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Tumescent Anesthesia with a Lidocaine Dose of 55 mg/kg Is Safe for Liposuction

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BACKGROUND. The safe upper limit of lidocaine dosage in tumescent anesthesia for liposuction has been reported to be 35 mg/kg.

OBJECTIVE. This study was undertaken to: 1) evaluate the safety of tumescent anesthesia in liposuction when lidocaine doses greater than 35 mg/kg are required, 2) determine the time interval when the peak plasma lidocaine level occurs following administration of tumescent anesthesia, and 3) assess if the safety of large volume tumescent anesthesia is due to significant lidocaine removed by liposuction.

METHODS. Sixty patients who underwent liposuction with a mean lidocaine dose of 57 mg/kg were prospectively evaluated for development of any signs or symptoms of lidocaine toxicity by multiple interviews over a 24-hour period. In addition, another 10 patients who received a mean lidocaine dose of 55 mg/kg had serial plasma lidocaine level measurements over a 24-hour period

following liposuction. The lidocaine level of the aspirate was also measured to assess any significant lidocaine removed by liposuction.

RESULTS. No evidence of lidocaine toxicity was found based on subjective evaluation of 60 patients as well as determined by plasma sampling of 10 patients. The peak plasma lidocaine concentration occurred at approximately 4 or 8 hours after infusion of tumescent anesthesia. The 24-hour plasma lidocaine level suggests that residual lidocaine is present in the subcutaneous tissue allowing for postoperative analgesia beyond this time. A negligible amount of lidocaine was removed by liposuction as determined by the lidocaine level of the aspirate.

CONCLUSION. This study suggests that tumescent anesthesia with a total lidocaine dose of up to 55 mg/kg is safe for use in liposuction. © 1996 by the American Society for Dermatologic Surgery, Inc. *Dermatol Surg* 1996;22:921-927.

Liposuction is an accepted procedure for removal of excess localized adiposity to achieve an aesthetically pleasing body contour.¹⁻³ Liposuction can be performed safely under local anesthesia by infiltrating large volumes of dilute lidocaine with epinephrine into the subcutaneous fat, which creates a firm, swollen, or tumesced tissue.⁴⁻⁶ The use of this form of anesthesia, known as tumescent anesthesia, is increasingly popular due to the avoidance of complications associated with general anesthesia, rapid patient recovery period, elimination of intravascular fluid replacement, long-lasting postoperative analgesia, and minimal blood loss due to the extensive vasoconstriction produced by the epinephrine contained in the tumescent anesthesia.⁷⁻⁹

The safe upper limit for lidocaine dosage in tumescent anesthesia for use in liposuction has been reported to be 35 mg/kg.^{10,11} However, individuals undergoing liposuction of multiple areas such as the abdomen, flanks, and extremities can routinely require a lidocaine dose that exceeds 35 mg/kg. Lillis has reported using lidocaine doses in the range of 60-90 mg/kg without any evidence of lidocaine toxicity based on plasma lidocaine level determination over a 1-hour period.⁷ However, the maximum plasma lidocaine level occurs beyond this time.

This investigation was therefore conducted to prove that the maximum safe dose of lidocaine in tumescent anesthesia for liposuction is higher than 35 mg/kg. This study also evaluated the time interval during which the peak plasma lidocaine level occurs following the administration of tumescent anesthesia. This information is valuable for assessing the time period during which the greatest potential for development of lidocaine toxicity exists. The percentage of lidocaine removed by liposuction was also measured in order to ascertain if the safety of large volume tumescent anesthesia is due to substantial lidocaine removal by the procedure.

