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Clinical Evaluation of Ketamine Hydrochloride for Immobilization in Bonnet Macaques (*Macaca radiata*)

Boon Allwin[1]*, Pradeep Nag BS[2], Kalaignan PA[3], Nishit S Gokarn[4], Gopikrishnan D[2] and Jahangir Basha Doddamani[5]

[1]*Department of Wildlife Science, Madras Veterinary College, TANUVAS, Chennai, Tamil Nadu, India*
[2]*Department of Veterinary Gynaecology and Obstetrics, Madras Veterinary College, TANUVAS, Chennai, Tamil Nadu, India*
[3]*Zoo Veterinarian, Bannerghatta Zoological Park, Karnataka, India*
[4]*Department of Surgery and Radiology, Madras Veterinary College, TANUVAS, Chennai, Tamil Nadu, India*
[5]*Department of Surgery, KVAFSU, Bidar, Karnataka, India*

Abstract

Bonnet macaques are old world monkeys and endemic to southern India. These animals constantly get into human settlements causing constant leading to human animal The study was carried out on 30 clinical cases of Bonnet Macaque of either sex referred for various surgical procedures. This paper aims at presenting a standard protocol of immobilizing bonnet macaques with injection ketamine hydrochloride. Time taken for ataxia was shorter 2.28 ± 0.22. Time for induction was 3.55 ± 0.10 minutes. The duration of anaesthesia was 39.50 ± 0.48 minutes. The mean recovery time was 44.17 ± 0.51 minutes. The quality of anaesthesia was smooth and uneventful. This clinical evaluation of ketamine hydrochloride for immobilization in bonnet macaques has been taken as a standard and can

Keywords: Bonnet macaques; Ketamine hydrochloride; Immobilization

Introduction

The bonnet macaque (*Macaca radiata*) is a macaque that is endemic to southern India. Its distribution is limited by the Indian Ocean on three sides and the Godavari and Tapti Rivers along with a related competing species of Rhesus Macaque in the north. These are Old World monkeys and diurnal in behaviour and weigh between 3.5-9 kg. Land use changes in the last few decades have resulted in changes in the distribution boundaries of these macaques, raising concern for its status in the wild and these animals are often found in human settlements causing menace resulting in a cumulatively growing Man-Animal conflict. This paper aims at presenting a standard protocol of immobilizing bonnet macaques with injection ketamine hydrochloride for restraining during various surgical procedures. Ketamine's neuropharmacology is complex. The compound interacts with NMDA and non-NMDA glutamate receptors, nicotinic, muscarinic cholinergic, monoaminergic, and opioid receptors. In addition there are interactions with voltage-dependent ion channels such as sodium and L-type Calcium channels. It is believed that the NMDA receptor antagonism accounts for most of the analgesic, amnestic, psychomimetic, and neuroprotective effects of the compound, but the exact mechanism of its anaesthetic action is not known. NMDA receptor activation is believed to play a role in the "memory" of the CNS, which is involved in the windup, hyperalgesia, and allodynia seen in certain pain syndromes.

Materials and Methods

The study was carried out on 30 clinical cases of Bonnet Macaque of either sex referred for various surgical procedures such as wound treatment, vasectomy, transport, radiography, presented to the Zoo Veterinary Hospital, Bannerghatta Zoological Park. The feeding history was neglected as often it was available when immobilizing these animals in the wild. The monkeys were administered inj. ketamine hydrochloride @10 mg/ kg, intramuscularly as recorded by Popilskis et al. [1] with either blow pipe, hand held syringe or darted with blowgun. Targets selected for were the muscles in the hip and thigh regions, or, in rare instances, the triceps or shoulder area of larger monkeys. The physiological and clinical parameters were assessed.

Results and Discussion

Time taken for ataxia was shorter 2.28 ± 0.22. Time for induction was 3.55 ± 0.10 minutes. The duration of anaesthesia was 39.50 ± 0.48 minutes. The mean recovery time was 44.17 ± 0.51 minutes. The quality of anaesthesia was smooth and uneventful. Ketamine at the dose rate of 10 mg/kg body weight respectively induced and maintained anaesthesia for a period of 39.50 ± 0.48 minutes. The rectal temperature reduced following induction ketamine. There was a slight elevation of the heart rate at the beginning of induction and the oxygen perfusion level was unaltered in all the cases. Prior to recovery hyperkinesia of all limbs, prolonged ataxia and distress vocalizations were evident 16% of the cases usually older animals.

