Circulatory Effects of Peridural Block:

I. Effects of Level of Analgesia and Dose of Lidocaine

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Effects of different levels of peridural analgesia on cardiovascular dynamics, blood gases and limb blood flow were studied in normovolemic man. Lidocaine, 2 per cent, was injected to achieve successively greater levels of analgesic block. During analgesia to T4 or below, MABP, TPR, and CO remained within normal limits; with T2–3 block, TPR decreased 15 per cent and CO increased 22.6 per cent, resulting in a 5 per cent increase in MABP; with blocks extending to T1 or higher, TPR decreased 18.7 per cent while CO remained slightly above normal, resulting in a 16.3 per cent reduction in MABP. Blood flow in the leg increased progressively to 292 per cent with T2–3 block, while blood flow in the arm decreased as much as 58 per cent. However, after extension of the block above T1, blood flow in the arm increased to 125 per cent above normal, while blood flow in the leg declined to 219 per cent above normal. The data suggest that cardiovascular responses to peridural block, unlike responses to subarachnoid block, are not the result of sympathetic blockade alone, but involve several other factors, including the dose of local anesthetic. When several doses of lidocaine result in arterial blood levels ranging from 4 to 7 μg/ml, most subjects develop increased CO. This may be sufficient to offset vasodilating effects of high sympathetic block so that MABP remains normal. (Key words: Peridural block; Hemodynamics; Sympathetic block; Lidocaine.)

DURING the past two decades peridural block has been used with progressively greater frequency. In many centers it has supplanted subarachnoid block as a major technique for production of regional anesthesia. Although many of the articles about it contain retrospective surveys of the incidences of arterial hypotension and other side-effects, data from well controlled studies of the effects of peridural block on body functions in man are scarce. Some aspects of the technique are still unclear, a fact emphasized by Bromage.[1] To help rectify this problem, we have studied systematically the cardiovascular, respiratory, renal, and hepatic effects of peridural block in normovolemic man.[2-6] The purpose of the present study was to determine the effects of different levels of peridural analgesia on cardiovascular dynamics, blood gases, and limb blood flow in normovolemic man.

Methods and Materials

Ten healthy male volunteers, 24 to 42 years of age, were studied. Several days prior to the study each subject was examined and was thoroughly informed about the nature and risk of the proposed investigation, and a written consent was obtained. When the study began each subject had fasted for eight hours and was unmedicated. The studies were performed with the subject supine in a quiet room. Intravenous infusion of 5 per cent glucose in lactated Ringer's solution was started. Catheters were inserted under local anesthesia into the brachial artery and basilic vein and advanced into the subclavian artery and superior vena cava, respectively. The catheters were connected to strain gauges and a Gilson recorder. Using the technique previously described,[7] two vinyl catheters were inserted into the peridural space, one with its tip located at the level of the second lumbar vertebra and

the other with its tip at the second thoracic vertebra. Whitney gauges were then placed around one forearm and one leg to measure limb blood flow.[8]

Following a 30-minute rest period, control measurements were made. Variables recorded continuously were arterial blood pressure (ABP), central venous pressure (CVP), heart rate (HR) and electrocardiogram (ECG); serial measurements were made of cardiac output (CO), left ventricular performance, limb blood flow and arterial blood gas and lidocaine levels. CO was determined by the indicator-dilution technique with indocyanine green as indicator. Arterial blood was sampled anaerobically for determination of Pa_{O_2} and pH. We calculated Pa_{CO_2} by the tonometric method of Astrup and base excess by the Siggaard-Andersen method.[9] Arterial blood levels of lidocaine were measured by gas chromatography according to a modified method of Beckett *et al.*[10] Stroke volume (SV) was calculated from CO and HR. Total peripheral resistance was calculated as follows:

TPR units (dynes/sec/cm^{-5})

$$= \frac{\text{MABP (mm Hg)}}{\text{CO (ml/sec)}} \times 1,332$$

Limb blood flow was measured by venous occlusive plethysmography with mercury in a silastic strain gauge (Whitney) as the transducer.[8] To evaluate ventricular function, maximum dP/dt in the subclavian artery was obtained by electronic differentiation.[11] Left ventricular minute work (LVMW) was calculated as: $CO \times MABP \times 0.0144$ (kg/m/min), and left ventricular stroke work (LVSW) as: $SV \times MABP \times 0.0135$ (g-meters).