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Table 1. Tumescent Anesthetic Solution Formula

Ingredient	Quantity	Concentration
Lidocaine	500-1000 mg	0.05-0.1%
Epinephrine	0.5 mg	1:2,000,000
Sodium Bicarbonate	10 mEq	
Triamcinolone	10 mg	
Normal saline	1000 mL	

Materials and Methods

Study Protocol

Sixty patients who underwent tumescent liposuction of the abdomen, flanks, and/or thighs with a total lidocaine dose exceeding 35 mg/kg were prospectively evaluated by telephone interview over a 24-hour period for development of any signs and symptoms of lidocaine toxicity. In addition, another 10 individuals volunteered to undergo multiple venous samplings for lidocaine level measurement. Blood samples were obtained at 4, 8, 12, and 24 hours after tumescent anesthesia was infused. These patients were also questioned for any subjective symptoms of lidocaine toxicity during each blood sampling time. Lidocaine level determination of the infranate, the slightly blood tinged liquid portion of the aspirate, was also taken in 8 out of 10 patients upon completion of liposuction in order to determine if any significant amount of lidocaine was removed by liposuction. Lidocaine levels were measured by enzyme immunoassay.

Formulation of Anesthetic Solution

Local anesthesia consisted of a 0.05-0.1% lidocaine solution with 1:2,000,000 epinephrine in normal saline (Table 1). Sodium bicarbonate (10 mEq) was added to each liter bag to neutralize the acidity of the solution and thus decrease the pain associated with anesthetic injection.¹² Triamcinolone, 10 mg/L, was also added to the anesthetic solution for presumed reduction in postoperative swelling and inflammation. Each bag was warmed to 40°C in an incubator prior to injection. Warming has been shown to reduce the discomfort associated with the infusion of the anesthetic solution.¹³

Procedure

Each patient was fully prepped and draped. Tissue tumescence was obtained by infiltration of the anesthetic solution

into the subcutaneous tissue of the preoperative marked areas with the aid of a 20-gauge spinal needle attached to a motor-driven peristaltic pump (Wells-Johnson Company, Tucson, AZ). An injection rate of 150 mL/min was used for the 10 patients who underwent plasma sampling since varying the rate of injection affects systemic absorption of the anesthetic. Approximately 90-120 minutes were required to complete the infusion of anesthetic. All areas were infiltrated with tumescent anesthesia prior to the start of liposuction. No preoperative sedatives or analgesics were necessary. Liposuction was performed with the use of small metal cannulas attached to a clear noncollapsible plastic connecting tube which is connected to a motor-driven high vacuum pump (Wells-Johnson Company).

Results

The total lidocaine dose ranged from 49.2 to 68.1 mg/kg in the 60 patients who underwent a prospective subjective evaluation over a 24-hour period following liposuction. The mean lidocaine dose used was 57 mg/kg. No signs or symptoms of lidocaine toxicity were noted by any of these patients.

The results for the 10 patients who underwent plasma sampling are given in Table 2. The lidocaine dose administered ranged from 47.2 to 76.7 mg/kg with a mean of 55 mg/kg. Peak plasma lidocaine concentration ranged from 1.1 µg/mL for a lidocaine dose of 47.2 mg/kg to 3.6 µg/mL for a lidocaine dose of 76.7 mg/kg. Peak plasma lidocaine concentrations obtained for all patients were below the 5-µg/ml threshold when objective signs of lidocaine toxicity develop. None of the 10 patients reported any unusual neurologic or behavioral changes suggestive of early lidocaine toxicity. The relationship between the lidocaine dose administered and the peak plasma lidocaine concentration is shown in Figure 1. Using statistical analysis, the calculated correlation coefficient (*r*) between these two variables is 0.54 out a perfect score of 1.0. Therefore, there is not a linear correlation between lidocaine dose and peak plasma lidocaine level. As a result, extrapolation

