EFFECT OF NITROUS OXIDE ALONE OR ITS COMBINATION WITH FENTANYL ON SPINAL REFLEXES IN CATS

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The effects of nitrous oxide alone and combination of nitrous oxide and fentanyl on spinal reflexes were studied in cats with transected spinal cord at the thoracic level. Nitrous oxide 33, 50 and 75% in oxygen depressed the amplitude of monosynaptic reflexes in a dose-dependent manner, but exerted little effect on polysynaptic reflexes. The addition of fentanyl 2.5 \( \mu \)g kg\(^{-1} \) during the administration of 75% nitrous oxide in oxygen depressed monosynaptic reflexes further. These results suggest that nitrous oxide or its combination with fentanyl has a depressant action on the transmission of monosynaptic reflexes in the spinal cord, but nitrous oxide might exert less effect on the spinal interneurones which mediate polysynaptic reflexes.

Simultaneous administration of nitrous oxide and narcotics increases the rigidity of skeletal muscle in man (Hamilton and Cullen, 1953; Gergis, Hoyt and Sokoll, 1971; Sokoll, Hoyt and Gergis, 1972; Freund et al., 1973; Askgaard et al., 1977). The H-reflex, which is a monosynaptic reflex contributing to the skeletal muscle rigidity, is usually depressed by nitrous oxide in man (Gergis, Hoyt and Sokoll, 1971; Sokoll, Hoyt and Gergis, 1972; Freund et al., 1973).

However, there have been no detailed studies of the effect of nitrous oxide and fentanyl on the spinal reflex in an animal devoid of higher controls and the effect of these drugs on monosynaptic and polysynaptic reflexes is not known in detail. In the present study, the effect of nitrous oxide alone and its combination with fentanyl on the spinal reflex was studied in cats with the spinal cord transected at the thoracic level.

METHODS

Eight cats of both sexes, weights 1.8–4.0 kg (mean 3.1 ±0.7 kg, SD) were studied. Tracheotomy was performed under ether anaesthesia and the femoral artery and cephalic vein cannulated. Arterial pressure was recorded throughout the experiment with a pressure transducer attached to the femoral arterial cannula. Arterial blood samples for gas analysis were drawn from this cannula. Fluid and drug administration was performed through the cephalic vein.

The cats were paralysed with gallamine 2 mg kg\(^{-1} \) and placed on a stereotactic apparatus. The lungs were ventilated with air using a Harvard ventilator. Arterial \( P_{O_2} \), \( P_{CO_2} \) and \( pH \) were maintained within normal ranges. Sodium bicarbonate was given i.v. if necessary to correct metabolic acidosis.

Points of the cat which were in contact with the stereotactic apparatus were infiltrated with 1% lignocaine solution. Additional local application of lignocaine and i.v. administration of gallamine were performed when necessary throughout the course of the experiment. After local infiltration of the overlying skin and tissue with 1% lignocaine solution, laminectomy was performed at T10 and the spinal cord was transected at this level. Laminectomy was then performed at L6–S1.

The ventral and dorsal roots of L7 were dissected and cut. The exposed spinal cord was covered with a paraffin pool. Rectal temperature of the animal was maintained at 37°C. The dorsal root of L7 was stimulated at 1 Hz with a square wave pulse of 200 \( \mu \)s duration. The intensity of the stimulus was set at 30% above the voltage at which the largest amplitude of the mono- and polysynaptic waves was obtained. This stimulation was considered as supramaximal.

Evoked potentials were recorded from the ventral root using a monopolar silver electrode. These spinal monosynaptic and polysynaptic reflexes were displayed on an oscilloscope and 32 waves were added by use of Adscope (Nihon-Kohden, Tokyo). Control observations were made at least 3 h after cessation of inhalation anaesthesia using controlled...
ventilation with 100% oxygen. After 15 min, nitrous oxide in oxygen was administered at concentrations of 33, 50 and 75% for 10 min at each concentration. Nitrous oxide was then discontinued and 100% oxygen was given for 30 min. The gas mixture was readjusted to 75% nitrous oxide in oxygen for 10 min and fentanyl (Fentanest, Sankyo Co., Tokyo) 2.5 μg kg⁻¹ was administered i.v.

Statistical analysis of the data was performed using Student’s t test for paired data.

