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Dose Response Curves of Althesin on Spontaneous Single Unit Activity of Various Dorsal Horn Rexed Laminae

(spinal cord/Althesin/anesthesia)

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Dose response curves of Althesin on single unit activities of various dorsal horn Rexed laminae were studied using an extracellular microelectrode recording technique in decerebrated spinal cats.

Althesin 33, 50, 100 and 200 μl/kg I. V. suppressed in a dose related manner spontaneous single unit activity in Rexed lamina 5, known to respond principally to noxious stimuli.

Althesin 100 μl/kg and 200 μl/kg depressed in a dose related manner spontaneous single unit activity in a lamina 4 and lamina 6, but a small dose of Althesin 33 μl/kg and 50 μl/kg I. V. did not suppress lamina 4 and lamina 6, with proprioceptive input, rather these units were adversely facilitated.

Althesin is a steroid anesthetic agent, now being clinically used even in Japan. The recommended dosage of Althesin is 40–150 μl/kg and 75–100 μl/kg I. V. for induction of anesthesia (1, 2). In a preliminary report (3), we observed changes in the spontaneous firing of neurons in the dorsal horn in decerebrated spinal cats, following administration of Althesin 100 μl/kg, infused through the femoral vein over a 30 sec period. Two to three min after administration of a dose of 100 μl/kg, the activities in all laminae were markedly suppressed, and a lamina specific suppression such as was seen in the case of ketamine hydrochloride and morphine sulfate was not apparent.

The present study was undertaken to determine a lamina specific suppression by Althesin. To obtain data on the dose response, each cat was given Althesin 33, 50, 100 and 200 μl/kg in turn, after recovery from the preliminary administration. A preliminary result was reported previously.

MATERIALS AND METHODS

Details of the experimental methods were as already reported (3, 5). Procedures specific to the present investigation were as follows.

Eleven cats of either sex, weighing 2.5 to 3.4 kg, were used. Halothane, nitrous oxide and oxygen anesthesia was used for tracheostomy, bilateral carotid artery ligation, cannulation of the right femoral artery and vein, and

laminectomy. Each animal was rendered decerebrate and unconscious by bilateral electrolytic lesions in the mid-brain reticular formation and the spinal cord was transected at L_1-L_2. These cats were then ventilated with 100% oxygen using a volume cycled ventilator connected to a non-rebreathing system. Adequacy of circulation and thermal control were assured by continuous monitoring of appropirate variables. A glass rod platinum sheathed Transidyne "Microtrode" microelectrode with a 1—2 micron exposed tip was then inserted by a hydraulic micromanipulator into the lumbar spinal cord near the L_7 root entry zone. Neurons were characterized by their evoked responses and spontaneous firing patterns.

To obtain dose response information, eleven animals were studied, four animals each with recording from lamina 4 and lamina 6 and three animals each with recording from lamina 5. Following observation during the control period, Althesin 33 μl/kg was infused over a 30 sec period, and the response was followed for 30 min. The second, third and fourth doses were 50 μl/kg, 100 μl/kg and 200 μl/kg, and each response was observed for 30 min. Signals recorded on magnetic tape were simultaneously monitored on a cathode-ray oscilloscope were counted electronically. Spike interval histograms and burst interval histograms were compiled according to the method described previously (6).

RESULTS

The salient features of physiologic characterization of the lamination of the dorsal horn were as previously reported. (5, 6). The overall characteristics of the spontaneous and gross modality of responsiveness were correlated with the anatomic lamination of Rexed (7).

Lamina 4 (Four Cats)

The average firing frequency of cells in lamina 4 was 17.7/sec. As shown

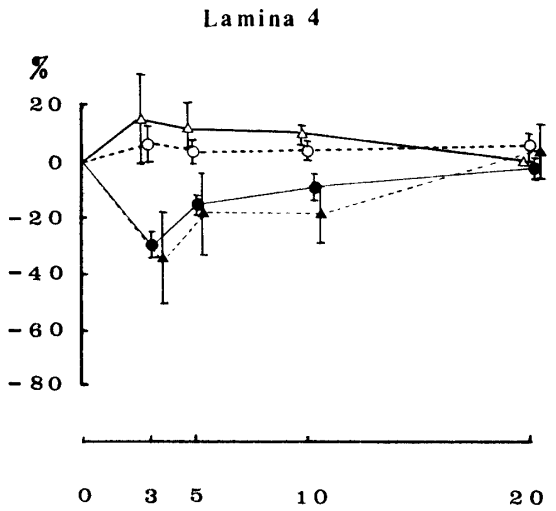

Fig. 1. Dose response curves of the effects of Althesin 33 μl/kg (○----○), 50 μl/kg (△—△), 100 μl/kg (●—●) and 200 μl/kg (▲----▲), on spontaneously firing single unit activity of lamina 4 in cats.

