

## DEATHS RELATED TO LIPOSUCTION

RAMA B. RAO, M.D., SUSAN F. ELY, M.D., M.P.H.T.M., AND ROBERT S. HOFFMAN, M.D.

## ABSTRACT

**Background** The technique of tumescent liposuction involves the subcutaneous infusion of a solution containing lidocaine, followed by the aspiration of fat through microcannulas. Although the recommended doses of lidocaine are as high as 55 mg per kilogram of body weight, few safety data are available. Since reporting of adverse events associated with tumescent liposuction is not mandatory, the incidence of complications and deaths is unknown.

**Methods** We identified 5 deaths after tumescent liposuction among 48,527 deaths referred to the Office of Chief Medical Examiner of the City of New York between 1993 and 1998. The patients' records and postmortem examination results were reviewed to identify common contributory factors.

**Results** The five patients had received lidocaine in doses ranging from 10 to 40 mg per kilogram. Other drugs, such as midazolam, were also administered. Three patients died as a result of precipitous intraoperative hypotension and bradycardia with no definitively identified cause. Postmortem blood lidocaine concentrations in two of the patients were 5.2 and 2 mg per liter. One patient died of fluid overload, and one died of deep venous thrombosis of calf veins with pulmonary thromboembolism after tumescent liposuction of the legs.

**Conclusions** Tumescent liposuction can be fatal, perhaps in part because of lidocaine toxicity or lidocaine-related drug interactions. (N Engl J Med 1999; 340:1471-5.)

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**L**IPOSUCTION is the most common cosmetic operation in the United States.<sup>1</sup> The technique of tumescent liposuction is a relatively new procedure that has gained popularity in the past decade, in part because of its purported safety.<sup>2,3</sup> Tumescent liposuction involves the subcutaneous infusion of a solution containing a local anesthetic drug, followed by the aspiration of fat through microcannulas.<sup>4</sup> The infusate typically consists of 1 liter of normal saline containing 500 to 1000 mg of lidocaine, 0.25 to 1.0 mg of epinephrine, and 12.5 mmol of sodium bicarbonate.<sup>4,5</sup> Its components provide prolonged local anesthesia and minimize blood loss. Large-volume liposuction, defined as the removal of more than 1500 ml of fat, may require the infusion of several liters of this solution.<sup>6</sup> Depending on the extent of liposuction and the patient's preference, it can be performed with the patient under conscious sedation or epidural or general anesthesia.<sup>4,5,7</sup> In contrast, older liposuction techniques were

performed under general anesthesia, used larger cannulas and no infusate, and often necessitated blood transfusions.<sup>6,8</sup>

Despite doses of lidocaine as high as 55 mg per kilogram of body weight,<sup>9</sup> few complications have been reported.<sup>10-14</sup> Fatalities have been alluded to in medical correspondence but not described.<sup>15-18</sup> We report here a series of five deaths related to tumescent liposuction.

## METHODS

We reviewed all autopsy reports from January 1, 1993, through December 31, 1996, and death-notification records from January 1, 1993, through March 1, 1998, at the Office of Chief Medical Examiner of the City of New York that had been identified by a computer search using the key words "liposuction," "cosmetic," "lipoplasty," "plastic," "lipectomy," "abdominoplasty," and "therapeutic complication." We also queried city medical examiners about liposuction-related deaths currently under investigation. Five cases were identified. We then sought information about concomitant drug therapy, medical conditions other than obesity, and the details of the liposuction procedures from the patients' medical and autopsy records. The amount of lidocaine each patient received was calculated from the volume and concentration of lidocaine in the infusate, or the total number of milligrams of lidocaine infused, if available in the medical record. A total dose of lidocaine per kilogram was then calculated.

## RESULTS

During the period investigated, a total of 48,527 deaths were accepted under the jurisdiction of the Office of Chief Medical Examiner of the City of New York. Of these, 1001 deaths were certified as due to therapeutic complications, 5 of them related to liposuction. All five occurred during or after tumescent liposuction. Four of the procedures were performed by plastic surgeons and one by a general surgeon, and anesthesiologists were present during all of them. Family consent was obtained to describe four of these cases. The fifth death was caused by complications of hypotension and bradycardia; specific data regarding this case are omitted, however, owing to our inability to obtain consent. In one of the four cases described here, both the liposuction and the autopsy were performed in another jurisdiction and subsequently referred to the medical examiner's office in New York for review and consultation.

