

CORRESPONDENCE

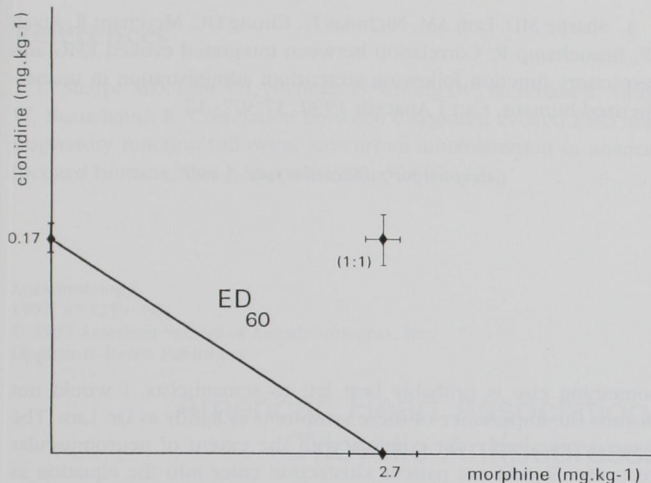


Fig. 1. Isobolographic representation of the interaction of morphine and clonidine combined in a 1:1 proportion, at 60% level of response. The axes indicate the mean doses (\pm SEM) of morphine (abscissae) and clonidine (ordinates) that individually produced 60% of maximal response. The diagonal line connects equi-effective doses of each drug alone, and the point to the right shows the doses of the combination (\pm SEM) that produced the same level of effect. The results demonstrate that the combination is antagonistic.

the figures, the small magnitude of the bars (SEM) and the different scales used in ordinates and abscissae made graphic representation sometimes difficult; it is also possible that when drawing the isoboles, a few millimeters were misplaced. However, in table 3 we included the statistical evaluation of the results, which was obtained by comparing the doses that produced the expected effects (additivity) and the actual doses that produced the observed effects (experimental data). A P value < 0.05 was considered statistically significant.

We sincerely regret the errors, and appreciate the considerate comments of Drs Asai and Mapleson.

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(Accepted for publication July 7, 1997.)

Anesthesiology
1997; 87:1257-8
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Lippincott-Raven Publishers

Visual Disturbance and Residual Paralysis

To the Editor:—It is with more than passing interest that I read the article on residual paralysis in volunteers by Kopman *et al.*¹ and the accompanied editorial by Brull.² The major significant finding was that visual changes (and subjective symptoms) persisted long after recovery of other functions. The authors are to be congratulated for observing and reporting this obviously common, yet always overlooked, phenomenon. As noted by Kopman *et al.*, we performed a similar study examining the correlation between respiratory function and electromyography in volunteers during atracurium infusion.³ Our primary objective was to examine respiratory function and other clinical tests (hand-grip, head-lift, and so on) but not visual symptoms; therefore, we did not record them systematically nor did we report them. As one of the participants in the study, I remember I had to delay going home because I continued to have diplopia 60 min after the end of the study when all other musculoskeletal functions were normal. Moreover, I attempted to correct the diplopia by self-administering 2.5 mg of neostigmine and 1.2 mg of atropine intravenously, which produced severe abdominal pain, but no improvement in my diplopia. It was not until another 60 min had elapsed before I could drive home. As far as I know, the persistence of diplopia after reversal with anticholinesterase has neither been reported nor studied.

On a rhetorical note, why is the persistence of diplopia surprising? And is it important or necessary to have complete recovery of the eye functions before we discharge patients home?

We know that 3 mg of tubocurarine ("precurarization" dose) would produce visual disturbance virtually in all patients, with preservation of respiratory and muscular functions in the majority of them. Is it surprising then that the visual disturbance persists after recovery of other muscle functions? The authors are correct in contending that train-of-four (TOF) during the onset of neuromuscular blockade cannot be equated to TOF during offset, but this does not detract from the previous observation because the visual symptoms occur not during the onset of muscular blockade but with a "nonparalyzing precurarization dose."

