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Research Article

EVALUATION OF PANCURONIUM AS MUSCLE RELAXANT IN BUFFALOES

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ABSTRACT

The present study was undertaken on five male buffaloes to evaluate pancuronium as a muscle relaxant. The drug was administered @ 26 µg/kg IV in all the animals after keeping them off-feed for 24 h and evaluated on the basis of a number of behavioral observations and various clinical, haematological and biochemical parameters. All animals showed ataxia at 0.97±0.13 min and sternal recumbency at 1.17±0.02 min. Complete muscle relaxation of animals was observed at 7.90±0.63 min. Early signs of recovery were noticed at 14.60±0.71 min as evident by tail movements. Complete recovery without ataxia took 42.46±2.70 min. A significant increase in heart rate and decrease in respiratory rate was observed at peak effect of the drug. There was a significant increase in haemoglobin and blood glucose level at peak effect of drug and significant increase in A:G ratio at recovery. There was a significant decrease in total plasma proteins and globulins at recovery. There was a non-significant increase in cortisol at peak effect of drug. Pancuronium bromide (26 µg/kg IV) resulted in rapid induction of muscle relaxation for longer duration action.

Key words: Buffalo, muscle relaxant, pancuronium

The muscle relaxants in veterinary practice have been first introduced in 1952 (Peshin, 2001). Manley *et al*. (1983) reported the efficacy of muscle relaxants (gallamine, pancuronium, and vecuronium) for anaesthetic management in humans, laboratory animals and small domestic animals. Neuromuscular blocking agents are most often used as adjuvants to anaesthesia to facilitate tracheal intubation, abdominal muscle relaxation, and orthopaedic manipulations, and as a component of balanced anaesthesia procedures to reduce the amount of general anaesthetic required in high risk patients (Taylor, 2006). In veterinary practice, it is necessary to restrain the animals and to produce adequate muscle relaxation so that the surgical interventions can be done easily. The rationale of the present study was to establish, whether or not pancuronium produces clinically useful neuromuscular blockade in buffaloes and, if it did, to determine the manifestations and duration of the blockade and its effects on body systems.

MATERIALS AND METHODS

The study was conducted with the prior permission of Institutional Animal Ethical Committee on five apparently healthy adult male buffaloes of 3-4 years of age to evaluate the muscle relaxant effect of pancuronium drug. The dose of pancuronium i.e. 26 µg/kg IV was standardized before actual experiment was undertaken. The animals were on fasting for 24 h before the experiment and then comfortably secured in standing position and pancuronium @ 26 µg/kg was administered intravenously. To evaluate the effect of pancuronium, following parameters were recorded at different time intervals: behavioural changes, heart rate, rectal temperature, respiratory rate, haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leucocyte count (TLC), platelet count, differential leucocyte count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), blood/plasma glucose, urea nitrogen, creatinine, bilirubin, cortisol, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, total plasma proteins, albumin, alanine amino transferase (ALT), aspartate amino transferase (AST), lactate dehydrogenase (LDH), gamma glutamyltransferase (GGT), alkaline phosphatase (AP), calcium, phosphorus, sodium, potassium and chloride. Statistical analysis of data was done by Students 't' test at 5 % level of significance.

RESULTS AND DISCUSSION

Means ±SE of time (min) of different behavioural characteristics and reflexes have been shown in Tables 1 and 2. A decrease in spontaneous activity with ataxia was seen in all the animals at 0.97±0.13 min of pancuronium administration and animals became recumbent at 1.29±0.02 min. This might be due to the blocking of endogenous neurotransmitter acetylcholine

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Table 1
Time intervals of behavioural characteristics after administration of pancuronium in male buffaloes

Parameters	Mean±SE (Min.)
Weak time	0.97±0.13
Down time	1.17±0.02
Chin on ground	1.23±0.02
Turning of neck	1.26±0.02
Lateral recumbency	1.29±0.02
Paddling of limbs	1.87±0.20
Salivation	2.48±0.18
Mouth gag application	6.66±0.73
Intubation	7.90±0.63
Extubation	30.54±4.12
Urination	21.95±2.90
Regaining of sternal recumbency	35.35±3.12
Standing with ataxia	35.59±3.09
Walking with ataxia	35.86±3.01
Walking without ataxia	42.46±2.70

