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Effects of Tahitian Noni Juice on Ketamine Anaesthesia in Some Local Rabbits

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Abstract: Tahitian Noni Juices (TNJ) from *Morinda citrifolia* is known with some therapeutic properties that include; anxiety and stress relief, production of calm and relax state, improvement of mood and sense of well being, and sleep restoration. This study attempt to evaluate TNJ effects in some ketamine sedated local rabbits. Six adult rabbits (1.5-1.7 kg) were given intramuscular injection of 5% ketamine hydrochloride (40 mg/kg), following which the quality of sedation was evaluated using: muscle relaxation/rigidity, presence or loss of pain sensation, quality of amnesia as well as heart rate, respiratory rate and temperature as control values. TNJ was administered orally at 2 mL/kg twice daily for 28 days during which period ketamine injection was repeated at 7 days interval. Presence of muscle relaxation or rigidity, presence or absence of pain sensation, quality of amnesia as well as heart rate, respiratory rate and temperature were evaluated. Duration of sleep before and after noni administration was 40.7±9.6 and 46.8±13.7 min, respectively. There was improved quality of amnesia and behavioral responses. Rough induction and recovery gave way to smooth induction and recovery, and spontaneous movement during anesthesia was minimized. Salivation was abolished in all except one rabbit. Mean basal heart rate before and after administration of noni were 204.8±48.4 and 264.4±35.6 beats per min, respectively. Basal respiratory rate also increased from 192±46.3 to 317.6±66.4 breaths per min. TNJ produced appreciable level of calmness, muscle relaxation, and loss of anxiety, and could be useful for premedication prior to aneasthesia.

Key words: Ketamine anaesthesia, local rabbits, tahitian noni juices

INTRODUCTION

In many developing countries, herbal medicines are assuming greater importance in primary health care and their international trade (WHO, 1996). Tahitian noni juice is one of such herbal medicines. Noni is the common name for *Morinda citrifolia* L (Family Rubiceae) and is also called Indian mulberry, Ba Ji Tian Nono, cheese fruit and Nhau in various cultures of the world. The fruit juice is in high demand in alternative medicine for different kinds of illnesses including; arthritis, diabetes, cancer, high blood pressure, muscle aches and pains, headaches, broken bones, menstrual difficulties, heart disease, AIDS, gastric ulcers, asthma, sprains, mental depression, senility, poor digestion, artherosclerosis, blood vessel problems and drug addiction (Bushnell, 1950; Whistler, 1992; Krauss, 1993; Wang *et al*., 2002).

In addition TNJ has been shown to relieve stress and anxiety, produce calmness and relaxation, improve mood and sense of well being (Deng *et al*., 2007). Its analgesic effect has also been reported to be 75% as strong as morphine (Younos *et al*., 1990). In a report from a compilation of over 200 health professionals (representing over 20, 000 Tahitian noni drinkers from over 50 countries) 87% (of 5622 drinkers) reported pain relief, and 74% (of 1,687 drinkers) reported restored/improved sleep (Solomon, 2002).

Ketamine hydrochloride is a dissociative anaesthetic agent used in clinical medicine. Ketamine as the sole anaesthetic produces catalepsia with nystagmus and intact corneal and light reflexes. Hypertonus, purposeful movements and vocalization may also occur. Ketamine produces profound visceral analgesia without somatic analgesia, and tonic-clonic spasms of limb muscles may occur even in the absence of surgical or other stimulations. Ketamine is therefore used in combination with muscle relaxants and analgesics (Hall *et al*., 2001) to produce a state of balanced aneasthesia (Hall *et al*., 2001). It was therefore hypothesized that TNJ could substitute as premedicant for ketamine aneasthesia. This study therefore reports the effects of TNJ on ketamine anaesthesia in some local rabbits.

MATERIALS AND METHODS

This study was conducted in University of Ibadan, Nigeria between July and August 2010. Six local rabbits (4 males and 2 females) with body weight ranging from

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1.5-1.7 kg were used for the study. They were obtained from a rabbitry in Ibadan, Nigeria, and housed in the experimental animal unit of the Faculty of Veterinary Medicine, University of Ibadan, Nigeria, in cages with ample room for ventilation and exercise. They were stabilized and adjudged to be in good health condition based on complete physical examination and laboratory data before the commencement of the experiment.