Table 2. List of Patients and Results

Patient	Sex	Age (yrs)	Weight (kg)	Total Lidocaine (mg)	Lidocaine Dose (mg/kg)	Peak Plasma Lidocaine Concentration (µg/mL)	Peak Time (hrs)
1. BS	M	27	81.8	4000	48.9	2.4	4
2. DA	F	51	47.7	2250	47.2	1.1	8
3. HZ	M	51	70.5	3750	53.2	2.5	4
4. KD	F	50	65.9	3750	56.9	2.2	4
5. KF	F	48	66.0	3000	47.2	1.3	8
6. SP	F	53	52.3	2750	52.6	1.1	4
7. SM	F	50	62.0	3500	57.0	1.1	8
8. RS	F	50	58.6	4500	76.7	3.6	4
9. WA	F	62	68.2	3500	51.3	3.4	8
10. ES	F	29	43.6	2500	56.7	1.7	4
				Mean:	55.0		

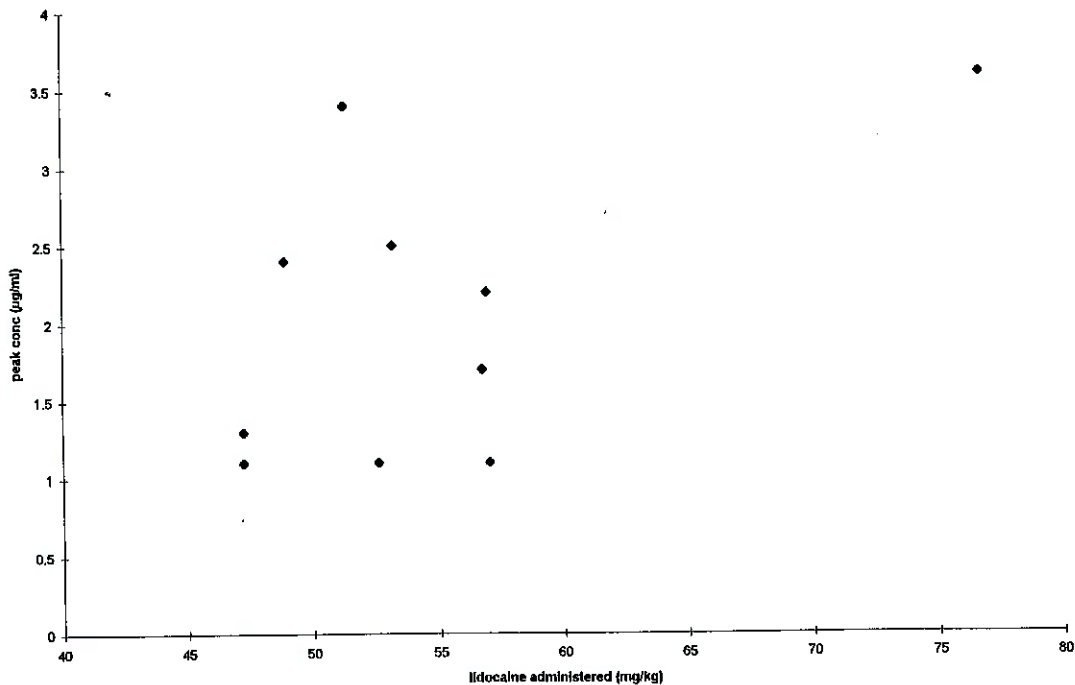


Figure 1. The relationship between lidocaine dose infused and peak plasma lidocaine concentration. There is no linear correlation ($r = 0.54$).

of maximum safe dose of lidocaine for use in liposuction cannot be made.

Figure 2 shows a plot of lidocaine infused (in milligrams) ignoring body weight versus the observed peak plasma lidocaine concentration. There is a strong correlation ($r = 0.74$) between these two variables ($P < 0.001$). Using linear regression analysis to draw the best

straight line that fits our data yields an equation that relates the amount of lidocaine administered in milligrams to the observed peak plasma lidocaine concentration:

$$\begin{aligned} \text{peak plasma lidocaine concentration } (\mu\text{g/mL}) \\ = \text{dose (mg)/1000} - 1.25. \end{aligned}$$

