its concentration gradient. When lidocaine is injected subcutaneously in mice, the higher the concentration, the smaller the lethal dose⁵⁶ (Table 7).

Table 7
Effect of Lidocaine Dilution on Fatal Toxicity in Mice After Subcutaneous Injection⁵⁶

Lidocaine Concentration(%)	LD ₅₀ of Lidocaine in Mice (gm/kg)
0.5	1.07
1.0	0.72
2.0	0.59
4.0	0.42

The 2% lidocaine in dental cartridges is appropriate for nerve blocks but is unnecessarily high for subcutaneous infiltration local anesthesia. A 0.5% lidocaine solution is sufficient for most forms of cutaneous surgery.⁵⁷ For liposuction by the tumescent technique a 0.5% lidocaine solution is sufficient.

Hyaluronidase is not a component of the anesthetic solution used with the tumescent technique. Hyaluronidase may accelerate systemic absorption of lidocaine and this increase the peak plasma lidocaine levels.^{58,59}

Excessively rapid subcutaneous infiltration of an otherwise safe dose of lidocaine can produce a potentially toxic plasma drug concentration. Lidocaine is a capillary vasodilator with a rapid onset of action.⁶⁰ Epinephrine is a vasoconstrictor with maximum clinical effect delayed approximately 10-15 minutes after injection. For several minutes after a rapid injection of a lidocaine and epinephrine solution, systemic lidocaine absorption will be rapid until the epinephrine-induced vasoconstriction has had sufficient time to occur.

The contrast between rapid and slow subcutaneous infiltration of lidocaine is well illustrated by the following four cases. In the first instance two patients received a combination of 1% and 0.5% lidocaine with epinephrine 1:100,000 injected rapidly in less than 5 minutes.⁶¹ Total doses of 800 mg and 1350 mg of lidocaine resulted in peak lidocaine blood levels of 4.2 and 6.3 µg/ml, respectively. These potentially toxic levels were attained within 15 minutes of completion of the infiltration (Fig.9).⁶²

In contrast, as illustrated by the present study, the slow infiltration of lidocaine over 45 minutes results in initial plasma lidocaine levels that are almost undetectable. When 900 mg of 0.1% lidocaine with epinephrine 1:100,000 was given over 45 minutes, the plasma lidocaine concentrations were negligible at 5, 15, and 30 minutes after initiating the injection (Fig.9). When 1000 mg of 1% lidocaine with epinephrine 1:100,000 was given over minutes, the peak plasma concentration of 1.5 µg/ml did not occur until 9 hours after initiating the infiltration (Fig.8). – not in this doc

Epinephrine is a potent vasoconstrictor. The anesthetic effect of lidocaine is prolonged, and its peak plasma concentration is reduced by the addition of epinephrine to the anesthetic solution.^{63,64} Using a lidocaine solution without epinephrine increases the risk of reaching toxic plasma lidocaine levels.

IMPAIRED LIDOCAINE METABOLISM

Diseases or drugs that decrease lidocaine metabolism are important causes of lidocaine toxicity. Diseases causing decreased hepatic metabolism can significantly delay elimination of lidocaine from the systemic circulation. Disease of liver parenchyma decreases lidocaine metabolism directly.^{65,66} Other diseases that diminish hepatic perfusion, such as heart disease,^{67,68} or diseases associated with hypotension,⁶⁹ decrease lidocaine metabolism indirectly.

DRUG INTERACTIONS

Drugs that decrease hepatic blood flow or otherwise decrease lidocaine metabolism can lead to toxic accumulations of lidocaine. Drugs commonly associated with such adverse interactions include cimetidine,^{70,71} beta-adrenergic receptor blockers,⁷²⁻⁷⁵ phenytoin, and procainamide.⁷⁶

Other forms of drug interactions, other than impaired metabolism, may be related to lidocaine toxicity. Diazepam (Valium, Roche Laboratories, Nutley, NJ) and other benzodiazepines reduce the risk of seizures associated with excessive plasma lidocaine concentrations.^{77,78} However, this should not be interpreted to mean that the concomitant use of benzodiazepines will allow a higher safe dose of lidocaine. In pigs, with either diazepam or midazolam (Versed)

premedication, the first sign of local anesthetic toxicity may be cardiovascular collapse with a decreased chance of successful resuscitation.⁷⁹

