Studies on Haemato-Biochemical Response to Fentanyl and Buprenorphine as Premedicant to Ketamine Anaesthesia in Large White Yorkshire Pigs

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Pigs commonly used in biochemical research are often subjected to complicate and invasive surgical procedures. The knowledge of appropriate analgesia and anaesthesia in pigs however is limited (Malavasi et al., 2005). Body and anatomy make manual restraint difficult, necessitating use of slings or chemical restraint agents.

Fentanyl is 4-acylanilino-piperidine compound and is 250 times as potent as morphine. It is a synthetic opioid analgesic related to pethidine. It is very short acting having peak effect lasting less than 30 minutes when used in anaesthetic doses. Fentanyl is widely used in veterinary medicine to produce complete surgical anaesthesia in dogs (Marsboon et al., 1964). Ketamine rapidly crosses the blood brain barrier quickly entering the brain and the brain/plasma concentrate ratio becomes constant in less than one minute (Cohen et al., 1973). Buprenorphine is a partial µ-opioid agonist–antagonist derived from thebaine. The onset of action is relatively slow requiring 20-30 min to reach full effect. Its analgesic action may last as long as 8 to 12 h. Reports regarding use of anaesthetic combination of Ketamine with fentanyl and buprenorphine in swines are limited.

Therefore, the research work was planned to evaluate the effect on various haematological and blood biochemical parameters using Ketamine with fentanyl or buprenorphine combination in pigs.

Materials and Methods

Fifteen clinically healthy Large White Yorkshire pigs of either sex weighing 25 to 65 kg body weight were randomly divided into three groups of five animals each. All pigs were dewormed with injection Ivermectin at a dose of 1ml per 33 kg bw and fasted for 12 h and drinking water with-held for 6 hours before the administration of anaesthesia. The animals of group I were kept as control, where atropine sulphate premedication was followed by Ketamine @ 15 mg/kg bw by slow intravenous injection through ear vein. In treatment groups i.e. II & III animals, premedication with atropine sulphate was followed by intramuscular injection of Buprenorphine @ 25 mg/kg and Fentanyl @ 10 µg/kg, anaesthetized 10 min later by Ketamine @ 15 mg/kg bw intravenously respectively.

The parameters estimated were haemoglobin, total erythrocyte count, total leucocyte count and differential leucocyte count for which 2 ml blood was collected from car vein in a clean sterile glass vial containing EDTA 1 mg/ml from the experimental pigs before the premedication and at 15, 30, 60, 120 and 240 min after induction of anaesthesia.

Four milliliters of venous blood was collected without anticoagulant in sterilized dry test tube and allowed to clot at room temperature. After two hours serum was separated with the help of pasture pipette and the following

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biochemical parameters were estimated using the serum from the pig at 0, 15, 30, 60, 120 and 240 min interval viz, blood glucose, total protein, serum urea nitrogen, creatinine, aspartate aminotransferase and alanine aminotransferase by standard procedures with the help of semiautomated analyzer (Logotech Techno-168).

The mean standard error of the recorded values were calculated and data was analysed using Analysis of Variance (ANOVA) for knowing any difference existing among the groups using standard procedure outlined by Snedecor and Cochran (1994) and ANOVA Single Factor Programme of M.S.Excel in the computer in Data analysis.

Results and Discussion

The haemoglobin levels (Table I) showed a significant (P<0.01) decrease up to 120 minutes in animals of group I form (11.50± 0.06 gm% to 10.08± 0.11 gm %), where as it increased significantly (P<0.01) up to 60 minutes from (11.44±0.10 to 12.72±0.10) in animals of group III where fentanyl was given along with ketamine, and subsequently decreased and approached near preanaesthetic administration level by 240 minutes. The decrease in the haemoglobin in pigs might have resulted due to spleenic pooling of blood which simulates with the observations recorded in ponies with the use of ketamine by Taylor et al. (1995).

A significant (P<0.01) decrease in total erythrocyte count was noticed following anaesthesia in animals of group I and III respectively, thereafter the values attained near normal levels. Total Leucocyte Count decreased significantly (P<0.01) up to 120 and 60 min in animals of group I and II respectively followed by gradual rise and return to base levels by end of study. Neutrophil count (36.8±0.97% to 39.4±0.87%) showed an increasing trend following anaesthesia up to 30 minutes and then decreased to normal level by 240 min, in animals of group III, where as the increase was marginal in group I anaesthetized with ketamine alone. However, the Neutrophil count decreased significantly at 60 min interval in animals of group II anaesthetized with ketamine and buprenorphine.

The significant (P<0.01) decrease in lymphocyte count in animals of group I given ketamine alone and III ketamine + fentanyl, up to 30 min following anaesthesia is relative to increase in number of neutrophils in various group of animals. A marked Lymphocytopenia was seen in various treatment groups with corresponding neutrophilia (Kaneko, et al., 1997). However, the variations in monocyte and eosinophils values were not of much significance. The observed changes in the differential leucocyte values are probably due to release of cortisone as a result of stress induced on pigs at the time of restraint and handling, since pigs are considered to be excitable animals by nature (Benjamin, 1985).