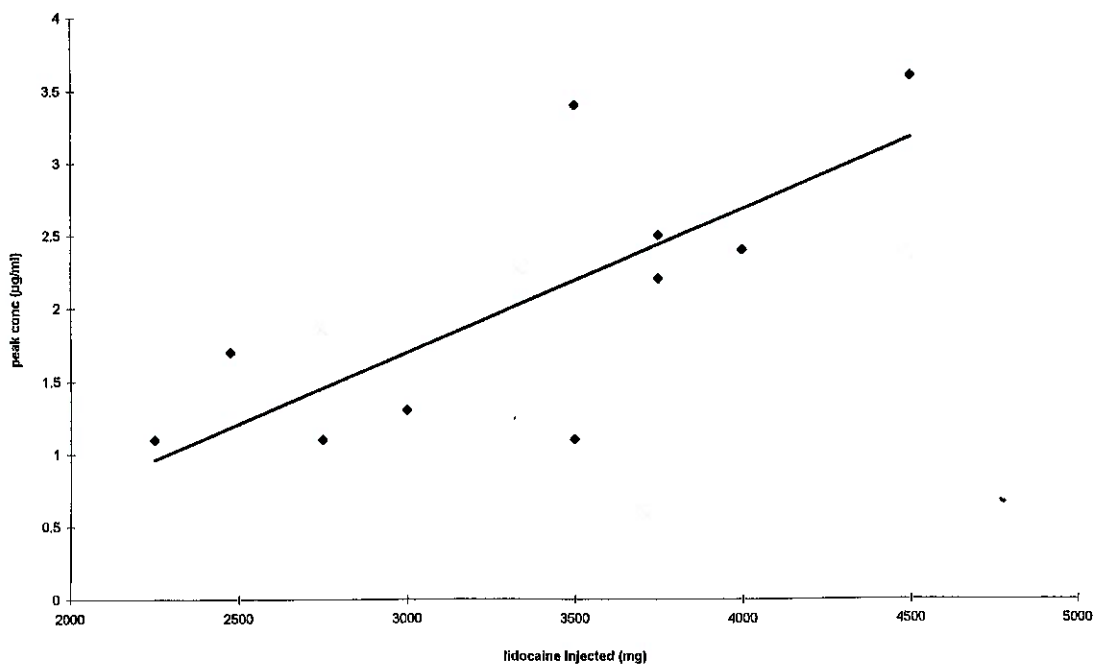


Figure 2. The linear correlation that exists between the lidocaine amount administered and peak plasma lidocaine concentration. The best linear fit is depicted by the line determined using the least-squares regression method ($r = 0.74$, $P < 0.001$).

Table 3. Serial Plasma Lidocaine Levels

Patient	Total Lidocaine (mg/kg)	Serial Plasma Lidocaine Measurements ($\mu\text{g/mL}$) at:			
		4 hrs	8 hrs	12 hrs	24 hrs
1. BS	48.9	2.4	1.8	1.0	1.1
2. DA	47.2	0.9	1.1	1.0	0.9
3. HZ	53.2	2.5	1.3	1.3	1.1
4. KD	56.9	2.2	1.8	1.7	1.8
5. KF	47.2	0.9	1.3	0.9	0.9
6. SP	52.6	1.1	0.9	0.9	0.9
7. SM	57.0	1.0	1.1	1.0	0.9
8. RS	76.7	3.6	2.6	2.4	2.6
9. WA	51.3	2.7	3.4	3.1	2.4
10. ES	56.7	1.7	1.6	1.1	0.9

The standard deviation for the peak concentration using this equation is $\pm 0.80 \mu\text{g/mL}$. This equation can be used to predict the peak plasma lidocaine concentration by knowing the total amount of lidocaine administered. This equation implies that, as a rule of thumb, there is an average $1\text{-}\mu\text{g/mL}$ increase in the peak for every 1000-mg increase in the lidocaine dose. This equation also implies that a dose of 5250 mg will produce, on average, a peak concentration of $4.0 \mu\text{g/mL}$. However, given that the standard deviation for the predicted peak is $\pm 0.80 \mu\text{g/mL}$, the dose whose upper 99th percentile is $4.0 \mu\text{g/mL}$ is about 4000 mg , while the predicted average peak at 4000 mg is about $2.7 \mu\text{g/mL}$. The predicted upper 99th percentile at 4000 mg is about $4.0 \mu\text{g/mL}$. For an average 70-kg individual, this translates to a maximum allowable lidocaine dose of 57 mg/kg .