The achievement of total sympathetic block was ascertained with the psychogalvanic reflex (PGR)[12] in the hand. The cardiac response to moderate hypercapnia induced by allowing the subject to rebreathe in a closed system for six minutes was determined. This procedure usually resulted in a Pa_{CO_2} of 65 to 75 mm Hg, which in normal man increases HR and CO significantly.

Following completion of control measurements, 10 ml of 2 per cent lidocaine without epinephrine were injected into the lumbar peri-

dural catheter at a rate of 0.5 ml/sec. This dose usually produced analgesia to T10–11. Beginning five minutes after injection, the level of analgesia was evaluated every two minutes by firm pinprick stimulation. When the level had been stable for five minutes (usually 22 to 25 minutes after injection), all variables were measured. In the last five subjects, blood samples for lidocaine measurements were obtained at 5- to 10-minute intervals. Once all measurements had been completed, the level of analgesia was extended cephalad in a stepwise manner to three or four more successively higher segments by injecting progressively greater volumes of 2 per cent lidocaine. The levels were categorized as T10–11, T8–9, T6–7, T4–5, T2–3, and T1 or above. The highest level of analgesia achieved required a double injection, one sufficiently large to produce block to T4–5 through the lumbar catheter and another of 5 to 7 ml through the upper thoracic peridural catheter. Measurements were made at each level after the block had been stable for five minutes. The times between injections averaged slightly more than an hour.

Computer analysis of the data was performed on a within-person basis, *i.e.*, using each subject as his own control. The calculations included individual differences and paired differences from control, test results expressed as proportions of control and logarithms of tests as proportions of control. Significance of the changes was determined by the use of the paired t test and by the Wilcoxon matched-pairs signed-rank test of differences.[13]

Results

Complete data at four or more levels of block were obtained from each subject (table 1). The total doses of lidocaine given ranged from 880 mg to 1,860 mg, with a mean for the group of 1,586 mg. On a body-weight basis the doses ranged from 11 to 20 mg/kg, with a mean of 16.8 mg/kg. Absence of data at one or two of the six levels resulted in part from the unpredictable responses of some subjects to the average dose. Thus, whereas 14 ml produced T6–7 blocks in five subjects, it produced higher or lower blocks in the other five. No data were obtained for four indi-

viduals with blocks of T1 or above: we terminated the experiment at T2 upon the request of one volunteer and at T4 in another because of signs of systemic toxicity. In the other two subjects we produced hypalgesia above T1 but could not achieve complete sympathetic interruption even after a second injection through the upper thoracic catheter. In these subjects the durations of successive blocks were significantly shorter than the preceding ones, so that by the fifth injection intensity was inadequate and duration less than 20 minutes. This suggests that these subjects probably developed increasing tolerance to repeated doses of lidocaine (tachyphylaxis) unusually rapidly.

The effects on circulation, blood gases and limb blood flow produced by various levels of block are summarized in table 2 and figures 1 and 2. The table contains the control average responses for the ten volunteers and the mean of the individual differences and standard error of mean differences from control obtained at each block level. Thus, the values at the T10 level are the averages of the eight differences from control for those (eight) volunteers who developed T10 analgesia and had measurements made at that level. The graphs show the quantity Δ, which is the geometric average of individual per cent responses. It deserves re-emphasis that these are based on means of individually calculated per cent differences and not per cent differences of the means.

During peridural block at T4 or below, all variables remained normal except HR, which was significantly increased at all levels except T6–7. When the block was extended to T2–3, TPR fell a mean of 14.6 per cent while CO increased a mean of 22.6 per cent, resulting in a 5 per cent increase in MABP. Two subjects had decreases of CO, while the other six had increases ranging from 21 per cent to 76 per cent, with a mean 41 per cent above control. The increase in CO resulted wholly from a 22 per cent increase in HR and was associated with a 26.7 per cent increase in LVMW and a 17.8 per cent increase in dP/dt. Except for heart rate, none of the changes was statistically significant. When analgesia was raised to T1 or above, TPR fell 18.7 per cent;

TABLE 1. Dosage of Lidocaine and Level of Peridural Analgesia

Level of Analgesic Block	Number of Subjects	Volume of 2 Per Cent Lidocaine (ml)	
		Mean	Range
T10–11	8	10.5	10–12
T8–9	9	12.0	10–14
T6–7	5	14.0	12–16
T4–5	8	15.5	13–18
T2–3	8	20.5	16–25
T1+	6	22.0	18–26

CO, HR, and SV remained near normal while MABP decreased a significant 16.3 per cent. There were also decreases of 19.5 per cent in LVSW, 13.7 per cent in LVMW, and 14.3 per cent in dP/dt. CVP remained normal with all levels except for increases of 11 per cent for TS–9 and 22 per cent with blocks above T1 (statistically significant).

