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Evaluation of Ketamine as a General Anesthetic for Domestic Fowl Chicks

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ABSTRACT

Ketamine is a cyclohexanone derivative with analgesic and anesthetic properties. The drug is recommended for use in a wide range of avian species. Studies on its effects on small birds, however, are apparently lacking. In this study, the drug was tested in 3-day-old domestic fowl chicks administered as a single intramuscular (i.m.) injection at 2.5, 5, 10 or 30 mg/kg body weight. A dose of 30 mg/kg was instantly lethal to these birds. Drug toxicity was expressed by the formula y = 1.191x + 1.375 using probit analysis with LD50 and LD99 values at 40.83 and 81.97 mg/kg, respectively. The therapeutic index (TI) was 24.4 indicating a wide margin of drug safety. The time for onset of anesthesia was rapid (10- 60 seconds) depending upon dose level with drug dose and response inversely related (y = -25x + 77.33). Recovery from anesthesia was consistently smooth and varied between 40-60 min also depending upon dose level. The dose and response, however, are positively correlated (y = 9.5x + 34). . Apart from transient salivation in one bird, no untoward effects were observed up to 3 weeks when the experiments were terminated. The domestic fowl (*Gallus domesticus*), as a species, is considered a unique experimental model in immunological research where surgical intervention at an early stage is the tool. This approach, however, requires an effective and a safe anesthetic agent for application in such small birds. Further clinical evaluation may prove ketamine a useful general anesthetic for domestic fowl chicks and perhaps other bird species.

INTRODUCTION

Effective general anesthesia is a prerequisite of all major surgical operations in birds and an important part of avian veterinary practice. It can be produced with either injectable or

inhalant anesthetic agents (Sinn, 1994). Both procedures have their advantages and disadvantages (Paul-Murphy and Fialkowski, 2001). Inhalation agents, for instance, provide rapid induction of anesthesia and smooth and rapid recoveries (Miller and Buttrick, 1999). However, the physiological and anatomical characteristics of the avian species render the use of inhalant anesthetics more hazardous than in mammals with the efficiency of the respiratory system likely to be compromised (Carter-Storm, 1987). There may also be other intricacies for application of inhalation anesthesia such as the unavailability of specialized delivery or monitoring devices particularly under field conditions. The use of injectable anesthetics, on the other hand, has several merits (Wendy and Buttrick, 1999). This includes the rapid mode of administration, the low cost and the minimal need for technical equipment. The greatest disadvantage of injectable anesthesia, however, is the inter-species variability in the response to therapeutic doses or even the variability at the individual level (Sinn, 1994; Miller and Buttrick, 1999; Paul-Murphy and Fialkowski, 2001).

Several injectable anesthetics are used in veterinary practice. Ketamine is a cyclohexanone derivative with analgesic and anesthetic properties. It is administered intravenously or intramuscularly to both mammalian and avian species. In most instances, however, the drug is used in combination with other injectable agents to reduce or eliminate many of the undesirable side effects if used alone (Maiti *et al*, 2006; Durrani *et al*, 2014). The drug is recommended for use in a wide range of avian species (Kittle, 1971; Flecknell, 2009) .When used alone, it is suitable for chemical restraint for minor surgical and diagnostic procedures (Ludders and Matthews, 2007). Despite the popularity of this drug, studies on its effects on small birds are apparently lacking. The present study was intended to assess drug performance when administered to domestic fowl chicks. Assessment was made in terms of drug basic toxicity, therapeutic efficacy, margin of safety, time for onset of anesthesia and duration of anesthesia.

MATERIALS AND METHODS

***Treatment*:** Twenty male, clinically healthy 3-day-old chicks of the Ross strain were allocated randomly to four groups each comprising 5 birds. They received single ketamine (Ketamine hydrochloride, ROTEXMEDICA GmbH, Trittau, Germany) intramuscular (i.m.) injections at doses of 2.5, 5, 10 or 30 mg/kg in the pectoral muscle.

Drug Toxicity: Toxicity was determined in terms of the median lethal dose (qualified as LD50 i.m.) and LD99 using probit analysis (Randhawa, 2009).

Drug Efficacy and Drug Safety*:* The two criteria were evaluated in terms of the median effective dose (ED50) and therapeutic index (TI), respectively.