Each rabbit was given intramuscular injection of 5% ketamine hydrochloride (Rotex Medica, Germany). Following onset of action, the heart rate (beats/min), respiratory rate (breaths/min) and temperature were taken at ten minutes intervals for one hour. The quality of amnesia based on degree of spontaneous movement during sleep and recovery were noted. The time interval between the loss and reappearance of righting reflex gave a measure of sleep time. Pain reflex was evaluated using pin prick and the presence or absence of salivation along with swallowing reflex was noted.TNJ was given orally at a dose rate of 2ml/kg twice daily for 28 days and ketamine injection was repeated at 7 days interval within the period of TNJ administration.

When noni juice administration stopped, the rabbits were still observed for two weeks. Physiological parameters were taken for 2 weeks beyond the period of TNJ administration to compare with control values.

RESULTS

The results of the study are summarized in Table 1-4. Table 1 summarizes the behavioral responses of rabbits to ketamine sedation before and during TNJ treatment. After two weeks of TNJ dose there was marked improvement in induction and recovery, rough induction and recovery gave way to smooth induction and recovery. Spontaneous movement during anesthesia was minimized and salivation abolished in some rabbits. Only one rabbit showed salivation at the end of the study. Pain and swallowing reflexes remained the same throughout the study.

There was a slight increase in time intervals for gain of righting reflex (sleep time) over the weeks of treatment (Table 2). A mean value of 40.7±9.6 was recorded before noni treatment while a maximum value of 51.7±4.7 was recorded one week after treatment. The values however dropped in subsequent weeks. There was also a moderate increase in basal respiratory rate from a control value of 192±46.3 to a maximum of 317.6±66.4 after two weeks of treatment (Table 3). This increase was also reflected in the heart rate which increased from a control value of 204.8 ± 48.4 to a maximum of 264.4±35.6 after three weeks of treatment (Table 4). An observation of the respiratory and heart rates after two weeks of withdrawal of the TNJ treatment showed a reversal to lower values of 199.7 for respiratory rate and 207.6 for heart rate similar to control values.

DISCUSSION

In this study injection of ketamine elicited violent struggles in the rabbits. The period of amnesia was also characterized by frequent turnings and cycling movements and recovery was rough. However, after the first week on noni juice treatment there was marked improvement in the quality of amnesia. The rabbits were relatively calm during ketamine injection and induction was smooth with less spontaneous movements. The recovery period was also characterized by less struggling and turning movements (Table 1). Noni juice seemed to have a calming effect on the rabbits. This supports result from traditional use of noni to relieve stress and anxiety. Noni fruit extracts have been shown to effectively bind to gamma amino butyric acid which produces the anxiolytic effects (Deng *et al*., 2007).

There was an increase in sleep time (40.7±9.6-51.7±4.7 min) after the first week of administering the juice compared to values obtained prior to treatment. However with continuous twice daily treatment with TNJ, the value dropped to 40.6 min in the third week. The animals seemed to adapt to the juice over time, thereby reducing the degree of response to the juice. The drop in values observed in the third week may be attributed to increased metabolism of the juice as a result of continuous administration. It may also be that the animals had developed some tolerance to the juice. An earlier animal study seemed to indicate that the fruit exerts a mild sedative effect (Hirazumi *et al*., 1996; Younos *et al*., 1990). Specifically, a polysaccharide component, damnacanthal is thought to be responsible for producing sedative effects in animal studies. From the result of this study, noni-ketamine combination transiently increased the sleep time produced by ketamine hydrochloride injection.

The analgesic effect of the juice was not apparent in combination with ketamine. This observation contrasted previous studies that the extract show a significant, dose-related, central analgesic activity in some mice. (Younos *et al*., 1990).

Basal heart-rates obtained before ketamine induction was observed to increase during TNJ treatment. There was a steady increase in normal heart rates of rabbits during the course of TNJ treatment. A value of 204beats/min was recorded as control, and by the third week the value was 264 beats/min.

