

## ORIGINAL ARTICLES

### Clinical Study on Effect of Electro-acupuncture Combined with Different Anesthetics on Auditory-evoked Potential Index

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**ABSTRACT** **Objective:** To observe the effect of electro-acupuncture (EA) on auto regressive with exogenous input model (ARX-model) auditory evoked index (AAI) in patients anesthetized with different anesthetics. **Methods:** Forty-eight adult patients undergoing scheduled surgical operation were enrolled and divided into two groups (24 in each group) according to the anesthetics applied, Group A was anesthetized with propofol sedation and Group B with Isoflurane-epidural anesthesia. Group A was subdivided into three groups of low, middle and high concentration of target effect-site of 1.0  $\mu\text{g}/\text{ml}$ , 1.5  $\mu\text{g}/\text{ml}$  and 2.0  $\mu\text{g}/\text{ml}$  through target controlled infusion (TCI) and Group B into 3 subgroups of minimum alveolar effective concentration of isoflurane (0.4 MAC, 0.6 MAC and 0.8 MAC for B1, B2 and B3 subgroups) respectively, with 8 patients in every subgroup. EA on acupoints of Hegu (LI4) and Neiguan (P6) was applied on all the patients during anesthesia, and the change of AAI at various time points was recorded. **Results:** In the three subgroups of Group A, levels of AAI were significantly elevated in the first few minutes after EA, and significantly lowered 20 min after EA in subgroup A2. While in the subgroups of Group B, except the elevating in Group B1 1-2 min after EA, levels of AAI remained unchanged at other time points. **Conclusion:** Pain response could be reflected by AAI during EA. EA could enhance the sedative effect of propofol in middle concentration, but its effect on isoflurane epidural anesthesia is insignificant.

**KEY WORDS** auditory-evoked potential index, electro-acupuncture, propofol, isoflurane

Auto regressive with exogenous input model (ARX-model) auditory evoked index (AAI) is an index that could continuously and accurately reflect the real-time degree of anesthesia, constituting some new content in anesthesia monitoring that has been studied extensively in recent years. But there has been so far no report published involving the effect of electro-acupuncture on AAI under different conditions of anesthesia. For this reason, the authors conducted a clinical observation on 48 patients undergoing scheduled surgical operation from April to June 2004.

#### METHODS

##### Criteria for Case Inclusion and Exclusion

Included in the study were patients who were ready to receive scheduled surgical operation of American Society of Anesthesiologists Physical Status grade (ASA) I - II, within the ages of 18-60 years and have not been medicated with any pre-operational medicine. And excluded were those who suf-

fered from hearing impairment, diseases of central nerve system, mental diseases, or had a history of long-term drinking or taking sedatives.

##### General Materials

All the patients enrolled were inpatients hospitalized between April to June 2004 in the authors' hospital for scheduled-operation, 48 in total, 26 males and 22 females. They were divided, according to the methods of anesthesia applied, into two groups, 24 patients in each group. Group A was the propofol sedative group, and Group B the Isoflurane-epidural anesthesia group. And all the patients in Group B were going to get upper abdominal operation. All the patients in either group were randomized by table into three subgroups, treated with low, middle

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and high concentration of anesthetics, with 8 cases in each group. Group A1, the low concentration propofol treated group consisted of 3 males and 5 females, aged 37-55 years,  $48.38 \pm 6.84$  years on average, with body weight of 48-71 kg,  $62.88 \pm 6.81$  kg on average; Group A2, the middle concentration propofol group, of the corresponding data of 3 males and 5 females, 27-59 years, averaged  $45.63 \pm 11.13$  years, 43-82 kg, averaged  $58.25 \pm 12.08$  kg; Group A3, the high concentration propofol group, of 3 males and 5 females, 48-58 years,  $50.13 \pm 3.64$  years on average, 53-77 kg, averaged  $63.38 \pm 9.62$  kg; Group B1, the low isoflurane group, consisted of 7 males and 1 female, 25-59 years, averaged  $44.75 \pm 11.82$  years, with their body weight at 49-85 kg, averaged  $65.63 \pm 10.35$  kg; Group B2, the middle isoflurane group, of 5 males and 3 females, 38-60 years, averaged  $47.38 \pm 6.28$  years, 48-72 kg, averaged  $61.13 \pm 9.33$  kg; and Group B3, the high isoflurane group, of 5 males and 3 females, 40-57 years, averaged  $48.13 \pm 6.20$  years, 55-71 kg, averaged  $62.88 \pm 5.25$  kg. The difference between Groups A and B in sex, age and body weight was insignificant, and so they were comparable.

