

21. O'Malley K, Crooks J, Duke E, et al: Effect of age and sex on human drug metabolism. *Br Med J* 3:607-609, 1971
22. Kangas L, Kanto J, Forsström J, et al: Protein binding of diazepam and *N*-demethyl-diazepam in patients with poor renal function. *Clin Nephrol* 5:114-118, 1976
23. Giles HG, Zilm DH, Frecker RC, et al: Saliva and plasma concentrations of diazepam after a single oral dose. *Br J Clin Pharmacol* 4:711-712, 1977
24. Kanto J: Plasma concentrations of diazepam and its metabolites after peroral, intramuscular, and rectal administration. Correlation between plasma concentration and sedatory effect of diazepam. *Int J Clin Pharmacol* 12:419-426, 1975
25. Hillestadt L, Hansen T, Melsom H, et al: Diazepam metabolism in normal man. I. Serum concentrations and clinical effects after intravenous, intramuscular, and oral administration. *Clin Pharmacol Ther* 16:479-484, 1974
26. Hunter AR: Diazepam (Valium) as a muscle relaxant during general anaesthesia: A pilot study. *Br J Anaesth* 39:633-639, 1967
27. Prensly AL, Raff MC, Moore MJ, et al: Intravenous diazepam in the treatment of prolonged seizure activity. *N Engl J Med* 276:779-783, 1967
28. Kanto J, Iisalo EUM: Diazepam as an inductive agent in two kinds of combination anaesthesia. The disappearance of diazepam and its metabolites from the plasma. *Ann Chir Gynaecol Fenn* 62:251-255, 1973
29. Brown SS: Studies of diazepam: An intravenous anaesthetic, Diazepam in Anaesthesia. Edited by PF Knight, CG Burgess. Bristol, John Wright and Sons, Ltd., 1968, pp 52-55
30. Randall LO, Heise GA, Schalleck W, et al: Pharmacological and clinical studies on Valium, a new psychotherapeutic agent of the benzodiazepine class. *Curr Ther Res (Clin Exp)* 3:405-425, 1961
31. Sellman R, Hurme M, Kanto J: Biliary excretion of diazepam and its metabolites in man after repeated oral doses. *Eur J Clin Pharmacol* 12:209-212, 1977
32. Kanto J, Sellman R, Haataja M, et al: Plasma and urine concentrations of diazepam and its metabolites in children, adults, and diazepam-intoxicated patients. *Int J Clin Pharmacol* 16:258-264, 1978

Anesthesiology  
51:159-160, 1979

## Objective Measurement of Succinylcholine-induced Fasciculations and the Effect of Pretreatment with Pancuronium or Gallamine

ERIK C. JANSEN, M.D.,\* AND PAUL HOWARDY HANSEN, M.D.†

Succinylcholine induces fasciculations at the onset of the depolarizing block. Pretreatment with a non-depolarizing agent *e.g.*, pancuronium or gallamine, is known to attenuate the fasciculations.

An objective method for measurement of fasciculations was not found in literature. A system was developed and applied in a clinical trial.

### MATERIALS AND METHODS

The circumference of the upper arm was chosen as the point of measurement. Variations in circumference were recorded by a strain gauge, an elastic tube filled with mercury (.015 × .040 inch, length

16 cm, from Parks Electronics, Beaverton, Oregon). The gauge was part of a bridge network. The signal was converted from a DC into an AC signal, as only the alterations of circumference were of interest. The signal was amplified and stored on a Philips Minilog® four-track tape recorder and later demonstrated on an x/y recorder. The system meets the safety requirements of IEC regulations. To obtain the wanted quantification of fasciculations we used a Tektronix® DC 504 pulse counter with variable threshold. The threshold was set so that all deflections larger than those of the brachial artery were registered by the pulse counter. In this way the fasciculation count consists of the muscular fasciculations and the transmitted movements associated with a few controlled respirations.

The study comprised three groups of 20 patients each, scheduled for elective surgical procedures. All patients were of ASA class I, and all body weights were similar. Patients with diseases of the arm were excluded from the study.

The patients were premedicated orally with diazepam (0.2 mg/kg). They were randomly allocated to one of three induction techniques: 1) Thiopental, iv, from

\* Clinical lecturer, Department of Anesthesia, Herlev Hospital, DK-2730 Herlev, Denmark.

† Assistant in Anesthesia, Department of Anesthesia, Herlev Hospital, DK-2730 Herlev, Denmark.