Onset of Anesthesia: Individual birds treated with different drug doses were observed closely to determine the time for onset of anesthesia measured from the instant of injection of the anesthetic to the moment the bird fell permanently on its side. Mean values were considered for different groups when results were analyzed.

Recovery from Anesthesia*:* Recovery time was recorded for individual birds in groups treated with different doses starting from the time of onset of anesthesia until the bird was fully awake showing normal physical responses. Mean values for different groups were analyzed.

RESULTS

Drug Toxicity: The i.m. administration of ketamine at doses of 2.5, 5 or 10 mg/kg was tolerated by birds. A dose of 30 mg/kg was instantly lethal to these birds. Probit analysis provided the formula y = 1.191x + 1.375 (Figure 1) with LD50 and LD99 values at 40.83 and 81.97 mg/kg, respectively. .

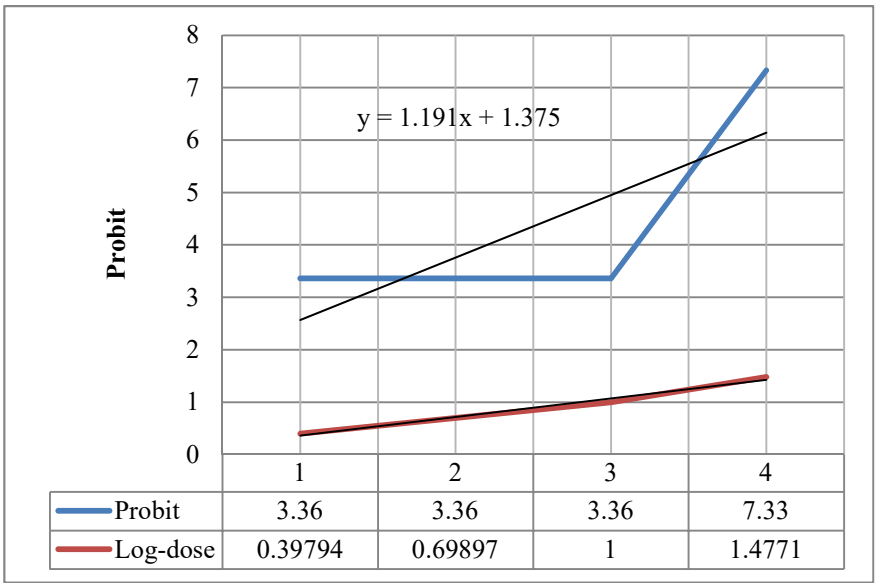

Figure 1: Toxicity of ketamine to 3-day-old chicks: Quantal log-dose response relationship.

LD50 and LD99 values = 14.1 and 20.7 mg/kg, respectively.

Drug Efficacy: Linear interpolation (MS Excel) for dose – response relationship provided the formula y = 30 x, with ED50 and ED99 equivalent to 1.67 and 3.30 mg/kg, respectively (Figure 2).

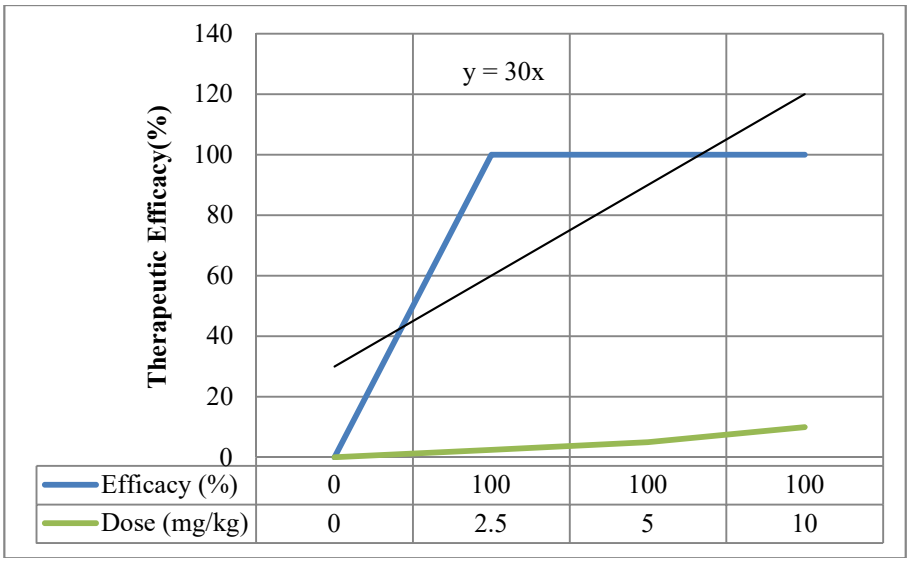

Figure 2: Therapeutic efficacy of ketamine administered to 3-day-old chicks.