Each patient underwent a complete autopsy, includ-

From the New York City Poison Control Center, Department of Surgery—Emergency Medicine, New York University Medical Center and Bellevue Hospital Center (R.B.R., R.S.H.); and the Office of Chief Medical Examiner of the City of New York and the Department of Forensic Medicine, New York University Medical Center (S.E.E.) — all in New York. Address reprint requests to Dr. Rao at the New York City Poison Control Center, 455 First Ave., Rm. 123, New York, NY 10016, or at raorama@pol.net.

ing appropriate microscopical examination and collection of blood from the heart. Pertinent data regarding the four patients are summarized in Table 1. Resuscitation was attempted in all patients. Only the postmortem findings thought to be functionally important are described. None of the autopsies identified laryngeal edema consistent with anaphylaxis. Complete cardiac examination in each patient revealed a normal heart weight for body mass and no contributory cardiac cause of death. Postmortem toxicologic testing of blood, urine, and other available fluids and tissues did not identify illicit substances in any patient.

#### Patient 1

Patient 1 was a 33-year-old man with a remote history of appendectomy who underwent tumescent liposuction of the abdomen and flanks under general anesthesia with elective intubation as an outpatient. Preoperative serum potassium, creatinine, and aminotransferase concentrations were normal. Despite an arterial oxygen saturation of 100 percent, bradycardia and hypotension developed simultaneously 2.5 hours into the procedure; asystole ensued. Postmortem examination revealed 250 ml of peritoneal fluid without an identifiable cause, and no fluid overload, as determined by normal lung weights. Staining for fat emboli was negative. A blood sample collected 47 hours after death was positive for laudanoline, a me-

tabolite of atracurium (0.3 mg per liter); meperidine (0.7 mg per liter); and lidocaine (5.2 mg per liter) (Table 1).

#### Patient 2

Patient 2 was a 40-year-old woman with asthma and normal liver function who underwent conscious sedation for tumescent liposuction of the flanks and back while prone as an outpatient. While speaking at a time when her arterial oxygen saturation was 96 to 97 percent, 2.3 hours into the procedure, she rotated to a supine position. Within 30 seconds, a wide-complex infranodal bradycardia developed; asystole ensued. Postmortem examination revealed no gross or microscopic abnormalities consistent with acute asthmatic bronchitis. Blood samples drawn 22.5 hours after death revealed midazolam and fentanyl, in concentrations too low to be quantified, and lidocaine (Table 1).

#### Patient 3

Patient 3 was a 33-year-old woman with an unspecified psychiatric disorder who was being treated with lithium, nortriptyline, buspirone, clonazepam, sertraline, trazodone, and carisoprodol. Her hemoglobin concentration was 12 g per deciliter. As an outpatient she received parenteral analgesia for bilateral augmentation mammoplasty and tumescent liposuction

TABLE 1. DEATHS RELATED TO TUMESCENT LIPOSUCTION.\*

PATIENT No.	HEIGHT	WEIGHT	ANESTHETIC ADJUNCT (DOSE)	FLUID VOLUME			DOSE OF LIDOCAINE	DOSE OF EPINEPHRINE	DURATION OF PROCEDURE	TIME TO CARDIAC ARREST†	LIDOCAINE CONCENTRATION‡
				SUBCUTANEOUS							
				IV	INFUSION	ASPIRATE					
	m	kg			liters		mg/kg	mg	hr		
1	1.75	100	Midazolam (5 mg IV), meperidine (100 mg IV), propofol (20 mg IV), isoflurane, nitrous oxide	3	4	4	10	2	2.5	2.5	Blood: 5.2 mg/liter; brain: 4.7 mg/kg; liver: 5.2 mg/kg; peritoneal fluid: 17 mg/liter
2	1.57	84	Midazolam (5 mg IV), fentanyl (150 µg IV), methohexital (40 mg IV), droperidol (125 mg IV)	1.7	2.4	2.4	14.3	1.2	2.3	2.3	Blood: 2 mg/liter
3	1.68	95.5	Morphine (18 mg IV), di- phenhydramine (25 mg IV), oxycodone-aceta- minophen (2 tablets po)	7.3	6	6.7	31.4	3	4.5	>48	—
4	1.83	102.3§	Meperidine, zolpidem, promethazine	NA	6	5.6	40	NA	7	25	Blood: 2.9 mg/liter; brain: 4.9 mg/kg; liver: 14.8 mg/kg; gastric contents: 2.7 mg/kg

\*IV denotes intravenous, po oral, and NA not available.

