BRONCHO ALVEOLAR LAVAGE (BAL) DURING SEVOFLURANE, ISOFLURANE AND HALOTHANE ANAESTHESIA

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SUMMARY

We have examined how sevoflurane anesthesia modified the number and morphology of cells in Broncho Alveolar Lavage (BAL) when compared to isoflurane and halothane anesthesia. 63 patients divided into three groups (n=21) undergoing elective abdominal and urological surgery were anesthetized with sevoflurane, isoflurane and halothane in 50% O_2/N_2O. The inhaled concentration was maintained at 1-2% MAC for isoflurane, 0.5-1% MAC for halothane and 2-2.5% MAC for sevoflurane. BAL samples were obtained before the inhalation agents were used (T1) and before the extubation (T2). During sevoflurane anesthesia the number of alveolar macrophages and, immature macrophages (T2) remained unchanged whereas the number of these cells increased after the inhalation of isoflurane and halothane anesthesia.

We concluded that sevoflurane anesthesia did not change BAL cell count and morphology when compared to isoflurane and halothane anesthesia.

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INTRODUCTION

Alveolar immune cells constituents one of the important lines of pulmonary defense system. Roughly 85% of the alveolar immune cells are macrophages (1). By phagocytosing inhaled foreign bodies and by secreting various cytokines, alveolar macrophages play an important role in preventing postoperative infection (2). Most of the previous studies of impaired immunologic defense problems focus on immunologic changes in the blood. Such changes suggest that anesthetic agents affect immune function. With respect to immunologic competence in the lung, several studies suggest that volatile anesthetics can suppress the cytotoxic and phagocytic response of alveolar macrophages (3).

Pulmonary alveolar macrophages PAM are the first phagocytic cells to encounter airborne pathogenic microorganisms. In previous studies isoflurane and halothane, widely used general anesthetic agents were shown to significantly inhibit the microbicidal oxidative activity of PAM at clinically releveant concentrations (4).

Previous studies have demonstrated that major surgery combined with anesthesia

caused marked changes in BAL fluid cell count and morphology (1). However few clinical reports have examined the effects of inhaled anesthetic agents on BAL.

Because of the contact of cilliated epithelial cells of the respiratory tract and alveolar macrophages would have with an inhaled anesthetic; we investigated the effects of commonly used general anesthetic agents, halothane - isoflurane and sevoflurane on BAL fluid because PAM play a key rol in the antibacterial defenses of the lung (2).

MATERIAL AND METHOD

After obtaining approval from the institutional ethics committee and informed consent we studied randomisely 63 patients undergoing elective surgery under general anesthesia. Exclusion criteria were: ASA II or more, patients more than 60 years of age, those receiving corticosteroid therapy or those with cardiac or lung disease. All patients received 10 mg diazepam the night before the surgery, 0.01 mg/kg midazolam + atropine 0.5 mg i.m. on the day of surgery as premedication.

On arrival in the operating room routine monitoring including arterial pressure ECG, capnogram and pulse oxymetry was established. Anesthesia was induced with 0.7 mg/kg pentothal + 1 mg/kg succhinylcholine after 100% O_2 pre oxygenation.

Atracurium was used for maintainance and ventilation was kept 10 ml/kg/min. end tidal CO_2 being 4.5-5%. Anesthesia was maintained with at 1-2% MAC for isoflurane, 0.5-1% MAC for halothane and 2-2.5% MAC for sevoflurane. Ventilation was provided mechanically to maintain an end expiratory CO_2 of 4.5-5%. Alveoar cells were harvested by bronchoalveolar lavage. BAL procedure was performed before the inhalation agents were used (T1), and before the extubation (T2) directly by routine endotracheal suctioning using an open ended catheter 40 cm catheter through the endotracheal tube and placing it in wedged position by turning the patients head to the left. Warmed sodium chloride 0.9% was instilled and gentle manual suctioning with 20 ml syringe was directly performed after each aliquat was administered. Lavage was repeated twice. Other cells harvested were bronchial cells, polynuclear cells lympocytes and red blood cells. The volume of the recovered fluid was immediately centrifugated. After May Grünvald Giemsa staining light microscopic assessment on Olimpus BX 50 was performed. Mann Whitney U and Wilcoxon test was used to analyse the data. $p<0.05$ was considered statistically significant.