The observed peak plasma lidocaine concentration occurred approximately 4–8 hours after tumescent anesthesia was infused. Table 3 gives the serial plasma lidocaine level measurements as a function of the total lidocaine dose. Figure 3 represents these serial measurements in graphic form. At 24 hours postinfusion,

there is still an adequate plasma lidocaine level indicating residual lidocaine in the subcutaneous tissue allowing for postoperative analgesia beyond this period.

The data collected on the aspirate are shown in Table 4. Lidocaine concentration of the infranate ranged from 49.8 to $166.0 \mu\text{g/mL}$. Lidocaine levels for two patients could not be included in the study because the aspirate was discarded prior to its lidocaine concentration sampling. The amount of lidocaine removed by the procedure was calculated by multiplying the lidocaine concentration of the infranate by the total volume of the aspirate. The percentage of lidocaine removed by liposuction was derived based on fraction of lidocaine in the aspirate compared with the total amount of lidocaine infused. The percentage of lidocaine removed by liposuction was negligible, ranging from 1.1 to 10% .

Discussion

Lidocaine toxicity is the most significant factor that limits the amount of tumescent anesthesia used in liposuction. This is in turn directly correlated to the peak

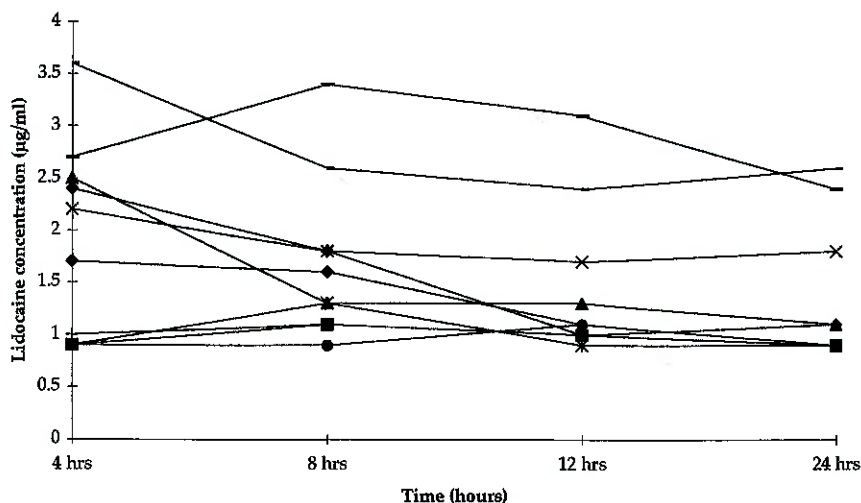


Figure 3. Serial plasma lidocaine levels measured over a 24-hour period. All levels were below the $5\text{-}\mu\text{g/mL}$ threshold for development of early signs of lidocaine toxicity.

Table 4. Aspirate Data

Patient	Total Lidocaine injected (mg)	Total Aspirate (mL)	Lidocaine Concentration of Infranate ($\mu\text{g/mL}$)	Amount of Lidocaine in Aspirate (mg)	% of Lidocaine Removed as Aspirate
1. BS	4000	950	70.5	67.0	1.7%
2. DA	2250	925	-*	-*	-*
3. HZ	3750	1900	-*	-*	-*
4. KD	3750	1700	72.0	122.4	3.3%
5. KF	3000	1800	166.0	298.8	10.0%
6. SP	2750	600	49.8	29.9	1.1%
7. SM	3500	3000	58.9	176.7	5.0%
8. RS	4500	1100	103.8	114.2	2.5%
9. WA	3500	1050	112.4	118.0	3.4%
10. ES	2475	900	53.6	48.2	2.0%