### Method of Anesthesia

Anesthesia applied to the three subgroups of Group A: The patients took the supine position in the operation room, connected with a A-line middle latency auditory evoked potentials (MLAEP) ARX-model monitor for continuous measuring of AAI and the pre-sedation baseline value of AAI was recorded after 10 min of rest. Propofol (with the trade name of Diprivan, produced by AstraZeneca S. P. A., Italy, batch number DJA055) was intravenously infused through cubital vein using a target concentration controlling infusion system. The concentration used for Group A1 was  $1.0 \mu\text{g/ml}$ , for A2,  $1.5 \mu\text{g/ml}$  and for A3,  $2.0 \mu\text{g/ml}$ . The AAI value before electro-acupuncture (EA) was

recorded 20 min after the target effect-site having gotten equilibrium with the concentration in effector chamber.

Needles were inserted into unilateral Hegu (LI4) point and Neiguan (P6) point separately, and connected with the impulse acupuncture therapeutic apparatus type KWD-808 II. EA was applied with continuous wave, 50 Hz in frequency and about 3V in strength. AAI values were recorded at the time points when EA was applied for 1 min, 2 min, 3 min, 4 min, 5 min, 10 min, 15 min and 20 min. Needles were withdrawn 20 min later, then the induction and intubation of anesthesia was started. Face-masked oxygen inhalation, with flow controlled to 3 L/min, was given to patients to maintain the saturation of blood oxygen ( $\text{SPO}_2$ ) in the normal range of over 95%, and of the patients lower jaw might have to be held up manually if necessary to keep the air pipe open.

Anesthesia applied to the three subgroups of Group B: the patients took the lateral recumbent position in the operation room. Epidural anesthesia was carried out by puncturing into the intervertebral space of  $\text{T}_{9-10}$  or  $\text{T}_{10-11}$  in accordance of what site was ready to be operated on, with the tube inserted for 4 cm pointing toward patient's head. Then the patient was turned to horizontal position and continuous epidural blocking was applied in the operational procedure.

After the baseline value of AAI was recorded by connecting the patient to A-line MLAEP ARX-model monitor and after the patient had rested for 10 min, AAI value before anesthesia was recorded.

The anesthesia was inducted with  $3 \mu\text{g/kg}$  of fentanyl,  $2 \text{mg/kg}$  of propofol and  $2 \text{mg/kg}$  of succinylcholine by quick intra-tracheal intubation under blankly direct-viewing, inhalation of isoflurane (produced by Yapei Pharmaceutical Ltd. Co., Shanghai, batch

number 6724B5U). Then the vaporizer was regulated as required by the operation, the muscles were kept relaxed by intermittently giving vecuronium bromide, the analgesic effect was maintained by local application of 1% lidocaine with 0.2% dicaine, and the end-expiratory CO<sub>2</sub> pressure was kept within 35-40 mmHg.

After the exploratory laparotomy was finished, the speed of vaporizer was regulated to induce the minimum alveolar concentration (MAC) of isoflurane to reach the scheduled degree, i. e. 0.4 MAC for Group B1, 0.6 MAC for Group B2 and 0.8 MAC for Group B3, and at the same time muscular relaxing agents and local analgesics were administered with the condition unchanged for 20 min. Then the AAI recorded was regarded as the value before EA.

EA was applied for 20 min and AAI recorded at various time points in the same method and procedure as what was done for Group A except that the strength was increased up to 6-7 V.

### Statistic Analysis

All data were expressed by mean  $\pm$  standard deviation, and managed with SPSS 11.0 software with one-way ANOVA, and  $P < 0.05$  was regarded as having significance.

## RESULTS

In the three subgroups of Group A, AAI showed no significant statistical difference before sedation, but it lowered significantly immediately before EA and at all the time points after EA ( $P < 0.01$ ), and the lowering was more significant in Group A3 than that in Group A1 ( $P < 0.05$ ). But when the values in Group A2 were compared with those in Group A1, significant difference only showed at the time points of 10, 15 and 20 min after EA ( $P < 0.05$ ). Moreover, when the value was compared immediately before EA, AAI raised

in Group A1 at the time points of 1 and 2 min after EA ( $P < 0.05$ ), and in Group A2 and A3 it was significantly raised at the time point of 1 min after EA, but significantly lowered at the time point of 20 min after EA in Group A2, with the difference not significant at the other time points ( $P > 0.05$ ). The data were listed in detail in Figure 1.