RESULTS

All 63 patients had surgical procedures involving abdominal surgery and urological procedures. For all patients the course of anesthesia was uneventful. No serious postoperative pulmonary complications had occurred by the time of patient discharge from the hospital.

There were no significant difference between the ages, sex and cigarette smoking of the patients.

Altough the number of alveolar macrophages and immun cell count (T2) did not change in sevoflurane group the number of these cells increased significantly in isoflurane and halothane group ($p<0.05$) (Table 1).

TABELLA I. *The number of cell count in BAL.*

	B.H.FSD	A.H.FSD	B.I.FSD	A.IFSD	B.S.FSM	A.S.FSD
Alv. Macr.	49.8±6.6	67.1±16	49.7±6.0	57.1±4.6	79.02±02	76.32±5
Imm. Alv. Macr.	30.3±3.6	45.5±3.2	34.5±3.3	52.2±4.1	19.32±09	15.45±2
PNL	66.0±11.7	74.2±17	62/3±7.9	68.3±6.3	24.42±01	28.42±5
Lenf.	2.3±0.5	3.3±0.6	2.9±0.8	2.3±0.4	0.28±35	0.09±0.1
Epi. cell.	101.7±2.1	97.0±17	118±8.3	107.8±37	253±23	146±19
Op. t.		95.7±4.3		94.7±10		91.57±9

BH: Before halothane inhalation; AH: After halothane inhalation; BI: Before isoflurane inhalation; AI: After isoflurane inhalation; BS: Before sevoflurane inhalation; AS: After sevoflurane inhalation.

DISCUSSION

In our study; it is resulted that sevoflurane anesthesia resulted with no change in BAL cell count where isoflurane and halothane anesthesia caused an increase in the number of immature alveolar macrophages which are known to be non functional in pulmonary defense system (fig. 1-2).

Pulmonary complications are a major cause of morbidity and death after anesthesia and surgery (6). The contribution of anesthesia alone to the pathophysiology

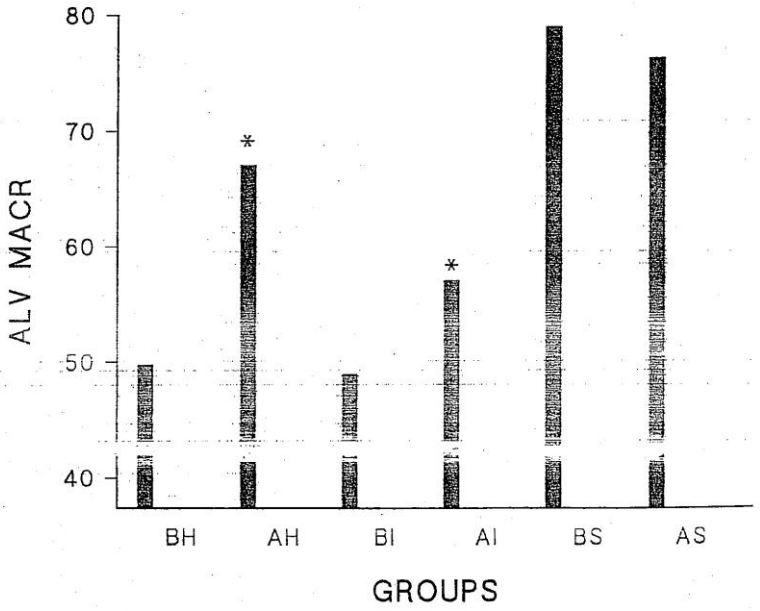


Figure 1. — Number of alveolar macrophages in groups. - (*) p<0.05.