RESULTS

Figure 1 shows spinal reflexes observed in one cat during administration of 100% oxygen, and 33, 50 and 75% nitrous oxide in oxygen. Figure 2 shows reflexes of the same cat recorded during the recovery period with 100% oxygen administration, during administration of 75% nitrous oxide for the second time and after the addition of fentanyl 2.5 μg kg⁻¹ i.v.

Nitrous oxide diminished the maximal amplitude of the monosynaptic reflex. Mean changes with SD compared with the control taken during oxygen administration were: -43.2 ± 20.7% with 33% nitrous oxide; -62.0 ± 14.8% with 50% nitrous oxide and -78.0 ± 11.2% with 75% nitrous oxide (fig. 3). These changes were all significant (P<0.001). The amplitude of the monosynaptic reflex during air administration did not change significantly from that measured during administration of oxygen (-0.7 ± 18.0%).

Polysynaptic waves were affected less with administration of nitrous oxide. The first wave of the polysynaptic reflex was taken as representative of polysynaptic waves. These first waves showed no statistically significant changes (-15.0 ± 13.2% with air; -9.3 ± 31.4% with 33% nitrous oxide; -12.0 ± 49.1% with 50% nitrous oxide; -29.1 ± 55.1% with 75% nitrous oxide, all compared with the oxygen control) (fig. 3).

After changing from nitrous oxide back to 100% oxygen, amplitudes of monosynaptic reflex waves recovered to -21.7 ± 27.8% of control. The second administration of 75% nitrous oxide in oxygen reduced the amplitude of the monosynaptic reflex to -72.4 ± 9.9% compared with the value taken during the second administration of 100% oxygen (P<0.01).

When fentanyl 2.5 μg kg⁻¹ was given the amplitude of the monosynaptic reflex was depressed (-26.7 ± 12.0% 1 min after fentanyl; -29.6 ± 16.8% 3 min after fentanyl; -36.5 ± 13.9% 5 min after fentanyl; all compared with the value taken during the second administration of 75% nitrous oxide). These changes are all statistically significant (P<0.01, P<0.05 and P<0.01 respectively). Polysynaptic reflexes after fentanyl administration became fused in some cases and it was difficult to identify the first polysynaptic wave.

DISCUSSION

In the present study, nitrous oxide decreased in a dose-dependent manner the amplitude of spinal monosynaptic reflexes in cats with transected spinal cord at the thoracic level. Amplitudes of polysynaptic reflexes were affected little with nitrous oxide.

It has been demonstrated that increased rigidity of skeletal muscle occurs when nitrous oxide, a narcotic or their combination is given to man...
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FIG. 3. Percent changes (means ± SD) from the control taken during administration of 100% oxygen, of the amplitude of monosynaptic reflexes (●—●) and the amplitude of the first wave of polysynaptic reflexes (○—○). Asterisks show significant changes (P<0.001).

It seems that the polysynaptic reflex is resistant to the depressive effect of nitrous oxide compared with the monosynaptic reflex. According to Bárány's theoretical analysis (Bárány, 1947), a multisynaptic chain in the central nervous system is always more vulnerable to the effect of anaesthetics than an oligosynaptic pathway, other factors being equal. Experimental evidence, however, showed that the number involved is not the only determinant of the effect of anaesthetic agents on the synapses in the central nervous system (Megirian, Vasey and Posternak, 1958; Somjen, 1967).

For instance, in Megirian’s experiments, ethanol and n-pentanol depressed the polysynaptic pathway to a greater extent than the monosynaptic pathway in the spinal cord. Ether and chloroform exerted no such selective action. According to Esplin (1959), carbon dioxide depresses the monosynaptic reflex but it has less effect on polysynaptic pathways. In this respect, the action of nitrous oxide demonstrated in the present study could be similar to that of carbon dioxide.

Sokoll, Hoyt and Gergis (1972) reported that fentanyl increased the amplitude of the human H-reflex. In Rudakov's experiment in cats (1971), decreased amplitude of the polysynaptic response was observed with administration of fentanyl 0.25 mg kg⁻¹. Monosynaptic reflex was unchanged.
even with larger doses of fentanyl. In the present study, fentanyl potentiated the depression of monosynaptic reflex caused by 75% nitrous oxide.

The results of the present study suggest that nitrous oxide or its combination with fentanyl depresses the spinal monosynaptic pathway, but spinal interneurones which transmit polysynaptic reflexes are affected less by nitrous oxide alone. This selective action might have some relation to the muscle rigidity observed with nitrous oxide and narcotics.

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REFERENCES