in Fig. 1, Althesin, 33 μl/kg and 50 μl/kg I. V., did not suppress the spontaneous firing frequency of lamina 4 cells. Althesin, 100 μl/kg and 200 μl/kg I. V., markedly suppressed the spontaneous activity by 30% and 36% at 3 min after the injection, respectively. After 20 min, the firing frequency were reverted to control values. Fig. 4 shows a histogram of findings with Althesin 33 μl/kg.

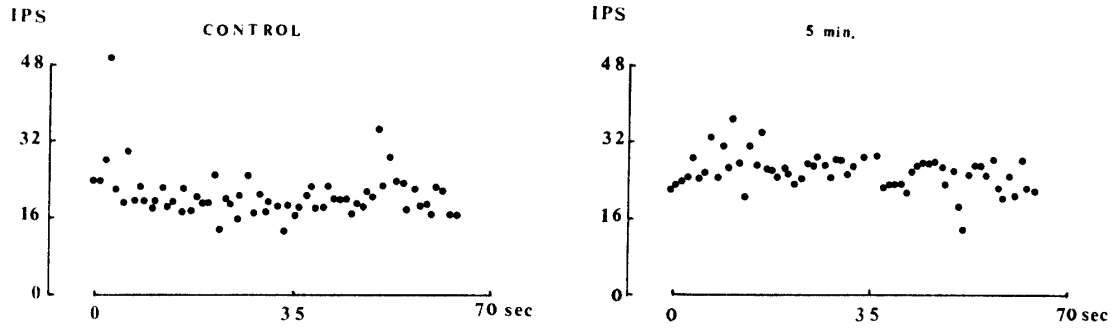

Fig 4. Histogram of single unit activity in lamina 4 during a control period and 5 min after administration of Althesin 33 μl/kg to cats.

Lamina 5 (Three Cats)

Lamina 5 cells could be identified by a sudden loss in response of the cell to the bending of hairs. The cell responded mainly to high intensity stimuli applied to the receptive field. Their spontaneous activity was characterized by bursts followed by steady firing, with an average frequency of 23.3/sec. As shown in Fig. 2, Althesin, 33, 50, 100 and 200 μl/kg I. V., markedly

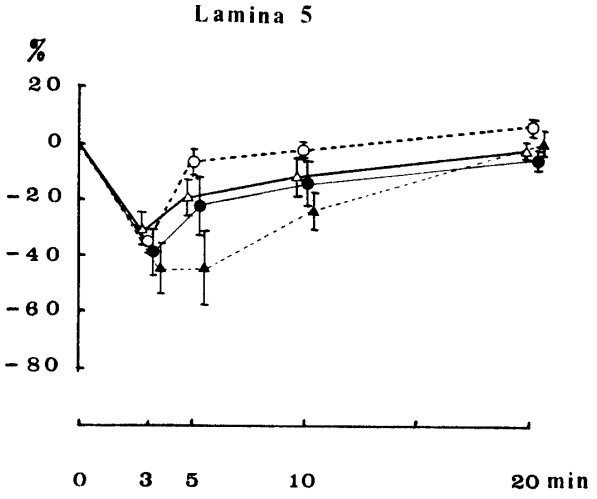

Fig. 2. Dose response curves of the effects of Althesin 33 μl/kg (○----○), 50 μl/kg (△—△), 100 μl/kg (●—●) and 200 μl/kg (▲----▲), on spontaneous firing single unit activity of lamina 5 in cats.

suppressed the spontaneous activity by 35%, 31%, 38% and 45% at 3 min. These firing frequencies returned to control values within 20 min.