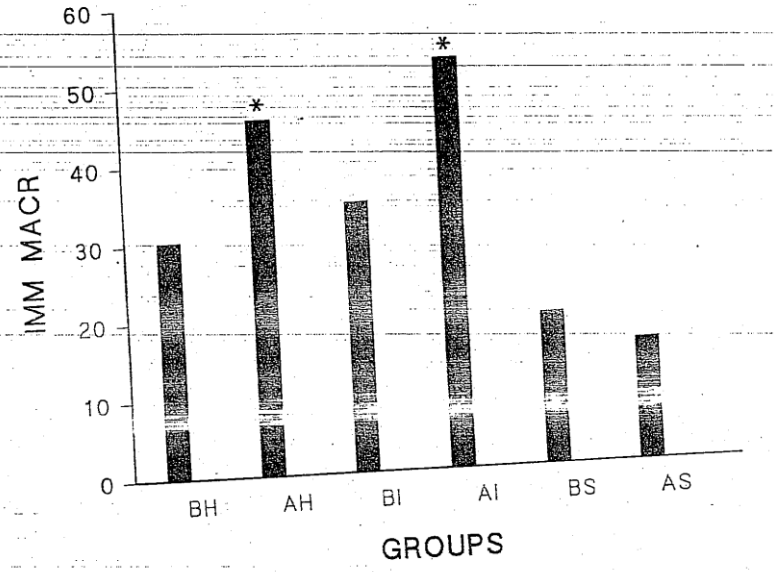
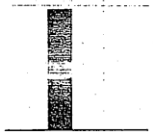


Figure 2. — Number of immature alveolar macrophages - (*) p<0.05.

of pulmonary complications is not clear. In previous studies the phagocytic system was chosen for evaluation because these cells are of primary importance in maintaining the sterility and normal function of the lungs and the system is known to be affected markedly by inhalation of anesthetics.

It was previously reported that halothane and isoflurane inhalation stimulated the liberation of substances those are chematic for phagocytes. Such notion has been proposed in regard to the mechanism that normally leads the lung macrophage population to increase in response to smoke inhalation [7, 8]. Active mobilization of PAM into airways may be the results of increased demand of airway clearence particulary of accumulated mucus after the anesthetic exposure. In our study isoflurane and halothane might have increased the demand of airway clearence more than sevoflurane. Our result is alike with previous studies showing that the alveolar macrophage function is adversly affected after exposure to halothane [7].

Previous studies suggested that the site of action of the anesthetic agents on the human PAM is in part the cell membrane and that they alter the response of the cells to surface stimuli [11]. In our study sevoflurane caused no response of pulmonary alveolar macrophages.



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The increase in the number of immature alveolar macrophages in isoflurane and halothane group might be due to impaired protein mobility in the PAM plasma membrane ([11]).

The results of invitro studies previously showed that PAM microbicidal oxidative activity inhibited by clinically releveant isoflurane concentration and this inhibition is reversible and that it only occurs during and after exposure. It was also previously reported that there was a strong correlation between loss of macrophage and the duration of surgery and anesthesia ([10]). On the contrary in our study we examined that the number of alveolar macrophages were increased but number of immature alveolar macrophages were increased. Although it was previously shown that halothane 4% caused dose dependent inhibition of proteine synthese in alveolar macrophages in vitro, these studies suggest that these volatile anesthetic can suppress the cytotoxic or phagocytic response of alveolar macrophages and this is reversible ([12, 13]). In our study isoflurane and halothane caused an increase in BAL immature alveolar macrophages which are known immunologically non functional but none of the patients had any pulmonary complications.

We concluded that isoflurane and halothane but not sevoflurane anesthesia changed the cell count of bronchoalveolar lavage. A larger study with strict criteria to define pulmonary complications anesthetic time and agents is needed to determine whether the number of alveolar and immature non functional macrophages correlates with the development of pulmonary complications or not.

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