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ANTAGONISM OF ACUPUNCTURE ANALGESIA BY NALOXONE IN UNCONSCIOUS MAN

BY

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ABSTRACT

The effects of acupuncture analgesia were studied using the change in halothane MAC in volunteers. Halothane MAC under electrical acupuncture stimulation was reduced to 86.2±11.1% from the control value. After naloxone administration the level of the MAC was raised to the control level and the increment was 19.1±14.8%. Naloxone itself did not change the halothane MAC in the same subjects. These results suggest that the changes in halothane MAC under acupuncture stimulation are caused by the release of an endogenous analgesic substance in the brain.

INTRODUCTION

In China, acupuncture analgesia was successfully employed in almost all kinds of operations, including chest surgery and open heart operations. The number of cases has been reported to be more than 400,000 and the success rate was announced to be quite high (Shanghai Acupuncture Anesthesia Coordinating Group [1]).

In Japan, acupuncture anesthesia was attempted for various operations, but its use was limited to operations on the anterior neck, maxillary sinus, tooth extraction, and obstetrics. However, a similar technique was widely applied clinically to intractable pain and its efficacy was recognized.

The mechanism of acupuncture analgesia was recently explored in the field of neurophysiology, biochemistry, anatomy and pharmachology, and the possible mechanisms were summarized as follows:

1. Hypnotic or autosuggestive effect
2. Local effect of needling (analgesic substance produced locally)
3. Presynaptic inhibition of sensory afferents (gate-control theory)
4. Modulating mechanism in CNS above the brainstem which activates the descending pain inhibitory system
5. Effect mediated by a Meridian

Recently, it was considered as a matter of significance that pain inhibition due to acupuncture was connected with the excretion of endogenous morphine-like factors (endorphins), in the periaqueductal gray or raphe nuclei (Mayer *et al.* [2]; Pomeranz [3]).

Previously, we studied the analgesic effect of hydroxyzine, diazepam, pentazocine, and nitrous oxide using the minimum alveolar anesthetic concentration (MAC) of halo-

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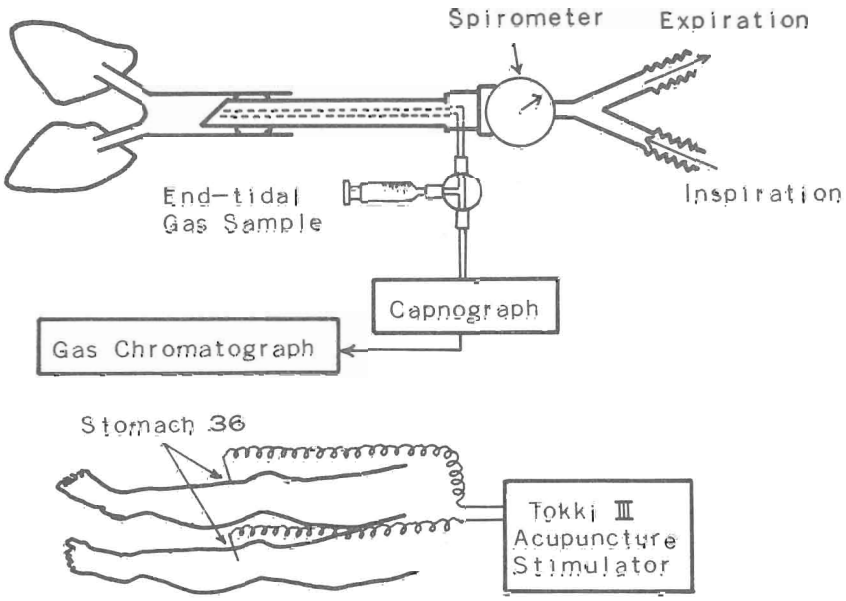

Fig. 1. Schema of the experiment.

thane as an index (Tsunoda *et al.* [4]).