* Data not available

plasma lidocaine concentration. Various signs and symptoms are experienced depending on the plasma lidocaine level¹⁴(Figure 4). Nonspecific subjective symptoms such as lightheadedness, dizziness, and drowsiness may appear with plasma levels between 3 and 5 $\mu\text{g/mL}$. The commonly reported threshold for objective signs of lidocaine toxicity is 5 $\mu\text{g/mL}$. These signs initially involve the central nervous system and include distal extremity muscle fasciculations, shivering, tremors, parasthesias, and tinnitus. Plasma lidocaine concentrations above 10 $\mu\text{g/mL}$ may result in seizures with slightly higher concentrations causing unconsciousness and coma. Lidocaine levels beyond 20 $\mu\text{g/mL}$ result in an inhibitory effect on cardiac and peripheral vascular smooth muscle with prolonged electrical conduction time resulting in an increased PR and QRS interval and depression of the sinus and AV node. This is translated clinically into bradycardia, heart block, hypotension, and cardiac arrest.

In order to prevent lidocaine toxicity, which occurs with a lidocaine level greater than 5 $\mu\text{g/mL}$, the manufacturer of Xylocaine (Astra Pharmaceuticals) recommends that maximal dosage for the use of lidocaine

with epinephrine should not exceed 7 mg/kg of body weight or 500 mg as a total dose.¹⁵ This information is based on the use of lidocaine in epidural, intercostal, and peripheral nerve blocks. These data have been applied for local anesthesia of the subcutaneous fat without any actual studies. However, data in the literature indicate systemic uptake of lidocaine are much slower from the subcutaneous fat than from epidural blocks.^{7,10,11,16} Lillis initially reported on the safe use of lidocaine doses in the range of 60 to 90 mg/kg.⁷ However this study was based on plasma lidocaine level sampling over a 60-minute period not accounting for peak levels that occur beyond this time. Based on plasma sampling over more than 24 hours, Klein estimated that 99% of patients receiving tumescent anesthesia will have peak lidocaine concentrations below the toxic threshold of 5 $\mu\text{g/mL}$ when given a lidocaine dose of 35 mg/kg.¹⁰ This has been the basis for the current 35 mg/kg recommendation as the safe upper limit of lidocaine dosage in tumescent anesthesia.

Our investigation evaluated the safety of lidocaine doses beyond this 35 mg/kg recommendation. In the plasma sampling arm of this study, a mean lidocaine dose of 55 mg/kg infused subcutaneously using the tumescent technique did not result in lidocaine levels beyond 5 $\mu\text{g/mL}$, suggesting the safety of tumescent anesthesia at this lidocaine dose. In addition, none of our 60 patients who received a mean lidocaine dose of 57 mg/kg experienced any subjective signs or symptoms of lidocaine toxicity upon prospective clinical evaluation. These findings suggest that a lidocaine dose of 55 mg/kg is safe when using tumescent anesthesia for liposuction. Figure 5 is a helpful graph that can be utilized preoperatively by the physician in order to determine the total amount of lidocaine that can be infused subcutaneously, depending on the patient's weight, to achieve a lidocaine dose of 55 mg/kg. It is noteworthy that patient no. 8, who received a lidocaine dose of 76.7 mg/kg, had no subjective signs or symptoms of lidocaine toxicity and that the peak plasma

