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Preoperative Stellate-ganglion Blockade to Prevent Hypertension Following Coronary-artery Operations

To the Editor:—The paper by Bidwai *et al.*¹ describing the prophylactic use of a right stellate ganglion block to prevent postmyocardial revascularization hypertension refers extensively to our work relating to that condition.² It's always gratifying to see one's observations confirmed and extended; however, we wish to underline a few points that could be forgotten in evaluating the initial success of a new method.

Perioperative hypertension can be due to many causes, as Bidwai *et al.*¹ would be the first to admit; all are not necessarily related to cardiovascular reflexes. Hypertension following cardiopulmonary bypass may be due to the lingering effects of increased serum catecholamines or changes in plasma renin activity.³ Hypertension in the postoperative period can be due to pain, anxiety, hypoxia, hypercarbia, hypothermia, shivering, and possibly hypervolemia.⁴ Therefore, therapy must be carefully designed for each individual case according to its merit. Further, careful evaluation of the risks of any procedure must be weighed against its possible advantages. The routine use of prophylactic stellate block to avoid some rise of arterial pressure that will otherwise occur in 30 per cent of patients should be carefully evaluated against possible other hemodynamic effects and complications of that procedure. In addition, one cannot always anticipate accurately the duration of cardiac surgical procedures, which

may unexpectedly outlast the duration of action of even a long-acting local anesthetic agent.

These remarks are not intended to belittle the importance of prophylaxis, but only to point out the many factors that must be examined before an overall recommendation can be accepted.

FAWZY G. ESTAFANOUS, M.D.

Department of Cardio-Thoracic Anesthesia

FETNAT M. FOUAD, M.D.

ROBERT C. TARAZI, M.D.

Research Division

The Cleveland Clinic Foundation

9500 Euclid Avenue

Cleveland, Ohio 44106

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More on the Pharmacokinetics and Dynamics of Muscle Relaxants

To the Editor:—The suggestion by Stanski and co-workers^{1,2} that recovery from nondepolarizing neuromuscular blockade can be totally explained in terms of competitive drug-receptor interactions leaves certain questions unanswered. These authors dispute the contention of Agoston, Feldman and Miller³ that a

dissociation rate constant for the relaxant-receptor complex is the rate-limiting step in isolated-arm experiments. They argue that the temporal disequilibrium between plasma levels of relaxant and observed effects can be explained by physical factors such as muscle perfusion (washout rate), and that the

rate of decrease in plasma concentration of relaxant determines the rate of recovery from paralysis. They calculated that on the basis of drug-tissue solubility and regional blood flow the half time for equilibration between plasma concentration and pharmacologic effect for *d*Tc should be 4.6 min ($t_{1/2}K_{eo} = 4.6$ min).

If drug-receptor interaction is instantaneous, as assumed by Stanski and Sheiner, then the recovery index (25 to 75 per cent recovery time) as determined by Feldman and Tyrrell⁴ should be essentially identical for all relaxants. This is not the case. While the recovery indices in isolated-arm experiments for nondepolarizing relaxants are similar (gallamine 9.8 ± 1.3 min, pancuronium 10.4 ± 1.4 min, *d*-tubocurarine 12.8 ± 1.3 min), the recovery index for decamethonium is significantly shorter (2.6 ± 0.3 min). A $t_{1/2}K_{eo}$ of about 4 min is compatible with the rapid recovery of function seen in isolated-arm experiments with decamethonium. It does not, however, explain the delayed recovery observed using nondepolarizing relaxants in this experimental model.

Although the exact relationship between receptor occupancy by neuromuscular blocking drugs and twitch depression is not clearly defined, there is general agreement that at less than 70 per cent receptor occlusion ($Y_B = 0.70$) no effect on single twitch tension is seen, and when Y_B exceeds 0.90, paralysis is essentially complete.⁵ The values of Y_B for 25 and 75 per cent depression for single twitch tension lie somewhere in between.

Shanks *et al.*⁶ state that during the offset of paralysis, when twitch depression is in the 20–80 per cent range, the rate of decline of paralysis is a function of the (log) plasma concentration. They found that recovery from 80 to 20 per cent twitch depression is associated with a decrease of less than 50 per cent in the plasma concentration of pancuronium. If this is so, then reasonable values of Y_B for 25 and 75 per cent recovery are 0.88 and 0.80, respectively.

Assuming an isolated-arm experiment (using *d*Tc as the test drug) is performed, and at the moment of tourniquet release paralysis is complete ($Y_B = 0.92$), then table 1 should describe the events during recovery. Initially, the plasma concentration of *d*Tc (in units of K_B , the dissociation constant) should be 11.0 (uK_B). If the $t_{1/2}K_{eo}$ is 4.6 min, drug concentration is less than 8.0 (uK_B) by 2 to 3 min after tourniquet release and 25 per cent recovery has occurred. Four minutes later, plasma *d*Tc concentrations are in the range of 4.0 (uK_B) and 75 per cent recovery is present. By 10 min following tourniquet release full recovery to 30 Hz stimulation is complete. These are not the

TABLE 1. Predicted Changes in Receptor Drug Concentration and Receptor Occupancy in Isolated-arm Experiment When Plasma Level is Zero and $t_{1/2}K_{eo}$ is 4.6 Min

Time Since Tourniquet Release (min)	Drug Concentration (in Units of K_B)	Receptor Occupancy (Y_B)*
0	11.0	0.92
1	9.5	0.90
2	8.1	0.89
3	7.0	0.88
4	6.0	0.86
5	5.2	0.84
6	4.5	0.82
7	3.80	0.79
8	3.3	0.77
9	2.84	0.74
10	2.44	0.71
12	1.81	0.64

* $Y_B = \frac{[B]}{1 + [B]}$, where [B] is drug concentration in units of K_B .

results observed by Feldman and Tyrrell.⁴ In fact, full recovery of neuromuscular function following *d*Tc often requires 30–45 min.

Physical washout may account for the rapid recovery from a depolarizing relaxant following tourniquet release, but then some other factor must be invoked to explain the significant difference in recovery times between decamethonium and pancuronium. The existence of a strong receptor dissociation constant for the latter drug still seems the most plausible explanation. Until these discrepancies between theory and observed results can be reconciled, the assumption that *d*Tc-receptor dissociation occurs instantaneously must be questioned.

AARON F. KOPMAN, M.D.
Attending Anesthesiologist
Long Island Jewish-Hillside Medical Center
New Hyde Park, New York 11042

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