In this study the changes in halothane MAC by acupuncture stimulation were measured in the unconscious state to exclude the hypnotic effects. At the same time the narcotic antagonist naloxone was given after acupuncture analgesia to investigate its antagonism to acupuncture.

Methods

Seven healthy young male volunteers were anesthetized with nitrous oxide and halothane after the administration of 0.5 mg of atropine sulfate. Using 8% lidocaine spray and a small amount of succinylcholine, an endotracheal tube was inserted and nitrous oxide was discontinued, anesthesia being maintained with halothane in oxygen at a constant concentration.

During the experiment, the respiration of the volunteer was assisted to maintain the end-tidal carbon dioxide concentration between 4% and 5%.

Figure 1 illustrates the schema of the experiment. The concentration of halothane in the inspired gas collected from the corrugated tube and the end-tidal gas sample collected through a thin tube inserted into the endotracheal tube were measured by a gas chromatograph (Shimazu GC-7A). Tidal and minute volumes were measured by a Wright spirometer, and the concentration of the end-tidal carbon dioxide was monitored by Capnograph®. Blood pressure, pulse, and respiratory rate were measured just before the nociceptive stimulation.

After endotracheal intubation, the concentration of halothane with 5 *l*/min oxygen was kept constant for over 20 minutes. Then the nociceptive stimulation was performed by electrical stimulation of 30 volt, 1 msec, 50 Hz given for 10 seconds through the needle electrodes inserted into the skin of the forearm.

The movement of the opposite arm, legs, or whole body was defined as a positive reaction. If a volunteer moved with this

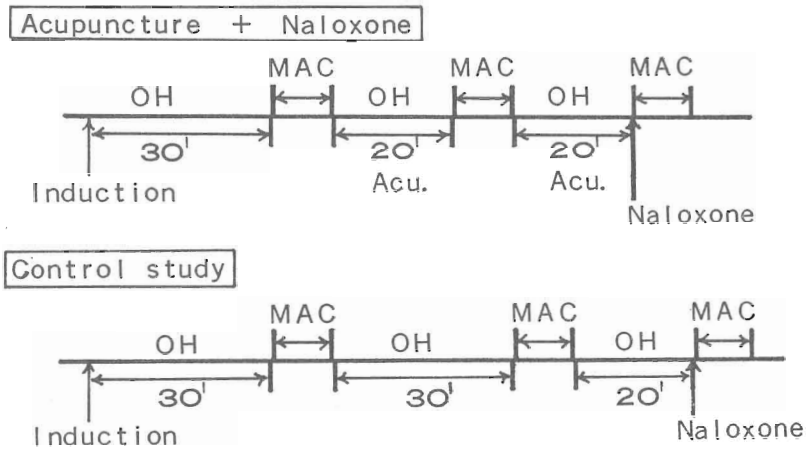

Fig. 2. Time schedule of experiment is illustrated.
The upper line shows the schedule of the measurements of halothane MAC; control value, with acupuncture stimulation and with naloxone administration. The lower line shows the schedule of control study of the time sequence and naloxone alone. (OH: Oxygen-Halothane anesthesia)

stimulation, the concentration of inspired halothane was increased and the same stimulation was repeated until the movements no longer occurred. The MAC was determined by the mean of two adjacent concentrations at which the subject did or did not respond to the stimulation.

After the control value of halothane MAC was determined, the acupuncture needles were inserted into the bilateral Stomach Meridian 36 (just lateral to the tibial tuberosity), and a plate electrode was placed on Conception Vessel Meridian 12 (midportion between the xiphoid process and the umbilicus).

Then acupuncture stimulation of 3 Hz, 1.5 mA (mean) was delivered for 20 minutes by tokki-III stimulator. After the cessation of electroacupuncture, the MAC of halothane under acupuncture was measured with the same method as the control value.

Electroacupuncture was applied again under halothane anesthesia for 20 minutes, the 0.4–0.6 mg of naloxone was injected intravenously and the changes in the MAC were measured.