Following withdrawal of the juice, the value fell back to 207 beats/min in two weeks. Though the blood pressure of the rabbits was not measured, the increase in heart rate observed could be as a result of the hypotensive effect of the juice. Earlier observations of the reciprocal relationship of blood pressure to heart rate formed the basis for Marey's law which states that a rise in blood pressure is followed by a reflex slowing of the heart rate and vice versa. The reflex speeding in response to a drop

Table 1: Rabbits Responses to TNJ under Ketamine Sedation

Responses	Control	Week 1	Week 2	Week 3	Week 4
Induction	Rough	Smooth	Smooth	Smooth	Smooth
Recovery	Rough	Smooth	Smooth	Smooth	Smooth
Spontaneous movement	Prominent	Minimal	Minimal	Minimal	Minimal
Salivation	+	+	±	±	±
Pain reflex	+	+	+	+	+
swallowing reflex	+	+	+	+	+

Table 2: Effects of TNJ on Ketamine Sedation: Average time intervals (min) for gain of righting reflex by the Rabbits

	Control	Week 1	Week 2	Week 3	Week 4
Forelimb	40.7±9.6	51.7±4.1	46.8±13.7	40.6±7.0	48.4±12.5
Hindlimb	78.3±10.3	93.3±11.0	76.2±10.3	73.2±13.9	87.4±20.2

Table 3: Respiratory rates: breaths/min of Rabbits during TNJ/Ketamine treatment

	0 min	10 min	20 min	30 min	40 min	50 min	60 min
Control	192±46.3	60.6±16.9	66.6±14.7	96±32.2	109.3±23.5	122.6±40.1	166.6±42.4
Week 1	290.6±43.4	106±57.5	115.3±77.6	145.3±86.1	194±45.8	250.6±55.2	242±32.3
Week 2	317.6±66.4	76.8±54.7	98.4±66.5	124±86.7	168±100	243±75.8	284±46.4
Week 3	275±13.7	66.4±53.6	91.2±63.4	124±84.8	168±95.6	212±106.6	220±96.8
Week 4	220±48.7	40±13.6	49.6±30.9	76±42.99	96±53.9	141.6±63.7	188.8±50.8

Table 4: Heart rate: beats/minutes of Rabbits during TNJ/Ketamine treatment

	0 min	10 min	20 min	30 min	40 min	50 min	60 min
Control	204.8±48.4	236.6±52.8	234.6±38.9	254±16.9	262±20.8	238±25.1	228.6±30.5
Week 1	244±30.3	264±18.8	237.6±22.5	232.8±22.3	233.6±9.2	249.6±19.1	249.6±16.9
Week 2	249.6±31.8	294.4±13.4	267.2±16.3	253.6±16.9	259.2±15.8	268±18.8	267.2±15.8
Week 3	264.4±35.6	284.8±43.6	251.2±34.1	241.6±28.1	253.6±30.9	259.2±40.5	276±29.7
Week 4	244±30.3	264±18.8	237±22.5	232.8±22.3	233.6±9.2	249.6±19.1	249.6±16.9

in arterial pressure is a mixed sympathetic-parasympathetic effect with some variation according to species (Roger and Robert, 1977). However Marey's law do not hold in physical exercise and emotional stress in which both blood pressure and heart rate are elevated. This result supports previous study on the hypotensive effect of noni (Bushnell, 1950; Whistler, 1992; Moorthy and Reddy, 1970). Moorthy and coworkers found that an ethanol extract of the Noni roots lowered the blood pressure in an anesthetized dog (Moorthy and Reddy, 1970).

The respiratory rate also increased from a control value of 192 breaths/min to 317 breaths/min by the second week. The increased respiratory rate during the course of TNJ administration could have occured as a result of the hypotensive effect of the juice. This is because respiratory rate increases in response to increased heart rate (Roger and Robert, 1977).

Results of this study showed the anxiolytic properties of TNJ. It also authenticates previous reports on the hypotensive properties and a mild antisialogogue effect of TNJ.

CONCLUSION

This study has shown that noni improves the quality and duration of amnesia produced by ketamine injection with a calming effect on the animal. The juice was also found to lower blood pressure and produce a mild antisialogogue effect, an observation that has not been previously reported. TNJ administration could therefore be useful for premedication prior to aneasthesia.

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