†Time was measured from the start of the procedure.

‡The concentration was measured by gas chromatography.

§The weight was measured post mortem.

of the posterolateral thorax, arms, back, abdomen, thighs, buttocks, and knees, with an estimated blood loss of 700 ml. Because of postoperative pain she was hospitalized, at which time her hemoglobin concentration was 5.8 g per deciliter. She received 2 units of packed red cells, morphine sulfate through a patient-controlled analgesic pump, and 5 percent dextrose in Ringer's lactate (100 ml per hour, intravenously, throughout a hospitalization of two days). Furosemide was administered for hypoxia, wheezing, and peripheral edema.

Two hours after hospital discharge, she reported worsening dyspnea and had a syncopal event. She was found in ventricular fibrillation; resuscitation restored her circulation but she remained unresponsive. Her serum potassium and creatinine concentrations were normal. A chest radiograph revealed pulmonary edema, an echocardiogram was normal, and serum cardiac-enzyme concentrations were normal. She remained in an anoxic coma and was pronounced dead three days later. Postmortem examination revealed severe pulmonary edema with a combined lung weight of 1560 g. No pulmonary thromboemboli were identified. Toxicologic testing for lidocaine was not performed.

#### Patient 4

Patient 4 was a 54-year-old woman who underwent tumescent liposuction of the back, flanks, abdomen, and thighs under general anesthesia. Eighteen hours postoperatively, she arose from bed and became "lightheaded" and then unresponsive. Cardiac electrical activity was identified, but the patient's pulse was unobtainable. Postmortem examination revealed deep venous thrombosis of the left calf with saddle and distal pulmonary thromboemboli. Blood drawn 22.6 hours post mortem was positive for meperidine (0.8 mg per liter), normeperidine (0.1 mg per liter), and promethazine (0.1 mg per liter). The gastric contents (123 g) included the following amounts of drug: 0.3 mg of zolpidem and 0.4 mg of meperidine. Lidocaine values are shown in Table 1.

#### DISCUSSION

The most striking aspect of this series is the incompletely explained deaths of Patients 1 and 2. Both had hypotension and bradycardia and then cardiac arrest. The differential diagnosis of hypotension and concomitant bradycardia includes primary myocardial dysfunction, disruption of the autonomic nervous system, end-stage systemic disorders (such as sepsis, hypoxia, and anaphylaxis), and toxic-metabolic causes. In these two cases, the first three categories can be ruled out by the case histories and pathological findings. Metabolic disturbances such as hypermagnesemia, hyperkalemia, and hypercalcemia are unlikely, because neither patient received any of these substances.

High doses of many drugs can cause hypotension

and bradycardia. These include beta-adrenergic antagonists, the non-dihydropyridine calcium-channel blockers, cardiac glycosides, and centrally acting alpha-adrenergic agonists, to name a few. In rare instances, propofol causes hypotension and bradycardia during induction,<sup>19</sup> but it is unlikely to account for the death of Patient 1, who tolerated the induction of anesthesia without incident.

Lidocaine can cause hypotension and bradycardia. It suppresses myocardial automaticity and causes some vasodilatation. When lidocaine is given to treat cardiac dysrhythmias, therapeutic plasma concentrations range from 2 to 5 mg per liter, and concentrations above 5 mg per liter are considered toxic.<sup>20</sup> Typically, neurologic signs such as paresthesias, somnolence, and seizures are correlated with antemortem plasma concentrations of 5 to 9 mg per liter, and cardiovascular collapse has been described at concentrations above 10 mg per liter.<sup>20</sup>

In tumescent liposuction, reported doses of lidocaine range from 10 to 88 mg per kilogram,<sup>8</sup> several times higher than the maximal recommended dose of 4.5 mg per kilogram (or up to 7 mg per kilogram with epinephrine) typically used for subcutaneous infiltration.<sup>21,22</sup> The 1991 guidelines of the American Academy of Dermatologists for tumescent liposuction suggested a maximal dose of 35 mg of lidocaine per kilogram,<sup>23</sup> which was increased to "at least 55 mg per kilogram" in 1997.<sup>24</sup> This increase was based on studies demonstrating that most patients had plasma concentrations below the toxic range, despite being given these high doses.<sup>5,9,25,26</sup>