Five of the same volunteers were examined again to find out whether the MAC was changed by the time sequence or by the administration of naloxone (Fig. 2).

Results

The halothane MAC under acupuncture stimulation was reduced to 86.2±11.1% from the control value in seven volunteers, which was statistically significant. After naloxone administration with the continuation of acupuncture stimulation, the level of halothane MAC was elevated close to the level of control value. The elevation was 19.1±14.8%, and this tendency was statistically significant when the acupuncture values were taken as a control (Fig. 3, Fig. 4).

As shown in Figure 5, the MAC value after 100 minutes of halothane inhalation was 97.3±4.1% of the control value. The MAC after 0.4 mg naloxone administration was 97.2±3.1% of the control. Neither of these values was significant. These data show that halothane MAC was not changed by the time sequence or by the administra-

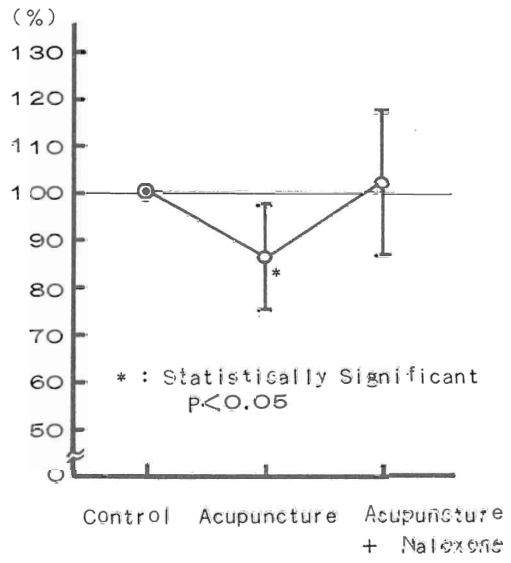

Fig. 3. Halothane MAC was reduced to 86.2~ 11.1% from the control value ($p<0.05$) and returned to the level of control after naloxone administration. (Horizontal axis: anesthesia method)

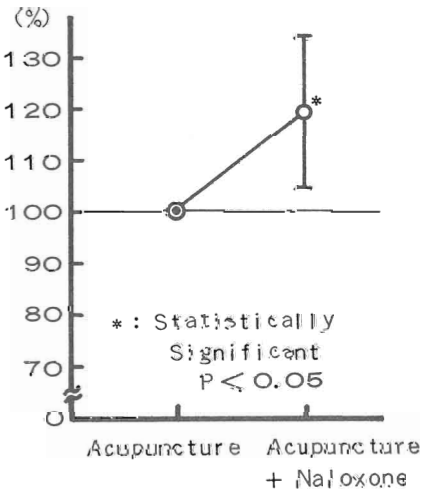

Fig. 4. Naloxone elevated halothane MAC 19.1~ 14.8% ($p<0.05$) from acupuncture value. (Horizontal axis: anesthesia method)

tion of naloxone, and so the above-mentioned changes in the MAC were caused solely by acupuncture stimulation.

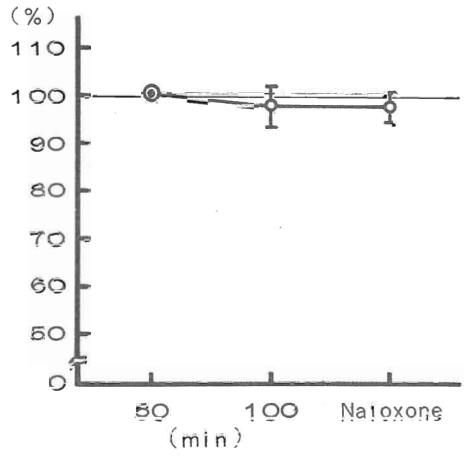

Fig. 5. 100 minutes of inhalation of halothane and naloxone administration alone did not change halothane MAC.