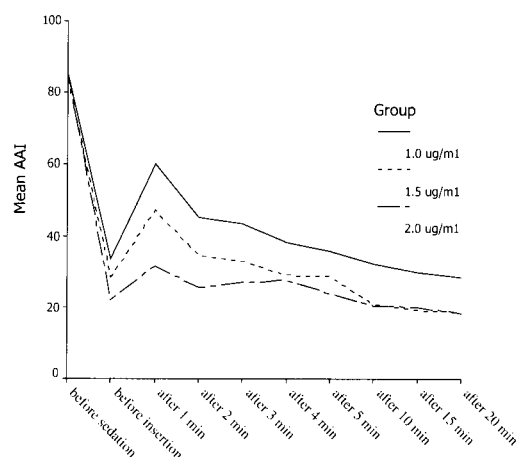


Figure 1. AAI at Each Time Point in Group A

In comparisons of AAI in the three subgroups of Group B, no statistical significance was shown between the three subgroups either before sedation or immediately before EA. AAI got lowered significantly after EA at all the time points in all the three subgroups as compared with that before sedation ( $P < 0.01$ ), but significant difference only showed in Group B1 at the time points of 1 and 2 min after EA, with no significance shown at other time points ( $P > 0.05$ ). The data were listed in detail in Figure 2.

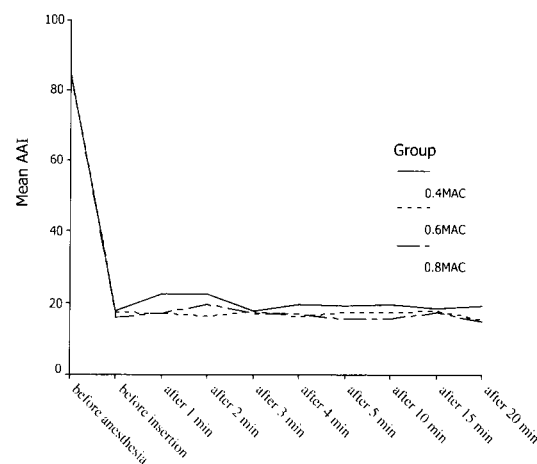


Figure 2. AAI at Each Time Point in Group B

## DISCUSSION

AAI, a continuous, real-time, accurate index capable to reflect the degree of anesthesia, is closely correlated with the sedative and narcotic effects of multiple general anesthetics for intravenous infusion or inhalation<sup>(1,2)</sup>. Nowadays, it has been proved by many reports that it could better detect the mutual transferring between the unconsciousness and consciousness, showing a rather high sensitivity to the fade out and comeback of understanding and consciousness in operations<sup>(3-6)</sup>. Its application in clinical practice has been approved by American Food and Drug Administration (FDA), USA, Council of Europe (CE), Europe, and State Food and Drug Administration (SFDA), China. Through a lot of clinical observations and studies, it has been recognized that AAI is 60-100 during consciousness, and it turns to 40-60 in sleep, 30-40 in light anesthetic and below 30 in clinical anesthetic manner.

It has been shown in this study that at the time immediately before EA patients in Group A were in the manner between light and clinical anesthesia, and the level of AAI in Group A3 was lower than that in Group A1, which means high concentration of propofol could depress the level of AAI more significantly. The result is in accord with those reported by other studies<sup>(7)</sup>, which have showed that the sedative effect of propofol shows a dose-dependent manner, and the variation of AAI level is accordance with that dose-dependent change. While in Group B who were Isoflurane-epidural anesthesia, the patients were in the clinical anesthetic status immediately before EA, and the comparison of AAI level between the three subgroups showed insignificant difference though it lowered along with the increase of MAC.

By stimulating the acupoints, EA could excite the receptor and nerve ending to produce signal of acupuncture. The signals are

conducted along the peripheral nerve fibers A and C into the spinal dorsal horn, arrive at the spinal anterior cross conjunct to the contralateral and go upward along the spinal abdominal lateral funiculus to the positions of brainstem, diencephalon and forebrain to activate the central regulating system in various levels, and then to exhibit the effects of EA by path of sympathetic nerve, parasympathetic nerve, body fluid and peptide hormones secreted from pituitary gland and adrenal medulla<sup>(8)</sup>.