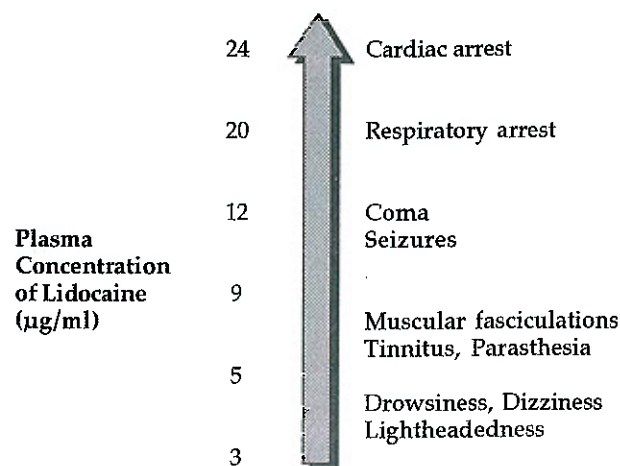


Figure 4. Common side effects associated with lidocaine toxicity depending on the plasma lidocaine concentration.

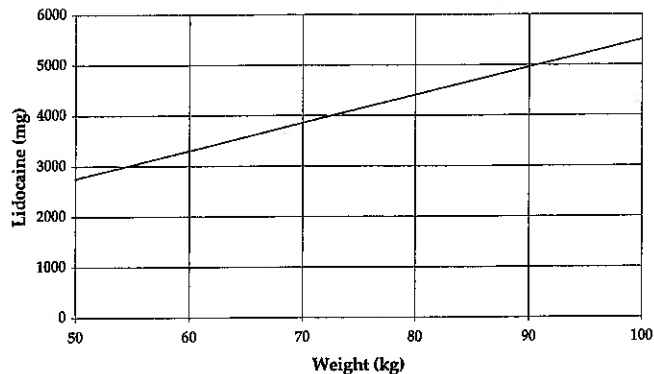


Figure 5. This diagram can be utilized to determine the total amount of lidocaine that can be infused, based on the patient's weight, to achieve a lidocaine dose of 55 mg/kg.

lidocaine level was below the toxic threshold of 5 $\mu\text{g}/\text{mL}$.

Our investigation did not demonstrate a linear correlation between the lidocaine doses used in this study and the peak plasma lidocaine concentration. Therefore, no extrapolation of our data can be made regarding the maximum safe dose of lidocaine in liposuction that can be administered, which consistently results in a plasma lidocaine level below the toxic threshold of 5 $\mu\text{g}/\text{mL}$. The reason for a nonlinear relationship between these two variables may be attributed to the unequal volume of distribution of lidocaine in the subcutaneous tissue of each patient resulting in potential differences in absorption among each individual. However, based on the linear correlation between total lidocaine infused in milligrams versus the peak lidocaine concentration, it is safe to assume that a total lidocaine dose of 4000 mg results in plasma lidocaine levels below toxic threshold in 99% of patients. It is important to note that this safe lidocaine amount is based on the weights of the volunteers in this study (43.6–81.8 kg) and therefore is only valid for this weight range.

Table 5 lists the factors responsible for the safety of large volume tumescent anesthesia. The very dilute nature of the lidocaine (0.05–0.1%) in the tumescent anesthetic solution, the relatively avascular subcutaneous fat compartment, the vasoconstrictive effect of epinephrine, the high lipid solubility of lidocaine and its strong binding affinity to adipose tissue, and vascular compression due to tissue tumescence all combine to delay systemic uptake of lidocaine.^{10,17-19}

Table 5. Factors Responsible for the Safety of Large Volume Tumescent Anesthesia

- Dilute nature of lidocaine
- Relatively avascular subcutaneous tissue
- Vasoconstriction due to epinephrine
- Lipid solubility of lidocaine
- Compression of vasculature due to infusion of tumescent anesthesia

This study also demonstrated that the plasma lidocaine concentration peaks approximately 4–8 hours after infusion of tumescent anesthesia. The significance of this delay is that by this time the patient is not in the physician's office and therefore is no longer under physician supervision. It is based on this premise that some physicians prescribe diazepam to be taken hourly for six to seven doses during this critical time period. The 4–8-hour delay in attaining peak lidocaine concentration is attributed to the slow systemic absorption of lidocaine, which in turn is dependent on its dilute concentration in each bag of anesthetic solution, the use of epinephrine, and the lipid solubility of lidocaine. It is noteworthy that plasma lidocaine levels in the patients studied still persisted at 24 hours postinfusion of tumescent anesthesia, indicating that residual lidocaine is present in the subcutaneous tissue allowing for postoperative analgesia beyond this time.