Diazepam may increase the incidence of malignant arrhythmias induced by local anesthetics.⁸⁰ The benzodiazepine midazolam reduces the incidence of lidocaine-induced convulsions but has no significant effect on mortality in rats.⁸¹

Maximum Safe Dose

Maximum safe dose of lidocaine for subcutaneous infiltration is dependent on local tissue vascularity. For infiltration into subcutaneous fat, which is relatively avascular, surprisingly high dosages are safe. The present study estimates that a dosage of 35 mg/kg, when infiltrated slowly and as a dilute solution, should correspond to a peak lidocaine plasma level of between 3 and 4 µg/ml. Although still higher doses might be safe, such safety has not been documented.

In one report of liposuction by the tumescent technique, doses as high as 90 mg/kg were used with serous toxicity.¹⁶ While some of these patients did experience nausea and vomiting approximately 12 hours postoperatively, these symptoms might have been the result of using oxycodone for postoperative analgesia, rather than side effect of lidocaine.⁸²

When a “standard recommended maximum safe dose” has a limited scientific basis in fact, higher doses may be quite safe. For lidocaine this inconsistency is the result of considering the absorption rate for regional nerve blocks (epidural, intercostal, or pericervical) to be the same as that for subcutaneous infiltration. The tumescent technique for liposuction is a specific example. Using this technique a maximal safe dose of lidocaine infiltrated into fat is 35 mg/kg. This is five times the maximum recommended safe dose of lidocaine with epinephrine for local anesthesia, 7 mg/kg, as listed in the Xylocaine package insert.

The total amount of a dose of lidocaine that is absorbed into the systemic circulation is represented by the area under the curve (AUC) of the graph of concentration vs. time. The AUC is an important parameter in the science of pharmacokinetics. For a given dosage, the AUC is constant. Thus, for a given dosage, accelerated absorption will result in both an early peak plasma lidocaine and a peak of increased magnitude. Similarly, a delay of the peak plasma lidocaine level will result in a diminished peak level.

Liposuction reduces the AUC and therefore reduces the total amount of lidocaine that is absorbed. The peak plasma lidocaine levels are not dramatically reduced. The removal of lidocaine by liposuction does not dramatically reduce the risk of lidocaine toxicity. It is the inherent slow rate of absorption from fat that accounts for the safety of liposuction by local anesthesia using high doses of lidocaine.

Hemostasis with the Tumescent Technique

Blood loss is minimal with the tumescent technique. After remaining undisturbed in the collection bottle for 15-30 minutes, the tissue removed by liposuction using the tumescent technique will separate into a supernatant layer of viscous yellow fat, and an infranatant layer of

blood-tinged anesthetic solution. In a recent study of the tumescent technique it has been found that for each liter of fat extracted by liposuction, there is approximately 12 ml of whole blood extracted¹⁰ (Fig 10). – not in doc

Because there is so little blood loss, there is frequently almost no postoperative bruising (Fig 11). – not in doc Patients may return to a desk-type job within 1-2 days following liposuction with the tumescent technique. Elastic support garments are only required for 4 days postoperatively, and exercising may be cautiously resumed 3 days after surgery.

CONCLUSIONS

- (1) A maximal safe dosage of dilute lidocaine using the tumescent technique is estimated to be 35 mg/kg.
- (2) Slowly infiltrating a local anesthetic solution of lidocaine and epinephrine minimizes the rate of systemic absorption and reduces the potential for toxicity.
- (3) When lidocaine (1%) with epinephrine (1:100,000) is slowly infiltrated into subcutaneous fat, the peak plasma lidocaine level occurs 9 hours after the initial injection.
- (4) Dilution of lidocaine (0.5% or 0.1%) and epinephrine (1:100,000) further delays absorption and reduces the magnitude of peak plasma lidocaine concentrations. Using the tumescent technique for liposuction, peak plasma lidocaine levels occur 12 hours after the initial injection. Clinically significant local anesthesia persists for up to 18 hours. For liposuction, it is necessary to use local anesthetics, which are longer acting and potentially more cardiotoxic than lidocaine.
- (5) Liposuction reduces both the amount of lidocaine absorbed systemically and the peak plasma lidocaine levels by approximately 10%-30%.
- (6) Using the tumescent technique, liposuction can remove large volumes of fat with minimal blood loss, and minimal patient discomfort.

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