In the present study the mean ± S.E was duration of anaesthesia was 39.50 ± 0.48 minutes**.** Darting is fast and effective, but has significant disadvantages, including stress, pain, and even trauma on injection. This may pre-excite the animal requiring higher dose. Bonnet macaques have relatively small target areas for darting and these can be difficult to hit, especially on a moving animal. Macaques have a large surface-area-to-body mass ratio; consequently, rapid body heat loss is common during anaesthesia. This is caused by drug suppression of hypothalamic thermoregulation and inhibition of physiological shivering to compensate for heat loss this was the reason for the lowering of rectal temperature after induction. Heat loss is most pronounced in small primate species like bonnet macaques.

***Corresponding author:** Boon Allwin, Research Scholar, Department of Wildlife Science, Madras Veterinary College, TANUVAS, Chennai, Tamil Nadu, India, Tel: +914425304000; E-mail: boonallwin@gmail.com

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There are few reports of reference ranges for primate heart rate, respiratory rate and blood pressure. Heart rates are approximately 100 to 200 beats per minute (bpm) for animals weighing greater than 1 kg, and 200 to 300 bpm for primates weighing less than 1 kg [2]. The respiratory rate is 20 to 50 breaths per minute for most species. In this study the mean heart rate and pulse rate slightly elevated when ketamine alone was administered in animals due to the stimulation of sympathetic nerve trunks. There was no significant deflection in the respiratory rate. However a distinguished breathing pattern termed "*apneustic breathing*", characterized by prolonged inspiratory duration and relatively short expiratory time was noticed.

A significant advantage of ketamine is its high therapeutic index. It has been used alone as an anaesthetic agent in most primates (10 to 100 mg/kg) [3,4]. It had also been given experimentally to five squirrel monkeys @ 250 mg/kg without any causality as reported by Greenstein [5]. It can be administered safely several days in a row for repeated anaesthesia as opined by Bree et al. [6]. The duration of effect is relatively short (depending on dosage), mainly owing to rapid redistribution from the central compartment. Ketamine is also rapidly metabolized in the liver and excreted by the kidneys. The variation is mainly size within the species related will be biggest challenge in computing dosages. It is noteworthy to mention that the suggested initial dosage for the bonnet macaques is 12 to 15 mg/kg [7]. Smaller the species higher dosage is the dosage. The duration of anaesthesia was 39.50 ± 0.48 minutes. The duration of anaesthesia was directly proportional to the plasma half-life of ketamine and the quick recovery from ketamine anaesthesia was due to the redistribution from the blood and the central nervous system to other tissues [8].

The mean recovery time was 44.17 ± 0.51 minutes. Luna et al. [9] reported that the early recovery from ketamine anaesthesia was attributed to ketamine induced catecholamine, which enhanced the basal metabolism leading to faster elimination of ketamine. Also the recovery period is prolonged and rough when high dosages were used alone [10]. This might result from emergence delirium, a severe and common side effect in humans [11], which occurs in approximately 5% to 30% of cases [12]. This state is associated with visual, auditory, proprioceptive, and confusional illusions [13]. The side effect is markedly reduced if ketamine is used in combination with sedative agents such as α2-agonists or benzodiazepines [14,15]. This also occurs when there is a lot pre excitation that the animal undergoes before immobilization. Therefore, a soft and calm induction was known to prevent traumatic recovery in many cases. Ketamine has been used alone in a wide variety of primates, and most reports describe it as safe and reliable. Effective intramuscular dosages vary from 5 to 12 mg/kg for chemical restraint, up to 10 to 30 mg/kg for surgical anaesthesia [7,16]. Some authors give a general recommendation of dosages from 5 to 40 mg/kg IM [17].

The mean time for induction in the present study was 3.55 ± 0.10 minutes after IM injection as recorded by West et al. [18]. Some suggest that induction time is dose related [5], whereas others state it is relatively constant with different dosages, but varies among species [4]. Duration and recovery time is mainly dose-dependent [4], but there is also a difference in sleep time among species [19]. In the present study it was observed that Mean ± S.E sleep time was 39.50 ± 0.48 minutes. Recovery from ketamine appears to be caused by redistribution and metabolism similar to the thiobarbiturates. Hepatic biotransformation to norketamine (metabolite I) and dehydronorketamine (metabolite II) is the major route of metabolism in most species studied [20].

Ketamine causes reliable immobilization, and maintains stable cardiopulmonary function and the laryngeal reflex. Smooth induction could be attributed to the effect of ketamine that altered the reactivity of the central nervous system to various sensory impulses without blocking sensory input at spinal or brain stem levels. However, there are no antagonists. This is a significant disadvantage in case of complications during immobilization or accidental over dosage [21]. Ketamine as a single drug can be administered intramuscularly to anesthetize bonnet macaques that are not easily given drugs intravenously. Thus on conclusion Intramuscular (IM) administration produces duration of anaesthesia that is enough to provide time for most minor surgical procedures and therapeutic managements, but the recovery is usually longer and can be accompanied by more dysphoria.

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