Earlier studies have reported varying time intervals for peak plasma lidocaine levels. These include 12–14 hours in one study¹⁰ and 6–12 hours in another.¹¹ The probable reasons for the earlier peak time observed in this study are the higher total lidocaine amount used, the lower dose of epinephrine used in each bag (0.5 mg), and the faster rate of anesthetic infiltration, which in our study was 150 mL/hour.

Published studies in the literature have suggested that the safety of tumescent anesthesia can be attributed to the fact that a major portion of lidocaine is removed by liposuction.²⁰ This is in contrast to other findings that only 10–30% of lidocaine is removed by the procedure.¹⁰ This study demonstrated that only 1–10% of the infused lidocaine was removed by liposuction. This finding suggests that a negligible amount of lidocaine is removed by the procedure and therefore liposuction does not play a significant role in the safety of large volume tumescent anesthesia. The reason for the low percentage of lidocaine in the aspirate is probably due to the high binding affinity of lidocaine to the adipose tissue and thus its retention in the subcutaneous compartment at the injected areas.

In conclusion, this study suggests that tumescent anesthesia with a lidocaine dose of 55 mg/kg is safe for use in liposuction. Peak plasma lidocaine concentration occurred between 4 and 8 hours following the infiltration of tumescent anesthesia. Negligible amount of lidocaine is removed by liposuction and does not contribute to the safety of large volume tumescent anesthesia. It is important to note that our findings are valid only for the use of tumescent anesthesia in liposuction of the abdomen, flanks, and thighs. Other more vascular body areas may require different doses of lidocaine to prevent lidocaine toxicity.

Survey of a larger series of patients is beneficial in order to provide conclusive findings regarding maxi-

mum lidocaine dose in tumescent anesthesia for liposuction. Future studies are also needed looking at the upper safe limit of lidocaine dose in tumescent anesthesia for use in procedures such as dermabrasion and hair transplantation, which involve more vascular body areas with increased risk of lidocaine toxicity.

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Commentary

Historically the recommended maximum dosage for the use of lidocaine with epinephrine in normal healthy adults was 7 mg/kg of body weight, or a maximum total dose not to exceed 500 mg. This dogma was ultimately challenged with the evolution of tumescent anesthesia for liposuction surgery. Injecting dilute solutions over a greater time interval into the relatively avascular subcutaneous tissue, the upper limit was exponentially raised. At the new level of 35 mg/kg, lidocaine toxicity was not reported and a new era using dilute local anesthesia was ushered in. This figure is now well-entrenched in the literature as the safe upper limit of lidocaine in tumescent anesthesia. However, sporadically reports and small studies appear, inching this figure even higher. Dr. Ostad and colleagues have greatly expanded much of the science initiated by Drs. Fournier, Klein, and Lillis regarding the safety threshold of lidocaine. Using many of the same parameters previously set forth, these authors have meticulously documented the safety of large volumes of dilute local anesthesia. Analyzing the amount of lidocaine removed and mon-

itoring patients over a longer time span for peak plasma levels and clinical signs of lidocaine toxicity has settled many controversies and simultaneously established a new upper limit of safety of lidocaine at a concentration of 55 mg/kg.

While this new upper limit has eloquently been substantiated and clearly improves our knowledge and capabilities for large-volume liposuction under local anesthesia, it is hopefully not an end point nor a figure to be misused. Perhaps in time this figure can be inched even higher with greater applicability, without additional patient risk. However, one central dogma, *primum non nocere*, "first, do not harm," should not be altered, and patient safety should always be kept a priority.

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