Received from the Department of Anesthesia, Herlev Hospital, University of Copenhagen, and Biomechanical Laboratory T<sub>2</sub>, Gentofte Hospital, University of Copenhagen, DK-2900 Hellerup, Denmark. Accepted for publication December 7, 1978.

Address reprint requests to Dr. Jansen: Biomechanical Laboratory T<sub>2</sub>, Gentofte Hospital, University of Copenhagen, DK-2900 Hellerup, Denmark.

TABLE 1. Results of Visible Fasciculation Count and Electric Fasciculation Count after Succinylcholine, and after Pancuronium-Gallamine and Succinylcholine

	Visible Fasciculation Rating	Fasciculation Counts
Succinylcholine (20 patients)		
Median	3	277.5
25th and 75th percentiles	2.25-3.0	135.3-312.0
Pancuronium (20 patients)		
Median	1	37.5
25th and 75th percentiles	0-1	11.75-67.0
Gallamine (20 patients)		
Median	1	50.5
25th and 75th percentiles	0-1	22.30-77.5

0-20 sec until loss of eyelid reflex. At 60-65 sec succinylcholine, 75 mg, was injected iv, and fasciculations were recorded until clinical relaxation occurred and endotracheal intubation was done. The patients were ventilated with N<sub>2</sub>O-O<sub>2</sub>, 7:3 l/min. 2) The same as 1), but preceded by iv injection of pancuronium, 1 mg, 180 sec before administration of thiopental. The dose of succinylcholine was increased to 100 mg. 3) The same as 2), but gallamine, 20 mg, was used instead of pancuronium.

To compare measured fasciculations with the clinical impression of fasciculations, they were rated: 0, none; 1, sparse; 2, some; 3, many. For practical reasons the observer could not be blinded as to the drugs administered, but he was blinded concerning the pulse count.

The fasciculation counts in the three groups were compared using the Mann-Whitney rank sum test for unpaired data. The relationship between fasciculation count and the visual ratings of fasciculations were evaluated by a rank correlation test.<sup>1</sup>

## RESULTS

Fasciculation rating and counting are shown in table 1. There was significant difference ( $P < 0.01$ ) between the fasciculation counts of the pretreated groups and the group not pretreated with a nondepolarizing agent. Responses to pancuronium and gallamine did not differ significantly. The correlation between fasciculation counts and visually observed effects was  $r = 0.78$  ( $P < 0.001$ ).

## DISCUSSION

The results showed a correlation between clinically observed fasciculations and the measured fasciculation count. There was clear difference between the undamped succinylcholine-induced fasciculation count and the count following pretreatment with a nondepolarizing muscle relaxant.

The tendency towards reduction of fasciculations after treatment with pancuronium compared with gallamine should be considered in the light of the difficulty of a very precise threshold adjustment of the pulse counter. The possible transmitted artifact due to the controlled ventilation may add approximately 12 counts during the recording time.

Visible fasciculation rating of the effect of pretreatment with pancuronium has been performed by Domaoal *et al.*<sup>2</sup> Cullen<sup>3</sup> made a similar study, which also included the effect of gallamine. Visible rating of fasciculations is difficult to perform, and most often a four-step rating system is used, as in the present investigation.

Our correlation between visible fasciculations and fasciculation counts may be considered moderate, probably because the fasciculations can vary in frequency and amplitude in the different patients. The difference between visible and electronically measured fasciculations will be most marked when the fasciculations are of hardly visible low amplitude and high frequency. The high sensitivity is the advantage of the strain-gauge system. In the present study the system supports a well-known clinical fact. Because of its sensitivity, the method offers possibilities in comparative and basic studies. The method of objective fasciculation counting may be used in assessing the effects of other drugs that interact with succinylcholine-induced fasciculations.

The strain-gauge technique provides sensitive, objective information about fasciculations induced by succinylcholine. The method confirms that pretreatment with pancuronium or gallamine has a uniform and significantly attenuating effect on such fasciculations.

## REFERENCES

1. Wulff HR: Rational Diagnosis and Treatment. Oxford, Blackwell Scientific Publications, 1976, pp 35-38
2. Domaoal AM, Weiniger FC, Wolfson MB: Precurarization using pancuronium. *Anesth Analg* (Cleve) 54:71-75, 1975
3. Cullen DJ: The effect of pretreatment with nondepolarizing muscle relaxants on the neuromuscular blocking action of succinylcholine. *ANESTHESIOLOGY* 35:572-578, 1971