Limb blood flows changed significantly. The increases in blood flow in the leg with different levels of analgesia were: 183 per cent at T10–11, 245 per cent at T8–9, 247 per cent at T6–7, 257 per cent at T4–5, and 292 per cent at T2–3. At these levels, blood flows in the arm were -27.5, -50, -32, -58, and $+4$ per cent from control, respectively. As the block was extended above T1, blood flow in the arm increased to 125 per cent above normal, while blood flow in the leg declined to 219 per cent above normal, indicating redistribution of flow.

There were no significant changes in Pa_{O_2} and Pa_{CO_2} with blocks of T4 or below, but a 10 per cent increase in Pa_{O_2} occurred with T2–3 block, and a 20 per cent increase in Pa_{O_2} and an 11 per cent decrease in Pa_{CO_2} occurred with analgesia above T1. There were significant decreases in pH at T6–7 and T4–5 and in base excess at all block levels above T9.

The arterial blood levels of lidocaine followed the previously established curves,[14-17] obviously related to the amount of the drug injected. Lidocaine was found in the blood as early as five minutes after peridural injection; a peak level was achieved in 10 to 30 minutes, followed by a rapid decay, so that 60 minutes after injection the blood level was

TABLE 2. Hemodynamic Responses and Blood Gases at Various

	Number of Subjects	MABP (mm Hg)	CO (l/min)	HR (beats/min)	SV (ml)	TPR (dynes/sec /cm⁻⁵)	CVP (cm H₂O)	dP/dt (mm Hg /sec)
Control value	10	94.6 ± 2.2	6.83 ± 0.46	67.4 ± 0.46	101.1 ± 3.4	1159 ± 94	8.5 ± 0.7	639 ± 40
								Mean Differences
T10-11	8	1.4 ± 1.4	0.42 ± 0.19	2.5 ± 0.7*	2.5 ± 1.9	−58 ± 47	0.0 ± 0.8	28 ± 33
T8-9	9	1.9 ± 2.3	0.00 ± 0.29	3.3 ± 1.4*	−4.6 ± 2.3	24 ± 41	0.9 ± 0.9	−18 ± 114
T6-7	5	−2.0 ± 2.0	−0.09 ± 0.43	2.0 ± 1.1	−3.6 ± 5.0	−48 ± 84	0.3 ± 1.1	63 ± 80
T4-5	8	1.8 ± 3.7	0.15 ± 0.25	5.8 ± 1.0*	−5.6 ± 2.6	−24 ± 40	0.9 ± 1.3	4 ± 30
T2-3	8	4.9 ± 4.6	1.41 ± 0.77	14.5 ± 3.8*	0.6 ± 6.2	−201 ± 121	1.1 ± 1.3	148 ± 88
T1+	6	−15.3 ± 5.3*	0.11 ± 0.85	4.0 ± 4.5	−3.0 ± 7.0	−241 ± 159	2.2 ± 0.9*	−74 ± 85

* P < 0.05.

