Effects of Electrical Stimulation of Respiratory Center in the Event of Termination of Its Natural Rhythmic Activity

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The possibility of restoration of the natural rhythmic activity of the respiratory system by transcutaneous electrical stimulation of the respiratory center after termination of spontaneous respiratory movements caused by narcosis was shown in experiments on mongrel cats of both sexes under nembutal anesthesia. Natural rhythmic activity of respiratory center was stopped by additional administration of sodium thiopental. The proposed method of electrical stimulation of the respiratory center allows maintaining the rhythmic respiratory movements and their recovery after narcotic apnea up to complete recovery of spontaneous respiration.

Key Words: *electrical stimulator; respiratory center; apnea*

Electrical stimulation is widely used in clinical and laboratory practice for diagnostics, treatment and maintenance of vital activity in animals and humans. Electronic stimulators differ by application and used in healthcare and in experimental investigations. It was established that electrical stimulation of respiration may be provided by stimulation of the respiratory system at different levels: medulla oblongata structures, spinal cord segments, diaphragm, and intercostal nerves [1,2]. It was shown in 1990s in animal experiments that recovery and maintenance of respiratory rhythmogenesis in case of apnea caused by barbiturates and narcotic analgesics may be provided by short series of electric pulses applied to pneumotaxic center area. Experimental approaches for restoration of spontaneous respiratory rhythm in animals by high frequency stimulation of the respiratory sites in giant-cell nucleus and nucleus tractus solitarius were proposed. Investigators noticed that electrical stimulation restored firing activity of respiratory center (RC) neurons and recovered respiratory movements. Currently, there are a lot of investigations where restoration and maintenance of respiratory movements is carried out by direct electrical stimulation of the spinal cord. Such studies are intensely performed in both animals [3] and humans [4-7].

Here we evaluated the possibility of recovering vital spontaneous rhythmic activity of the respiratory system after narcotic apnea by transcutaneous electrical stimulation of RC area in cats.

MATERIALS AND METHODS

Experiments were performed on sodium pentobarbital-anesthetized (40-50 mg/kg intraperitoneally) mongrel cats of both sexes weighting 1.8-4.0 kg (n=10) with preserved natural respiration. Body temperature was maintained with 1°C accuracy within the range 37.0-38.5°C. Tracheotomy was performed at the level of upper third of the trachea; the inserted cannula was connected to a transducer for measuring external respiration parameters. Main respiratory parameters, such as minute volume of respiration (MVR), respiration rate (RR), and pneumotachogram, were recorded with an MX-01 polygraph under BTPS conditions. Systemic blood pressure (BP) and heart rate (HR) were measured using a catheter introduced into the femoral artery and connected to an MX-01 tensiometric transducer. Intraesophageal pressure (IEP) was measured with another catheter with a water-filled elastic

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balloon introduced into the esophagus and connected to an MX-01 transducer. Pressure in the esophageal catheter was set in such a way that during passive expiration it was 0 mm Hg. Electrical activity of diaphragm (EMGd) was recorded using electromyograph M-42 (Medikor) via bipolar hook-shaped electrodes fixed to the costal part of the diaphragm at the right side. Electrical stimulator of respiration ESD-2P was used for electrical excitation of RC. Stimulating burst frequency was set close to background (initial) spontaneous respiration rate. Control stimulation of RC was performed in each experiment to determine the optimal magnitude of stimulation impulses. Respiratory arrest was induced by intravenous administration of freshly prepared 5% solution of sodium thiopental (thiobarbiturate) 10 min after control stimulation. Stimulating electrodes were placed on the skin between occipital bone margin and first cervical vertebra, projecting the irritation to the RC area in the medulla oblongata. RC electrical stimulation was periodically interrupted to assess the moment of restoration of spontaneous respiratory movement. Experimental data was registered using an H3031-6 ink recorder. Results were statistically analyzed and expressed in terms of arithmetic mean±error of the mean ($M \pm m$). Significance of differences was evaluated using Student's t test ($p<0.05$).

RESULTS

It appeared to be possible to maintain and then to restore respiration rhythmogenesis by transcutaneous electrical stimulation of RC area in medulla oblongata during respiration arrest. According to EMGd and IEP data, the respiratory movements caused by stimulation can be produced and maintained at a satisfactory level long enough during apnea. We believe that electric current affected directly RC of the medulla oblongata, and stimulation was conducted to the diaphragm what resulted in preservation of vital parameters of external respiration (Tables 1 and 2). Benefit of this reanimation method was demonstrated by the fact that stimulation restored the respiratory rhythm in all animals even after the longest respiration arrest (more than 75 min). Most of them were exposed to repeated respiration arrest (sodium thiopental administration) and repeated stimulation again restored spontaneous respiration.