When an organism suffers from injurious stimulation, the monitoring function of AAI, depending upon the infracortical conducting passage, could quickly show the occurring and vanishing of response, by which the body movement during dermatotomy is predictable<sup>(9)</sup>. For this reason, AAI is considered to be capable in reflecting the EA induced stimulation. It has been found in this study that AAI is significantly raised at the first several minutes after EA in Group A. Since the anesthetic degree in Group A1 is the lightest, the response of patients to pain is the most sensitive, and so the elevation of AAI is the highest and its lasting time is the longest, while the elevation and lasting time of AAI in Group A2 and A3 is rather lower and shorter. As for AAI in Group B, significant elevation only showed at the first 2 min in Group B1, the patients in which were in light anesthetic condition, and in Groups B2 and B3, AAI level in patients in the clinical anesthetic condition was not changed at all. It is therefore deduced that when anesthetized with propofol, because the needling sensation still remains, EA could be used to help relax the patients' emotion. But when Isoflurane-epidural anesthesia is applied, the circulation of qi-blood and Ying-Wei in the whole body are blocked by the suppressive action of muscular relaxing agents and anesthetics and the needling sensation is obviously weakened due to the retardance of Jing-qi, acupuncture could not play its regular action at this time. There-

fore, to patients anesthetized by different anesthetic methods, different time points for applying acupuncture should be selected properly, though they are all in the anesthetic condition.

Hegu and Neiguan are acupoints with intensive needling sensation, and should always be chosen for acupuncture anesthesia and are actually widely applied in surgical operations on various localities of the body. Studies have showed<sup>(10)</sup> that the two acupoints could effect the activity of brain cortex to suppress direct cortical electric response. In this study, it has been shown that when anesthesia was carried out with propofol, the level of anesthesia was evidently deepened along with the prolonging of EA time applied in Group A2, while in Group A1 and A3, although a decreasing tendency of AAI was shown, it was of no statistical significance as compared with that immediately before EA. The change of AAI in Group A3 was the least, which may be due to the biphasic regulatory action of EA, that is, when the central nerve systematic suppressive process was intensified, acupuncture generally showed an effect in alleviating or weakening the intensified process. As for why EA didn't show a sedation enhancing effect in Group A1, it is a problem that remains to be further explored.

Owing to the impropriety of time chosen of insertion for Isoflurane-epidural anesthesia, EA showed insignificant effect on the degree of anesthesia.

The conclusion is: AAI can sensitively

reflect pain response during EA. EA stimulation in surgical operation could strengthen the degree of the sedative effect of middle dose propofol, but its influence on Isoflurane-epidural anesthesia is insignificant.

## REFERENCES

1. Thornton C, Sharpe RM. Evoked responses in anaesthesia. *Br J Anaesth* 1998;81 : 771-781.
2. Mantzaridis H, Kenny GN. Auditory evoked potential index: a quantitative measure of changes in auditory evoked potentials during general anaesthesia. *Anaesthesia* 1997; 52 : 1030-1036.
3. Urhonen E, Jensen EW, Lund J. Changes in rapidly extracted auditory evoked potentials during tracheal intubation. *Acta Anaesthesiol Scand* 2000;44 : 743-748.
4. Davies PW, Mantzaridis H, Kenny GN, et al. Middle latency auditory evoked potentials during repeated transitions from consciousness to unconsciousness. *Anaesthesia* 1996;51 : 107-113.
5. Gaj raj RJ, Doi M, Mautzaridis H, et al. Comparison of Bispectral EEG analysis and auditory evoked response for monitoring depth of anaesthesia during propofol anaesthesia. *Br J Anaesth* 1999;82 : 672-678.
6. Gaj raj RJ, Doi M, Mantzaridis H, et al. Analysis of the EEG bispectrum, auditory evoked potentials and the EEG power spectrum during repeated transitions from consciousness to unconsciousness. *Br J Anaesth* 1998;80 : 46-52.
7. Ge SJ, Zhuang XL, Wang YT, et al. Changes in the rapidly extracted auditory evoked potentials index and the bispectral index during sedation induced by propofol or midazolam under epidural block. *Br J Anaesth* 2002;89 : 260-264.
8. Han JZ. Exploration into mechanism of acupuncture anesthesia based on molecular physiology. *Jiangsu J Tradit Chin Med* 2002;23(3) : 27-28.
9. Katoh T, Suzuki A, Ikeda K. Electroencephalographic derivatives as a tool for predicting the depth of the sedation and anesthesia induced by sevoflurane. *Anesthesiology* 1998;88 : 642-650.
10. Zhu LY. Chinese electro-acupuncture. Xi'an: Shaanxi Science and Technology Press, 1983 : 70.

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