30 to 40 per cent of the peak value. With subsequent injections, peak levels increased above those of preceding injections, the final values ranging from 4.0 to 6.65 μg/ml. A curve from one subject representative of the group is shown in figure 3.
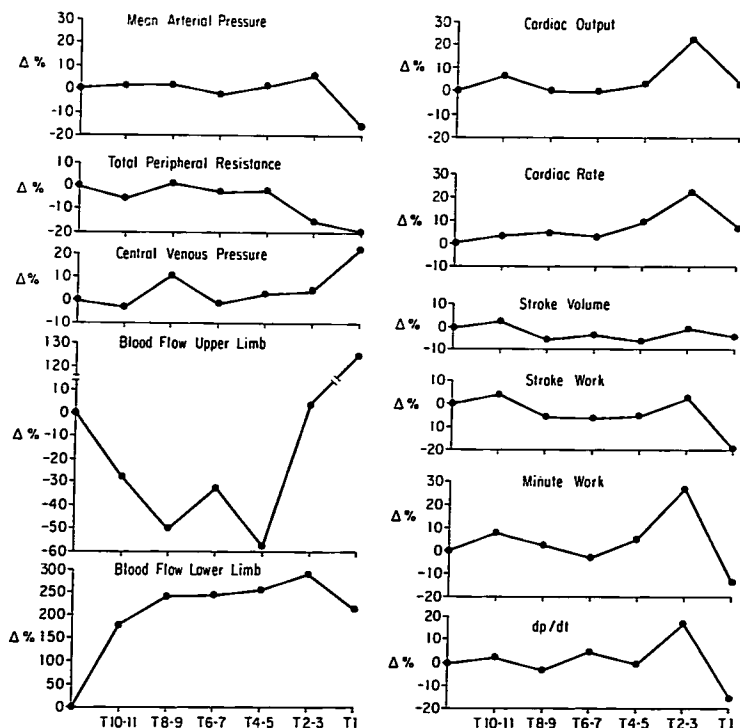

FIG. 1. Circulatory responses to various levels of peridural analgesia.

Levels of Peridural Analgesia in Ten Subjects (Mean ± SE)

ABF (ml/100 ml tissue/min)	LBF (ml/100 ml tissue/min)	SW (g-meters)	MW (kg/m/min)	PaO₂ (mm Hg)	PaCO₂ (mm Hg)	pH	BE (mEq/l)
4.1 ± 0.8	3.0 ± 0.7	137.0 ± 3.3	8.7 ± 0.6	87.3 ± 2.9	37.8 ± 0.7	7.38 ± 0.00	−2.1 ± 0.3

from Control

ABF	LBF	SW	MW	PaO₂	PaCO₂	pH	BE
−1.3 ± 0.5*	6.4 ± 2.2*	5.4 ± 2.0*	0.7 ± 0.2*	0.6 ± 2.8	−1.5 ± 0.8	0.00 ± 0.00	−0.7 ± 0.3
−2.0 ± 0.5*	7.9 ± 1.8*	−3.7 ± 8.3	0.1 ± 0.5	1.3 ± 1.7	−1.8 ± 0.8	0.00 ± 0.01	−0.6 ± 0.2*
−1.4 ± 0.8	8.8 ± 3.0*	−7.2 ± 8.6	−0.2 ± 0.7	3.4 ± 5.3	1.1 ± 0.8	−0.02 ± 0.00*	−0.7 ± 0.1*
−2.1 ± 0.7*	8.6 ± 1.9*	−14.9 ± 8.4	0.3 ± 0.6	1.1 ± 2.7	−0.9 ± 1.1	−0.01 ± 0.00*	−0.9 ± 0.3*
1.3 ± 1.9	6.7 ± 1.3*	7.9 ± 12.7	2.4 ± 1.4	8.8 ± 2.3*	−1.4 ± 0.7	0.00 ± 0.01	−0.7 ± 0.3*
3.7 ± 1.2*	5.3 ± 1.8*	−25.3 ± 10.0	−1.2 ± 1.2	20.8 ± 13.1	−3.9 ± 2.1	0.02 ± 0.02	−0.8 ± 0.6

Discussion

Until recently, cardiovascular responses to peridural block, like those to subarachnoid block, were believed to be due primarily to the effects on sympathetic nerves.[18-20] Many assumed, therefore, that the cardiovascular changes associated with peridural anesthesia were similar to those of spinal anesthesia. Data from our previous study of human volunteers showed that this was not the case and suggested the involvement of other factors, including the use of epinephrine, the local anesthetic employed, and perhaps the increase in peridural pressure during and following injection.[2] Bromage[1] has suggested five ways that peridural analgesia can influence cardiovascular dynamics: 1) dilatation of resistance and capacitance vessels; 2) paralysis of cardiac sympathetic fibers from the upper four thoracic segments, resulting in bradycardia with reduction of cardiac output; 3) vascular absorption of local anesthetics, which causes a decrease in cardiac output owing to beta receptor blockade and peripheral vascular smooth muscle depression; 4) beta receptor stimulation owing to vascular absorption of epinephrine if present, increasing CO and decreasing TPR; and 5) sudden elevation of cerebrospinal fluid pressure owing to peridural injection, producing transient reflex increases in vasomotor tone and cardiac output. We have shown the important role played by epinephrine[2, 6] and the lack of effect of increased peridural pressure.[4]