(ACh) to activate nicotinic cholinergic receptors of skeletal muscle cells, thereby inhibiting receptor–coupled trans-membrane ion movements necessary for muscle contraction (Bouzat *et al*., 2004; Unwin, 2005). The end result of this action led to skeletal muscle paralysis and muscular relaxation (Kita and Goodkin, 2000). Ataxia and lateral recumbency was also reported in buffalo calves after administration of pancuronium bromide (Manuja *et al*., 2012). The onset of action was rapid similar to other species such as dogs (Hall and Clarke, 1991), horses (Manley *et al*., 1983) and cattle calves (Hildebrand and Howitt, 1983).The fore limbs (3.38±0.70 min) relaxed earlier than the hind limbs (4.52±0.72 min). Apnoea was not seen in any of the animals in the present study. However, apnoea has been reported in dogs at a dose of 0.06 mg/kg (Hall and Clarke, 1991). Corneal reflex and palpebral reflex were intact in all the animals throughout the experiment. Pin pricks in the region of abdomen and thorax showed the presence of cutaneous

Table 2
Time intervals for loss and gain of different reflexes after administration of pancuronium in male buffaloes

Reflex	Loss of reflexes Mean±SE (min.)	Gain of reflexes Mean±SE (min.)
Tail	2.87±0.27	14.60±0.71
Fore limb withdrawal	3.38±0.70	17.97±1.48
Hind limb withdrawal	4.52±0.72	13.66±1.66
Prepuce reflex	8.59±1.17	19.73±1.79
Scrotal reflex	10.73±1.00	25.74±1.19
Jaw reflex	7.39±2.17	30.62±4.12
Muzzle dryness	15.78±1.01	38.10±3.51

reflex because the muscle relaxants do not have analgesic property (Melegar, 2006). Peak time of the drug effect with profound relaxation of jaw muscles was observed at 7.39±2.17 min. Manuja *et al.* (2012) reported the peak duration of pancuronium-induced muscle relaxation at 10.98±0.34 min. Endotracheal intubation was done after moderate relaxation of jaw at 7.90±0.63 min and extuabtion was done at 30.54±4.12 min. Endotracheal intubation was done to see the relaxation of muscles and for assisted ventilation, if needed, however, no assisted ventilation was required during the experiment. The early sign of recovery i.e. spontaneous movement of tail were noticed at 14.60±0.71 min. All the animals returned to sternal recumbency at 35.35±3.12 min. and stood up on their own and walked with ataxia at 35.86±3.01; normal i.e. without ataxia at 42.46±2.70 min. Similar observations were reported by Manuja *et al*. (2012) in buffalo calves after administration of pancuronium bromide.

Values of rectal temperature, heart rate and respiratory rate before and at different intervals after administration of pancuronium have been shown in Table 3. There was a significant increase in heart rate (102.80±8.14 beats/min) at 5 min of pancuronium administration as compared to the base value (50.20±4.79 beats/min). The pancuronium is known to increase the

Table 3
Various clinical parameters (mean±SE) at different time intervals after administration of pancuronium in male buffaloes

Parameters (Units)	Before drug administration	At 5 min.	At 10 min.	At 15 min.	At 20 min.	At 25 min.	At 30 min.	At 35 min.	At recovery	At 24 h of recovery
Ambient temperature (°C)	22.80^{a}± 0.49	22.80^{a}± 0.49	22.80^{a}± 0.49	22.80^{a}± 0.49	22.80^{a}± 0.49	22.80^{a}± 0.49	22.80^{a}± 0.49	22.50^{a}± 0.50	22.80^{a}± 0.49	23.20^{a}± 0.49
Rectal temperature (°C)	37.92^{a}± 0.37	38.02^{a}± 0.41	37.98^{a}± 0.41	37.88^{a}± 0.31	37.78^{a}± 0.23	37.72^{a}± 0.24	37.66^{a}± 0.28	37.63^{a}± 0.36	37.66^{a}± 0.29	38.02^{a}± 0.34
Heart rate (beats /min.)	50.20^{c}± 4.79	102.80^{a}± 8.14	70.60^{b}± 6.66	60.20b^{c}± 4.86	55.40^{c}± 2.89	53.20^{c}± 3.38	52.80^{c}± 3.72	53.25^{c}± 4.66	51.60^{c}± 4.49	50.60^{c}± 3.83
Respiratory rate (breaths/min.)	22.20^{a}± 3.85	12.00^{b}± 2.19	9.60^{b}± 2.69	7.60^{b}± 2.34	6.20^{b}± 1.11	6.60^{b}± 0.98	8.60^{b}± 1.21	8.25^{b}± 1.03	13.20^{b}± 2.15	21.00^{a}± 2.93