Lamina 6 (Four Cats)

Cells located in the most ventral portion of the dorsal horn were characterized by increased spontaneous activity in maintained bursts, with an average frequency 24.8/sec. As shown in Fig. 3, Althesin, 33 μl/kg and 50 μl/kg

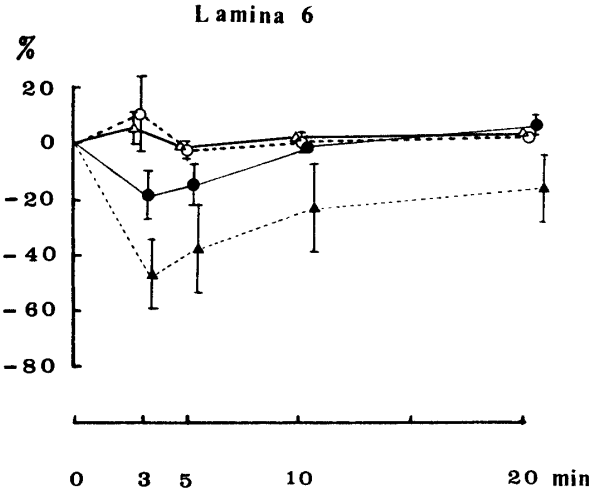

Fig. 3. Dose response curves of the effects of Althesin 33 μl/kg (O----O), 50 μl/kg (△—△), 100 μl/kg (●—●) and 200 μl/kg (▲----▲), on spontaneous firing single unit activity of lamina 6 in cats.

I. V., had no discernible effect on lamina 6 cellular activity, While Althesin 100 μl/kg and 200 μl/kg I. V., markedly suppressed the spontaneous activity of lamina 6 cells. A significant suppression of unit activities, occurring in a dose related manner (33, 50, 100 and 200 μl/kg), was demonstrated in lamina 5, but in other laminae. Fig. 5 shows a histogram of findings with Althesin 33 μ/kg.

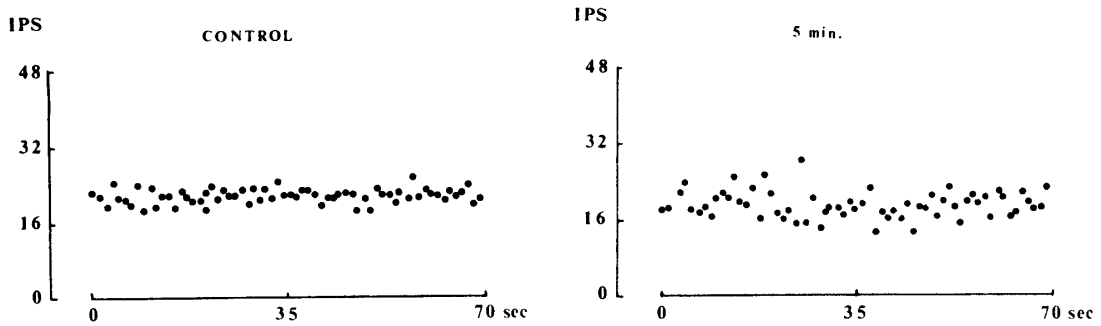

Fig. 5. Histogram of single unit activity in lamina 6 during a control period and 5 min after administration of Althesin 33 μl/kg to cats.

DISCUSSION

Althesin possess several features acceptable to the anesthesiologist. There is a very large dosage range (40 to 150 μl/kg) in which Althesin can be used

as an induction agent. With smaller doses, patients may not lose consciousness, while marked respiratory depression occurs frequently with doses over 150 μl/kg (2). As in the case of barbiturates, complications increase in frequency and severity with increasing dosages, this being particularly noticeable with regard to muscle movement (2). Studies by Samuel and Dundee have shown that a fast rate of injection predisposes to an increased incidence of excitatory phenomenona, but this is of lesser importance than the high dosage in causing these side effects (8). Other workers have studied the effect of Althesin on the central nervous system (2, 9), however, there are few data with regard to the spinal cord cells (2, 10).

The present studies have shown that a small dose of Althesin facilitates activity of lamina 4 and lamina 6 cells, with proprioceptive input. The cause of Althesin induced involuntary muscle movement remains unknown. There results suggest that spinal cord cells, except for lamina 5 cells are facilitated by a small dose of Althesin.

The facilitation of dorsal horn cells by anesthetics have been observed with administration of a small dose of thiopental (11), and also during the induction period of halothane and nitrous oxide anesthesia (12). Shimizu, *et al.* assumed that the involuntary movement which occurs in cases of Althesin anesthesia is due to an increased activity of the spinal interneurons which depend on efferent effects from the upper spinal levels, however, these workers provided no data on the spinal cord cells (10).

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