The results of the present study indicate that with continuous peridural block achieved with lidocaine alone, the problem is even more complex than proposed by Bromage. Apparently, factors other than the extent of sympathetic

block and depressant effects of local anesthetics are involved. Moreover, the factors interact and the net effect varies with circumstances. Peridural block extending to T4–5 usually is not associated with significant hypotension. Normovolemic man apparently can maintain cardiac output near normal or even increase it and compensate for vasodilatation in the anesthetized part of the body by vasoconstriction in the unanesthetized part. Results of many studies of spinal anesthesia[21] and several studies of single-dose peridural block[2, 22] confirm this observation. Thus, Shimosato and Etsten[22] found that both spinal and peridural blocks to sensory levels between
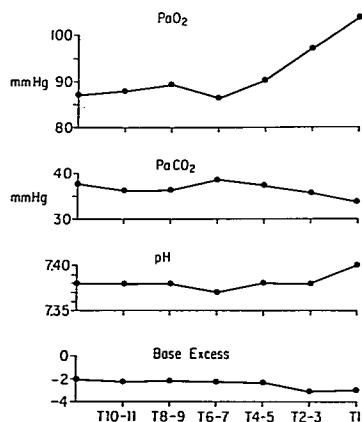

FIG. 2. Arterial blood gases and acid–base balances during various levels of peridural analgesia.
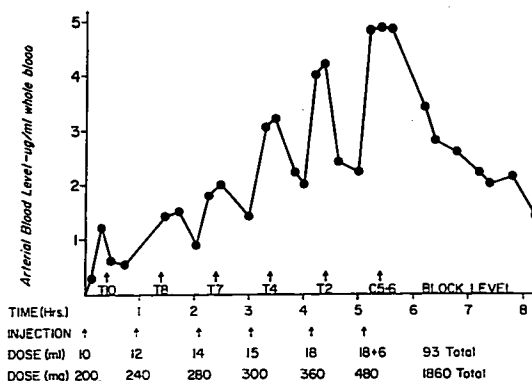
Fig. 3. Blood levels of lidocaine in one subject following several peridural injections.

TIME (Hrs.)	1	2	3	4	5	6	7	8
INJECTION ↑	↑	↑	↑	↑				
DOSE (ml) 10	12	14	15	18	18+6	93 Total		
DOSE (mg) 200	240	280	300	360	480	1860 Total		

T4 and T7 were associated with a 16 per cent decrease in mean arterial pressure, a 12 per cent decrease in peripheral resistance, but no significant change in stroke volume index, heart rate and, consequently, cardiac index. In previous studies [2, 6] of peridural block with lidocaine without epinephrine, we found that T5 analgesia was associated with decreases of about 5 to 10 per cent in mean arterial pressure and peripheral resistance, whereas cardiac output remained within 5 per cent of normal.

The cardiovascular alterations with analgesia to T2–3 in the present study were quite unexpected. Because such blocks presumably involved three or four of the five cardiac sympathetic segments, significant reductions in HR and SV, and with them CO, were anticipated. Instead, we saw increases in HR and CO and commensurate increases in LVMW and in dP/dt. The mechanism of these unexpected cardiovascular effects of high peridural block achieved with several injections of lidocaine is not known. One may speculate that they represent the action of lidocaine on the cardiovascular system.

Although lidocaine is generally believed to produce direct cardiovascular depression, ample evidence now indicates that moderate arterial blood levels of lidocaine are usually associated with increased cardiac output and slight hypertension. This was first suggested by Kimmey and Steinhaus,[23] who found in-

creased blood pressures in patients given intravenous lidocaine (1 to 2 mg/kg body weight) during general anesthesia. This was subsequently confirmed in human volunteers by Foldes and colleagues [24] and Jorfeldt and associates,[25] who reported that blood levels of lidocaine ranging from 3 to 6 μg/ml were associated with increases in arterial pressure, cardiac output and tachycardia. Similar results were found in patients receiving single intravenous injections of lidocaine for treatment of cardiac arrhythmias.[26, 27]