As for the importance of visual symptoms, because we advise patients not to drive or otherwise engage in activities that require mental and intellectual capacity for 24 h and because the major complication of residual muscle paralysis is compromised respiratory function, why should we not be satisfied with complete recovery of respiratory function only? I would suggest that we warn the ambulatory patients about the persistent visual disturbances and not interpret this as "residual weakness."

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2. Kopman AF, Yee PS, Neuman GG: Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *ANESTHESIOLOGY* 1997; 86:765-71

Anesthesiology
1997; 87:1258
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Lippincott-Raven Publishers

In Reply:—Dr. Lam's inability to antagonize residual diplopia with neostigmine after atracurium administration is fascinating because we have had a similar experience. Before the 10 cases that we reported,¹ we did a pilot study using rocuronium as the test drug. One individual (a man aged 26 years and weighing 70 kg) complained of pronounced visual disturbances despite a measured train-of-four (TOF) fade ratio of 0.93 at the end of the study. At this time, the subject was given 0.4 mg of atropine and 5.0 mg of edrophonium intravenously. The TOF ratio promptly returned to a value of 1.00, but the subject reported that if anything his vision got worse. Blurred vision persisted for an additional 60 min.

This observation, if it can be reproduced, raises several questions. What is the effect (if any) of intravenous atropine, glycopyrrolate, neostigmine, and edrophonium alone or in combination on visual acuity and extraocular muscle function? Is it advisable to attempt to reverse diplopia if that is the sole residual effect of an administered relaxant? Is it even possible to do so? Certainly this is an area deserving of further investigation.

The question of whether persistent visual disturbances after the use of nondepolarizing relaxants represents "residual weakness" or

3. Sharpe MD, Lam AM, Nicholas FJ, Chung DC, Merchant R, Alyafi W, Beauchamp R: Correlation between integrated evoked EMG and respiratory function following atracurium administration in unanesthetized humans. *Can J Anaesth* 1990; 37:307-12

(Accepted for publication July 7, 1997.)

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(Accepted for publication July 7, 1997.)

Anesthesiology
1997; 87:1258-9
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Lippincott-Raven Publishers

In Reply:—Thank you for the opportunity to comment on Dr. Lam's correspondence and very interesting observations. Dr. Lam correctly identified that subjective symptoms of visual changes such as diplopia are "obviously common, yet always overlooked, . . ." More importantly, he reports that his own symptoms of diplopia (after participation as a volunteer in an electromyographic study¹) persisted for 60 min after self-administering anticholinesterase reversal.

Although his questions were rhetorical, I would nevertheless like to respond: the persistence of diplopia^{2,3} was surprising because in some cases it was evident for up to 90 min after the train-of-four (TOF) ratio had returned to a value of 1.0. This persistence was evident after administration of a drug (mivacurium) that has a spontaneous recovery index of 7-8 min. This is as surprising as Dr. Lam's finding that atracurium-induced diplopia was not improved by anticholinesterase reversal. As to whether "it is important or necessary to have complete recovery of eye functions before we discharge patients home," it is perhaps not imperative to do so if patients received an ultra-short-acting muscle relaxant. Would we feel as

comfortable discharging our patients after administration of one of the older (and cheaper), long-acting relaxants, as we are increasingly being "encouraged" to do?

Finally, as to whether we warn ambulatory patients about "persistent visual disturbances," and not interpret them as "residual weakness," it is really a matter of semantics. I doubt that the patients' subjective symptoms would be dramatically improved by our warning, regardless of what we call these symptoms. In the present era of expanding ambulatory surgery, when emphasis is placed on rapid recovery, quick discharge, and patient satisfaction scores, even "persistent visual disturbances" may be perceived by our patients (and managed care organizations) as undesirable.

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