ED50 and ED99 = 1.67 and 3.30 mg/kg, respectively. Therapeutic Index = 8.44.

Drug Safety: The Therapeutic Index (LD50/ ED50) equals 24.4.

Onset of Anesthesia: The time varied between 10-60 seconds in different

groups depending upon dose level. Dose and response are inversely related (y = -25x + 77.333) (Figure 3).

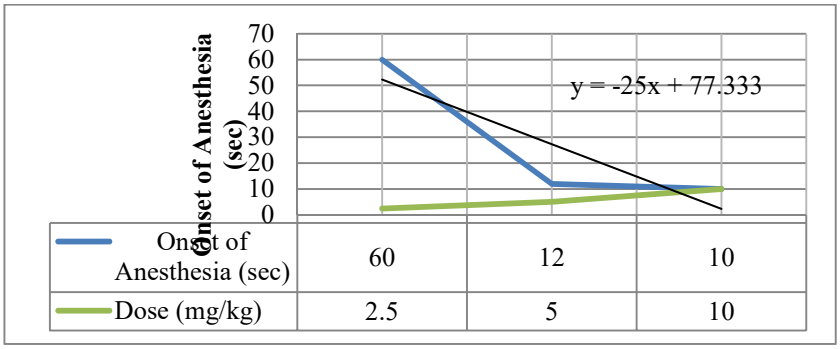

Figure 3: Onset of ketamine –induced anesthesia in 3-day-old chicks.

Onset was rapid not exceeding 60 seconds. Onset is a function of dose.

Recovery from Anesthesia*:* Recovery lasted 40-75 minutes in different groups also depending upon dose level. The dose and response, however, are positively correlated (y = 19.7x-9.5) (Figure 4).

DISCUSSION:

The present study shows that ketamine can be used effectively and safely as a general anesthetic to young chicks following i.m. injection. Doses of 2.5, 5 or 10 mg/kg appeared to be well tolerated by birds with LD50 and LD99 calculated at 40.83 and 81.97 mg/kg, respectively. The drug also had a therapeutic index of 24.4.suggesting a wide margin of drug safety. Onset of drug action was rapid not exceeding 60 seconds regardless of dose level. Such a rapid mode of action may be considered an advantage of the drug. Recovery from anesthesia lasted 40-75 min depending upon drug dose (y = 19.7x-9.5). This enables the level of drug dose to be determined in advance according to the duration of anesthesia required. Recovery was consistently smooth. Apart from salivation in one bird during the induction phase, no untoward reactions were recorded for up to 3 weeks when the experiments were terminated.

The practical significance of testing ketamine in young chicks is that the domestic fowl (*Gallus domesticus*), as a species, is considered a unique experimental model in immunological research where surgical removal of the bursa of Fabricius at an early stage results in depletion of the B-cell lineage and a permanent reduction in antibody production. Schusser *et al* (2013) described an advanced molecular technique leading to loss of antibody production and a block in B-cell development. Surgical bursectomy of newly hatched chicks, nevertheless, combined with sublethal whole body x-irradiation, still remains an economically and a technically feasible technique to produce agammaglobulinemia. This surgical approach, however, requires an effective and a safe anesthetic agent for application in such small birds. Ketamine has been recommended for use in a wide range of avian species (Kittle, 1971; Paul-Murphy and Fialkowski, 2001; Flecknell, 2009). Studies on the effects of this drug on small birds, however, are apparently lacking. Elowni and Hopkins (1981) used sodium pentobarbitone i.p. injection to anesthetize 1-day-old chicks for bursectomy. The anesthetic, given at 40 mg/kg, diluted in Hanks'

Balanced Salt Solution, was effective in inducing and maintaining anesthesia for at least 2 hours, a period sufficient for operation and the subsequent irradiation of the immobilized birds. The present study suggests that ketamine, when given intramuscularly, has the potential to be used effectively and safely as a general anesthetic for domestic fowl chicks.

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