TABLE 1. Dependence of Apnea Duration on Sodium Thiopental Dose

Thiobarbiturate dose, mg/kg	Apnea duration, min	Number of cases
7.5-13	15-25	5
14-18	26-30	6
19-72	31-75	8

After administration of sodium thiopental, the respiratory arrest in some animals was observed immediately, while in others it occurred 5-10 min later. Electrical activity of the diaphragm and changes in IEP disappeared from the beginning of apnea. In our experiments, 19 cases of apnea were observed in 10 cats (Table 1). Administration of sodium thiopental produced a dose-dependent effect on activity of the respiratory system (lowest dose was 7.5 mg/kg, highest dose 72 mg/kg), therefore the duration of stimulation depended on apnea duration (Table 1).

An insignificant increase in lung ventilation (up to 30%) associated with increase in respiratory rate was observed during control RC stimulation. The increase in external respiration parameters during control stimulation was determined, according to IEP and EMGd data, by stimulation activity of respiratory muscles added to normal animal breathing. Thus, stimulation potentiated natural activity of respiratory muscles. More precisely, alternation or summation of spontaneous and stimulated respiratory movements was observed at the time of control stimulation. It is characteristic, that systemic BP was virtually unaffected under these conditions (Table 2).

Sodium thiopental (similarly to other anesthetic drugs) rapidly decreased lung ventilation by almost 1.5 times, mean BP decreased by 20% ($p<0.05$, Table 2). At the moment of respiratory arrest, heart activity appreciably dropped and mean BP decreased 2-fold ($p<0.001$) in comparison with baseline values.

Stimulation of RC was started 1-2 min after apnea onset and recovery of natural rhythm was checked in all episodes of apnea. In 11 cases, natural rhythm recovered within 30 min (Table. 2).

During apnea, electrical activity of diaphragm and changes in IEP were resumed with the onset of RC stimulation, a clear-cut tendency to improvement of lung ventilation was noted (Table 2). MVR increased by 2 times 25 min after the start of electrical stimulation. Lung ventilation decreased 1.5 fold in comparison with background values ($p<0.05$) after the end of stimulation and resumption of spontaneous respiration.

During stimulation, MVR increased due to deeper breathing; the volume of respiration tended to increase (Table 2) and attained 83 and 91% by minutes 25 and 30, respectively. After termination of stimulation and resumption of spontaneous respiratory rhythm, the depth of respiratory movements returned to baseline values.

As it was previously noticed, the rate of respiratory movement set by investigator using stimulator remained unchanged, but after resumption of spontaneous breathing the rate of respiration decreased by 30% ($p<0.05$; Table 2).

TABLE 2. Parameters of External Respiration and Mean Systemic BP during RC Stimulation in Apnea Produced by Administration of Sodium Thiopental ($M \pm m$)

Parameter	BP, mm Hg	MVR, ml/min	RV, ml	RR, min^{-1}
Baseline	94±5	9.4±1.1	0.93±0.11	11±1
CS	109±7	12.2±2.3	1.04±0.19	14±1*
Administration of sodium thiopental	76±6*	6.6±1.0	0.98±0.16	9±1
Apnea onset	49±5***	–	–	–
Stimulation against the background of apnea, min				
1	58±6*	13.3±2.6	1.18±0.24	12±1
3	62±5***	13.0±2.4	1.15±0.21	12±1
5	65±5***	15.3±3.0	1.23±0.22	12±1
10	73±7*	15.8±3.8	1.39±0.32	11±1
15	82±9	13.1±2.3	1.21±0.21	11±1
20	67±7**	15.4±3.7	1.41±0.29	12±2
25	81±4	20.0±7.6	1.70±0.40	12±2
30	82±3	15.7±5.2	1.78±0.43	11±3
SR	83±4	6.2±0.9*	0.95±0.16	8±1*

Note. RV: respiratory volume; SR: spontaneous respiration; CS: control stimulation. *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared to baseline values.

No significant changes in BP were detected during the experiment. The mean BP in systemic circulation slightly decreased during the first 10 min after the start of stimulation: the maximum BP drop (by 40%, $p<0.05$) was observed by the end of the first minute, while after 10 min the reduction was only 20% ($p<0.05$, Table 2). Twenty-five minutes after stimulation onset, BP returned to baseline level and did not differ from that after termination of stimulation.

Thus, transcutaneous electrical stimulation of RC appeared to be effective for maintaining life in cats during very long time (up to 75 min) in the absence of natural breathing.

Thus, the proposed method allows maintaining respiration not only during narcotic overdose, but also in deep toxicoses and other urgent cases, and eventually it provided subsequent resumption of natural rhythm of respiratory movements. Beneficial effect manifested as stable restoration of breathing in extreme circumstances associated with respiratory rhythm disturbances in animals and, in perspective, in humans.

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