The cardiac stimulating effects of lidocaine may be produced through central nervous system action or potentiation of endogenous epinephrine or norepinephrine, or may simply be a compensatory reflex response to vasomotor blockade. A central mechanism is suggested by the studies of Kao and Jalar,[28] who found that intravenous lidocaine in doses of 1 to 2 mg/kg body weight produced significant increases in cardiac output and blood pressure. The increase in cardiac output did not occur after midbrain transection, suggesting a central action of the drug. This hypothesis was substantiated by their results in cross-circulation experiments in which they were able to isolate the effects of lidocaine on the central nervous system from those on heart and peripheral vessels. The potentiating mechanism is suggested by studies of Van Dongen [29] and D'Amato and Truant,[30] who found that lidocaine, cocaine, and some other local anes-

thetics consistently potentiated the effects of exogenous epinephrine and norepinephrine on blood pressure. These results prompted Austen and Moran [31] to suggest that, conceivably, the rise in blood pressure following administration of lidocaine may be due to potentiation of endogenous catecholamines. Currently we are studying this problem in man.

Our data suggest that in normal man arterial blood levels of lidocaine ranging from 4 to 7 μg/ml are usually associated with an increase in cardiac output which may be sufficient to offset the vasodilating effect of high sympathetic block, provided some cardiac sympathetic nerves remain intact. Because such blood levels usually develop following single peridural injections of 400 to 500 mg or following several injections of 200 to 300 mg of lidocaine,[14-16, 19] these findings have obvious clinical implications. They are especially important in patients receiving "continuous" peridural block for extensive surgical intervention or prolonged labor, for which injections are usually repeated hourly. Since man requires considerably more than an hour to metabolize and eliminate lidocaine,[32-34] the drug will accumulate to a significant level in blood and body tissues.

Our results with peridural block extending above T1 are not quite in accord with those of McLean and associates,[35] who published the only other hemodynamic study of total sympathetic block achieved with peridural anesthesia. In seven patients scheduled for major operations, they studied the separate and combined hemodynamic effects of segmental cervicothoracic (C5 to T4) peridural block and total peridural block (C5 to S5) achieved by supplementing the former with an extensive thoracolumbar peridural block. Total sympathetic block decreased CVP 26 per cent, TPR 6 per cent, HR 8 per cent, SV 13 per cent, CO 19 per cent and MABP 20 per cent. In contrast, in our subjects, CO remained slightly above normal, whereas TPR decreased 20 per cent, resulting in a 15 per cent decrease in MABP. The differences between the results of the two studies may be related to differences between the subjects' conditions, the agents used, and total doses injected. Their patients had a mean age of 49 years, had pathologic conditions requiring surgical

treatment, and were given mepivacaine (Carbocaine) in doses of 5 mg/kg, whereas our ten volunteers had a mean age of 32 years, were healthy, and received lidocaine in total doses averaging nearly 17 mg/kg.

In conclusion, because our data were obtained in young healthy subjects they should not be extrapolated to sick surgical patients. Furthermore, the cardiovascular responses of individuals to different levels of sympathetic blockade vary widely, depending upon degree of sympathetic tone prior to the block, whether blood volume is normal, the efficiency of neurogenic homeostatic mechanisms, and the condition of the heart. Patients with high sympathetic tone provoked by apprehension, injury, or disease, or with hypovolemia, have much greater hemodynamic changes. Patients in whom circulatory homeostatic mechanisms are dampened by narcotics, intravenous anesthetics, and other depressant drugs may not be able to mobilize compensatory mechanisms as effectively, and consequently will develop greater degrees of cardiovascular depression. Finally, with serious myocardial disease the reserves of both the extrinsic and intrinsic cardiac regulatory systems are decreased as the heart dilates and resting sympathetic tone increases.[36, 37] Under these conditions, removal of sympathetic tone is poorly tolerated. This is especially true of patients with congestive heart failure in whom there is significant arteriolar and venular constriction modulated by increased sympathetic activity to complement the heart's reduced performance.[38] Since the increase in total peripheral vascular resistance in heart failure is an important compensatory mechanism for maintaining arterial pressure when cardiac output is low, extensive sympathetic blockade in these patients may prove disastrous.

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