Means with different superscripts for a parameter in a row vary significantly ($p<0.05$)

Table 4

Haematological parameters (mean±SE) at different time intervals after administration of pancuronium in male buffaloes

Parameters (Units)	Before drug administration	At peak effect of drug	At recovery	At 24 h of recovery
Haemoglobin (g/dl)	9.50^{b}±0.15	10.22^{a}±0.32	8.86^{c}±0.09	9.12^{bc}±0.20
Packed cell volume (%)	32.58^{ab}±0.74	36.18^{a}±1.88	31.82^{b}±0.76	31.32^{b}±1.54
TEC (x10^{6}/mm^{3})	7.25^{ab}±0.15	7.92^{a}±0.20	6.93^{b}±0.13	6.98^{b}±0.42
TLC (x10^{3}/mm^{3})	9.19^{a}±0.85	10.32^{a}±1.26	8.33^{a}±0.85	9.65^{a}±0.78
Total platelets count (x10^{3}/mm^{3})	240.00^{a}±20.49	235.4^{a}±33.22	225.00^{a}±24.34	267.00^{a}±42.91
Lymphocytes (%)	51.20^{ab}±3.73	58.4^{a}±2.97	59.8^{a}±2.57	49.40^{b}±2.27
Monocytes (%)	1.00^{a}±0.00	1.00^{a}±0.00	1.00^{a}±0.00	1.00^{a}±0.00
Granulocytes (%)	47.8^{ab}±3.73	40.6^{b}±2.97	39.2^{b}±2.57	49.6^{a}±2.27
MCV (fl)	46.62^{a}±1.26	47.86^{a}±1.31	46.46^{a}±1.29	46.64^{a}±1.25
MCH (pg)	13.7^{a}±0.32	13.78^{a}±0.43	13.4^{a}±0.28	14.34^{a}±0.59
MCHC (%)	28.74^{a}±0.74	28.52^{a}±1.12	28.06^{a}±0.80	29.96^{a}±1.04

Means with different superscripts in a row for a parameter vary significantly ($p<0.05$). TEC=Total erythrocyte count; TLC=Total leucocyte count; MCV=Mean corpuscular volume: MCH=Mean corpuscular haemoglobin; MCHC=Mean corpuscular haemoglobin concentration

heart rate by its cardiac vagolytic action on the postsynaptic cholinergic receptors of the heart (Punnen *et al*., 1984) and the blocking of noradrenaline re-uptake (Domenech *et al*., 1976). Usually no other significant changes are observed in cardiovascular function after administration of pancuronium (Brown *et al*., 1973). However, the drug had been reported to cause slight increase in blood pressure in human beings (Coleman *et al*., 1972). Significant tachycardia was also recorded during the peak effect of the pancuronium in buffalo calves by Manuja *et al*. (2012). There was a significant decrease in respiratory rate at 5 min of pancuronium administration (12.00±2.19 breaths/min), which remained significantly lower till recovery with a minimum value of 6.20±1.11 breaths/min at 20 min as compared to the base value of 22.20±3.85 breaths/min. The decrease in respiratory rate is due to relaxation of respiratory muscles. Other workers have also reported a significant decrease of the respiratory rate at peak effect of drug in buffalo calves (Manuja *et al*., 2012). Mean ±SE values of different haematological and biochemical parameters before and at different intervals after administration of pancuronium in buffaloes have been shown in Tables 4 and 5, respectively. There was a statistically significant increase in Hb level at peak effect of drug but the values remained within the normal physiological limit. Other haematological parameters also remained within the normal physiological limits. Manuja *et al*. (2012) also found no significant variations in any of the haematological parameters after pancuronium administration in buffalo calves. There was a significant increase in blood glucose level at peak effect of drug which may be due to increase in cortisol level in the blood. Cortisol counters insulin by encouraging higher blood sugar and stimulating gluconeogenesis (Toshihiko *et al*., 1996). There was a significant decrease in total plasma proteins and globulins at recovery and significant increase in A:G ratio at recovery but the values remained within the normal physiological limits. Other biochemical parameters did not vary significantly.