Discussion

Though the mechanism of acupuncture analgesia has been studied for a long time, no definite conclusion has been reached. Acupuncture analgesia has some peculiarities, as follows:

1. Special needle sensation (Te-Chi, Toki); weakness, swelling, heaviness, and numbness must be obtained by twirling the needle at the Meridian point to establish a better analgesic effect.
2. Analgesia may be produced at the distant portion of the body which has no spinal segmental relationship.
3. It takes 15–20 minutes to establish acupuncture analgesia for the operation, but the therapeutic effect of acupuncture in a pain patient can be established instantaneously.
4. The effects of acupuncture analgesia are not disturbed by the use of small amounts of narcotics, tranquilizers, or local anesthetics.
5. The effects of acupuncture analgesia are poor unless a mutual understanding is established between the patient and doctor.

In our study the subjects were anesthetized by halothane, and then the hypnotic effects were excluded but the special needle sensation (Te-Chi) could not be obtained. The points (Stomach-36) were useful to establish analgesia in the face and neck but not in the forearm, which has a poor connection in the spinal segment or in the Meridian. If an analgesic effect in the forearm occurs, it should be the generalized elevation of the pain threshold.

The localized effects of acupuncture in the lower legs have no way of arriving at the forearm, unless locally produced analgesic products are carried by the blood stream to a distant part of the body. Generalized analgesic effects of acupuncture in the extremities occur even when the blood stream of the extremities is obstructed, which contradicts the local humoral theory of acupuncture.

An increase in the presynaptic inhibition of the sensory afferents was postulated as the mechanism of acupuncture. However, analgesia can be established in an area where the spinal segment has no relation. Moreover, it takes 15–20 minutes to establish acupuncture analgesia, which suggests the existence of a humoral factor rather than direct control in the spinal cord exerted by acupuncture stimulation.

Recent reports of stimulation-produced analgesia in the periaquaductal gray and raphe nuclei, and reports also of endogenous morphine-like substances (endorphins), have begun to throw light on the mechanism of acupuncture analgesia (Liebeskind *et al.* [5]; Oliveras *et al.* [6]; Terenius and Wahlström [7]).

Mayer reported on the antagonism of acupuncture analgesia by naloxone, and postulated that acupuncture stimulation increased the somatosensory input into the brain and the release of an endogenous substance from the periaquaductal gray or raphe nuclei, and that the endorphins activated the descending pain inhibitory system (Mayer *et al.* [2]).

Pomeranz also proposed the hypothesis that acupuncture analgesia was mediated by endorphins (Pomeranz [3]). He found a naloxone reversal of acupuncture effects on the spinal cord firing in response to painful stimuli, and postulated that acupuncture activates the deep muscle receptors which drive the sensory system to release endorphins from the pituitary or midbrain. Endorphins are released into the blood and reenter the brain to block the synaptic transmission in the nociceptive pathways.

To prove the above hypothesis halothane MAC was used as an indicator of pain threshold in this study. The subjects were unconscious but responded to nociceptive stimuli under light halothane anesthesia; the psychological effect which might be one of the factors of acupuncture was completely excluded.

If halothane MAC were reduced by electrical acupuncture stimulation and this reduction were antagonized by naloxone, it can be postulated that this change was caused by the release of an endogenous analgesic substance mediated through the central nervous system.

Fink reported that a large dose of naloxone increases the MAC of halothane, cyclopropane, and enflurane in the rat (Fink *et al.* [8]). His results were questioned by many authors because the dosage of naloxone was large enough to work as an analeptic (Bennet [9]).

In summary it can be postulated that the decrease in halothane MAC under electrical acupuncture stimulation was caused by the release of an analgesic substance from the periaquaductal gray or raphe nuclei which subsequently activated the descend-

ing pain inhibition system. But the extent of the MAC decrease was only 16% in this experiment, and this would not be enough to establish complete clinical analgesia. The magnitude of the analgesic effects was small and much less than the effects obtained in a conscious state. We can postulate that a CNS center higher than the midbrain has some potentiating effects on acupuncture.

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