There was a significant (P<0.01) increase in serum glucose (Table II) immediately following anaesthesia in animals of group I (56.39± 0.67 to 73.85 ± 0.90), II (56.11± 0.89 to 72.93 ± 0.65) and III (55.54 ± 0.62 to 70.84 ± 1.10) (Table 2) from 0 min to 30 min. The significant (P<0.01) decrease in total protein up to 30 min was recorded in animals of group I from (6.59±0.09 to 5.85±0.09), where as it increased significantly (P<0.01) up to 60 min interval in animals of group III (5.92±0.17 to 6.72± 0.26) and non significantly in group II. The rise in blood glucose level at various time intervals could be attributed to the increased adrenocortical hormones during anaesthesia as a result of stress, mobilization of liver glycogen under the influence of increased adrenaline level, decreased glucose utilization or impaired insulin activity (Stenyn, 1969, Tranquilli, et al., 2007). Increase in the level of serum total proteins in different treatment groups II and III at various intervals might be due to stress causing rise in glucocorticoids. Similar findings have been also reported by Shinkar (2002) after administration of detomidine as premedicants to propofol anaesthesia in canines.

A constant and significant (P<0.01) rise in the serum urea nitrogen and creatinine
values were observed up to 120 min in animals of group II and III. Thereafter, the serum urea nitrogen and creatinine levels declined but remained little higher than base value till the end of the experiment. The increase in the serum urea nitrogen during anaesthesia in animals of all the groups might be due to transient and mild depression of the kidney function with decreased renal blood flow and consequent decrease in the glomerular filtration rate (Thurmon et al., 1972).

The significant (P<0.01) increase in the values of aspartate aminotransferase and alanine aminotransferase was observed in animals of group I and II up to 60 and 120 min post anaesthesia, respectively, thereafter the levels approached the base values. The transient increase in the level of AST indicated the probable leakage of this enzyme through plasma membrane of hepatic cells rather than release from the damaged cell. Alanine amino transferase is employed as a marker of hepato cellular damage and is considered as more sensitive indicator of liver cell injury than aspartate amino transferase (Cohen and Kaplin, 1971). The increased permeability of ALT through plasma membrane of hepatic cell, in anaesthetized animals might be occurred due oxidative transformation of these drugs in liver during the process of elimination leading to increased level of activity of these enzymes in the present study (Kaneko, et al., loc. cit). Ganter and Kanngiesser (1991) also found increased levels of AST during xylazine-ketamine anaesthesia in pigs. However, Lim et al. (2000) found non significant changes in AST in pigs under propofol anaesthesia.

**Summary**

Fifteen healthy Large White Yorkshire pigs of either sex weighing between 25 to 65 kg were used to study the haematological response to fentanyl and buprenorphine as premedicants to ketamine anaesthesia. The animals were randomly divided into 3 groups of 5 animals each. Ketamine @ 15 mg/kg bw administered intravenously in animals of group I (Control),
Fentanyl @ 10 µg/kg bw and buprenorphine @ 25 mcg/kg bw were administered intramuscularly as preanaesthetics, 10 minutes prior to ketamine anaesthesia in animals of group II and III respectively. The administration of Ketamine alone and along with fentanyl and buprenorphine resulted in decrease in various hematological parameters viz. haemoglobin, packed cell volume, total erythrocytic count, total leucocyte count and lymphocytes. However, increase in haemoglobin was observed in animals of group III. Serum glucose, total protein, urea nitrogen, creatinine, alanine aminotransferase and groups whereas the value of protein decreased significantly up to 30 min interval in animals of group I. The increase in various hematological parameters and decrease in different biochemical parameters attained the base values within 240 min. Thus, fentanyl and buprenorphine as premedicants to Ketamine anaesthesia can be safely used in pigs for general anaesthesia as they caused transient haematobiochemical alterations which reached normal physiological values in few hours.

References


Japanese quail (*Coturnix coturnix japonica*) is the smallest avian species having high market value for its table delicacy. Japanese quail farming in India is not an organized integrated sector as that of chicken farming. The production cost of commercial quail meat and egg is mainly depending on the feed cost since it occupies more than 70 per cent of total production cost. To overcome all these, Japanese quail are subjected to physical feed restriction during early weeks of life and followed by normal *ad lib* feeding. If the low feed consumption is maintained after the short period of feed restriction without affecting the normal growth rate which leads to better production performance that could lead to reduction in production cost and increase in profit margin.

**Materials and Methods**

A total of two hundred and forty straight-run one-day-old Japanese quail chicks belonging to single hatch were randomly allotted into four treatment groups with three replicates of 20 chicks in each. All chicks were fed *ad lib* until two weeks of age. Quantitative feed restriction was followed from 3rd to 5th week of age based on the previous day total feed consumption of full fed control group. The treatment groups consisted of *ad lib* fed control (T₁) and 10 per cent (T₂), 20 per cent (T₃) and 30 percent (T₄) feed restriction. After the completion of feed restriction period, nine females from each replicate were selected and reared separately feeding *ad lib* up to 17 weeks of age and the egg production parameters.