Title : EFFECTS OF KETAMINE AND HALOTHANE ANESTHESIA ON MORTALITY DUE TO PSEUDOMONAS PNEUMONIA IN GUINEA PIGS

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Introduction: Bacterial clearance in the respiratory tract is performed by the aerodynamic filtration of the upper airway, by the mucociliary escalator system and the phagocytic action of alveolar macrophages. Impairment of pulmonary antibacterial defense mechanisms by halothane (1) and other volatile anesthetics (2) have been reported. Whether depression of immune mechanisms of the lung will result in an increased incidence of respiratory infections and/or an increased mortality in experimental animals remain to be established. Since ketamine has been reported to be devoid of any depression of immune functions in vitro (3), we have attempted to evaluate in a guinea pig model the comparative effect of single and multiple administration of ketamine and halothane anesthesia on the mortality rate of these animals, infected endotracheally with Pseudomonas aeruginosa. The effect of additional trauma, i.e. surgical incision or 20% surface burn was also investigated. Guinea pigs were chosen because 1. a successful burned and infected model has been developed in these animals, 2. their immunologic responses are closer to man than other common laboratory animals.

Methods: Preparation of Pseudomonas aeruginosa, strain 1244: Strain 1244 is a non-mucoid-producing Pseudomonas, virulent in rats and guinea pigs. 0.1 ml of standard stock of P. aeruginosa, strain 1244, kept at -70°C, was added to 50 ml of trypticase soy broth and strongly agitated in a 37°C water bath for 18 h. The bacteria were then collected by centrifugation, washed twice with normal saline and resuspended in normal saline. All procedures were aseptic. The yield from 50 ml broth was approximately 1-2 x 10^{11} bacteria.

Guinea pigs, female Hartley outbreds, weighing 350-400 g were anesthetized in a special plexiglass box into which halothane 1.5% in humidified air was delivered at a flow rate of 5 L/min. (1 or 3 exposures at three day intervals or to a single exposure). Another group of animals received 44 mg/Kg ketamine once or three times. All animals, including untreated control guinea pigs, were instilled endotracheally using a laryngoscope and catheter, with 10^6 - 10^{11} C.F.U. (colony forming units) i.e. live Pseudomonas aeruginosa. Alternatively, animals were instilled transtracheally after a surgical incision, with P. aeruginosa. Each experimental set consisted of 3 groups of 8-10 guinea pigs each (A, B, and C). Group A and B were anesthetized either with Halothane 1.5% in air for 1.5 hrs. or Ketamine 44 mg/Kg intraperitoneally, allowed to recover, then administered Pseudomonas endotracheally under direct vision. The animals were followed up to 1 week after infection, with mortality being the endpoint. Group C = control.

Burn procedure: Scalding in a 95°C water bath for 20 seconds was accomplished by placing the anesthetized guinea pigs in a metal cradle which had an open template on the dorsum of the guinea pig equal to 20% of the body surface area resulting in a full thickness, 3° burn. After scalding, the animals were resuscitated with 10 ml of Ringer's i.p. No deaths occurred following this procedure.

Controls: Control animals received no anesthesia, but were burned and/or infected at the same time and with the same batch of bacteria.

Results: The following results were obtained.

1. No statistically significant difference in mortality between anesthetized (halothane or ketamine) and control (unanesthetized) guinea pigs was observed, i.e. approximately 10% in each group.
2. Decrease LD_{50} up to a difference of 5 log or more, i.e. 10^6 C.F.U. of Pseudomonas vs. 10^{11} or more C.F.U. occur when Pseudomonas was injected intratracheally after small surgical incision in the neck $p < 0.001$.
3. Addition of 20% scald surface burn in guinea pigs, later instilled with Pseudomonas endotracheally and anesthetized with either halothane, 1.5% in air or receiving ketamine, 44 mg/Kg, did not significantly change the mortality compared to controls.
4. Multiple exposures to either halothane (x 3) or ketamine (x 3) at a short interval, (i.e. 3 days) over a period of two weeks in non-burned guinea pigs did not change mortality rate in a statistically significant manner.

Discussion and Conclusions: Factors such as CO_2, temperature, humidity, PO_2, blood pressure play a role in the efficiency of bactericidal function of the lungs and must be controlled. However, in our preliminary experiments even with the absence of rigorous controls of all these parameters, no significant difference in mortality was obtained between animals anesthetized with ketamine or halothane and unanesthetized animals. Repeated anesthesia at a short interval with halothane or ketamine over a period of 2 weeks did not alter the mortality rate. The only important and relevant parameter was the use of a surgical incision, which pinpoints the contribution of surgical trauma or the interaction of anesthesia and operation to post-operative depression of immune defenses and/or increased morbidity and mortality in this experimental model.

References:

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