In tumescent liposuction, plasma lidocaine concentrations have been found to rise for 16 hours,<sup>6,9,25-27</sup> or even 23 hours.<sup>28</sup> The sampling intervals were often wide,<sup>6,9,27</sup> and regression analyses were used to extrapolate maximal safe doses of 35 mg per kilogram<sup>27</sup> and 55 mg per kilogram.<sup>9</sup> These analyses failed to consider that hepatic metabolism of lidocaine by means of CYP3A4 is saturable.<sup>29</sup> Once saturation occurs, absorption exceeds elimination, and plasma lidocaine concentrations increase precipitously. Administration of other drugs that are metabolized by or inhibit CYP3A4 can also alter lidocaine metabolism.<sup>29</sup> Midazolam, in particular, may compete with lidocaine for enzymatic metabolism, protect against lidocaine-induced seizures, and alter mental status,<sup>29</sup> delaying the diagnosis of lidocaine toxicity until the onset of cardiovascular collapse. General anesthesia or conscious sedation can also mask the early clinical signs of toxicity, as may have occurred in the cases of Patients 1 and 2. In some reports, "drowsiness" or "syncope," which may represent neurotoxicity, was attributed to other causes.<sup>6,30</sup>

Interpreting the postmortem blood lidocaine concentrations in Patients 1 and 2 is difficult.<sup>31</sup> No data regarding the stability of lidocaine in postmortem blood and tissue are available<sup>31,32</sup>; concentrations as

low as 4 and 6 mg per liter have been reported in deaths attributed to the drug.<sup>32,33</sup> In our series, the reported values may not reflect the concentrations in myocardial tissue at the time of cardiovascular collapse, owing to the redistribution half-life of the drug (8.5 minutes)<sup>20</sup> and the effects of attempted resuscitation. Data on the active metabolite of lidocaine, monoethylglycinexylidide, are unavailable and may be relevant. Given the available clinicopathological information, we think lidocaine toxicity or lidocaine-related drug interactions are a possible explanation for the deaths of Patients 1 and 2.

The American Society of Plastic and Reconstructive Surgeons reports that the number of liposuction procedures performed by plastic surgeons increased by 200 percent from 1992 to 1997, with 149,042 procedures performed in 1997.<sup>2</sup> The proportion involving the tumescent liposuction technique was not reported. The most recent survey from the American Academy of Cosmetic Surgery, representing several surgical disciplines, reported that 292,942 liposuction procedures were performed in 1996, an increase of more than 300 percent from 1990. Of these, 92 percent involved tumescent infusions, roughly half with general anesthesia.<sup>3</sup>

Deaths associated with earlier liposuction methods resulted primarily from pulmonary thromboembolism or fat emboli.<sup>34,35</sup> A forerunner of tumescent liposuction, the "wet technique," involved the subcutaneous infusion of a dilute solution of epinephrine.<sup>28</sup> We found no reports of concomitant hypotension and bradycardia during or after liposuction with these methods.

During earlier liposuction procedures, the amount of intravenous hydration was based on the volume of fat aspirated. In tumescent liposuction, however, the infusate not only serves as a potential source of absorbable fluid, but also provides a tamponading effect, limiting fluid losses.<sup>5,6,30</sup> Overhydration puts patients at risk for serious or fatal consequences,<sup>13</sup> as occurred in Patient 3, whose severe hemodilution was erroneously attributed to blood loss alone.

Extensive tumescent liposuction of the abdomen and lower extremities can cause impedance of venous flow, release of local tissue factors, and postoperative immobilization. These can contribute to venous stasis and thrombogenesis, as occurred in Patient 4.

Anecdotes in the lay press suggest that these deaths after tumescent liposuction are not unique. According to press accounts, patients have died from "tumescent anesthesia," epinephrine or lidocaine toxicity, hypothermia, and fluid overload.<sup>36-39</sup> Editorials in the medical literature have mentioned deaths secondary to tumescent liposuction that were due to cardiac "depression," pulmonary edema, and lidocaine toxicity,<sup>15-18</sup> but these cases were not formally reported. There is no mandatory reporting or review of adverse events associated with this privately performed

procedure, so the true incidence of complications and death is unknown.

Tumescent liposuction is not a trivial procedure, because it has the potential to kill otherwise healthy persons. Drug absorption and drug interactions, fluid management, prothrombogenic factors, and liposuction volume should be reevaluated for this popular cosmetic procedure. Deaths due to cosmetic surgery should be a matter for serious public concern.

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