Similarly, Manuja *et al*. (2012) also found no significant variations in any of the biochemical parameters after pancuronium administration in buffalo calves. A non-significant increase in cortisol level was also observed at peak effect of drug and at recovery which may be due to the release of ACTH from the anterior pituitary gland due to hypoxia condition caused by pancuronium (Castognoli *et al*., 1961; Brunt and Ganong, 1963). On the basis of finding of this study, it can be concluded that pancuronium bromide (26 µg/kg IV) results in rapid induction of muscle relaxation for longer duration of action without much changes in haemato-biochemical parameters in buffaloes. Therefore, pancuronium can be used for those surgical procedures in buffaloes where muscle relaxation is required.

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Table 5

Blood biochemical parameters at different time intervals after administration of pancuronium in male buffaloes

Parameters (Units)	Before drug administration	At peak effect of drug	At recovery	At 24 h of recovery
Glucose (mg/dL)	51.38^{b}±3.53	125.02^{a}±20.34	123.52^{a}±13.32	54.78^{b}±5.10
Triglycerides (mg/dL)	16.8a^{b}±1.49	20.60^{a}±1.6	17.80^{ab}±2.01	13.20^{b}±2.47
Total cholesterol (mg/dL)	74.20^{a}±3.49	70.80^{a}±2.90	70.40^{a}±2.04	68.60^{a}±3.90
HDLC (mg/dL)	34.7^{a}±1.53	33.54^{a}±1.33	31.84^{a}±2.09	33.64^{a}±2.23
LDLC (mg/dL)	17.32^{a}±0.92	16.92^{a}±0.84	16.26^{a}±0.87	15.34^{a}±1.09
Cortisol (ng/L)	100.06^{a}±20.60	154.47^{a}±40.52	151.88^{a}±48.31	92.46^{a}±20.75
LDH (IU/L)	426.98^{a}±45.71	446.96^{a}±44.25	439.22^{a}±43.58	430.76^{a}±45.20
ALT (IU/L)	32.62^{a}±3.25	35.80^{a}±3.54	33.58^{a}±3.09	33.18^{a}±2.15
AST (IU/L)	39.78^{a}±3.34	44.60^{a}±3.10	42.34^{a}±2.87	41.00^{a}±3.17
ALP (IU/L)	69.00^{a}±2.02	70.80^{a}±5.38	67.40^{a}±2.56	68.00^{a}±3.11
GGT (IU/L)	17.68^{a}±3.21	21.32^{a}±1.34	19.86^{a}±1.67	20.30^{a}±1.15
Bilirubin direct (mg/dL)	0.18^{a}±0.04	0.19^{a}±0.03	0.11^{a}±0.01	0.13^{a}±0.03
Total protein (g/dL)	9.82^{a}±0.24	9.47^{ab}±0.33	8.55^{b}±0.55	9.66^{ab}±0.47
Albumin (g/dL)	3.53^{a}±0.06	3.48^{a}±0.06	3.78^{a}±0.40	3.49^{a}±0.05
Globulin (g/dL)	6.29^{a}±0.24	5.99^{a}±0.39	4.77^{b}±0.44	6.17^{a}±0.45
A:G ratio	0.56^{b}±0.02	0.59^{b}±0.05	0.82^{a}±0.12	0.57^{b}±0.04
BUN (mg/dL)	39.36^{a}±4.04	36.98^{a}±4.58	40.38^{a}±3.45	37.18^{a}±5.80
Creatinine (mg/dL)	0.10^{a}±0.00	0.11^{a}±0.00	0.10^{a}±0.01	0.09^{a}±0.00
Sodium (mmol/L)	142.94a±2.83	142.14^{a}±2.61	140.36^{a}±2.28	140.60^{a}±3.01
Potassium (mmol/L)	4.18^{ab}±0.12	4.72^{a}±0.35	4.00^{b}±0.17	4.45^{ab}±0.15
Chloride (mmol/L)	109.74^{a}±2.91	107.24^{a}±2.03	105.66^{a}±2.30	106.60^{a}±3.37
Calcium (mg/dL)	8.62^{a}±0.44	9.08^{a}±0.45	8.46^{a}±0.51	9.70^{a}±0.34
Phosphorus (mg/dL)	3.95^{a}±0.34	4.90^{a}±0.39	4.70^{a}±0.46	4.67^{a}±0.52

Means with different superscripts in a row for a parameter vary significantly ($p<0.05$). HDLC=HD Cholesterol; LDLC=LD Cholesterol; LDH= Lactate dehydrogene; ALT=Alanine aminotransferase; AST=Aspartate aminotransferase; ALP=Alkaline phosphatase; GGT=Gamma glutamyl transferase; BUN=Blood urea nitrogen

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