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Research Article

EVALUATION OF VECURONIUM AS MUSCLE RELAXANT IN BUFFALO BULLS

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ABSTRACT

Study was undertaken for evaluation of vecuronium (40µg/kg IV) as muscle relaxant in five buffalo bulls. All animals showed ataxia at 1.11±0.02 min and sternal recumbency at 1.28±0.04 min. Complete relaxation of animal was observed at 7.90±0.63 min. Early signs of recovery were noticed at 19.77±1.94 min. as evident by tail movements. Complete recovery without ataxia took 30.10±0.75 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 glucose at peak effect of drug and significant increase in Albumin: Globulin at recovery. There was significant decrease in total plasma proteins and globulin at recovery. There was a non-significant increase in cortisol at peak effect of drug.

Keywords: Buffalo, Bulls, Muscle relaxant, Vecuronium

A muscle relaxant is a drug which affects skeletal muscle function and decreases the muscle tone. The use of neuromuscular blocking drugs have increased the safety and improved the results of many established surgical procedures. 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). Neuromuscular blocking agents interfere with the effectiveness of the endogenous neurotransmitter acetylcholine 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).

Vecuronium is one of the newer muscle relaxants, the pharmacology of which has been described by Bowman (1980). Non-depolarizing relaxants have advantages over the depolarizing ones, because the former don't cause muscle fasciculi and concurrent change in intra-abdominal pressure that increase risk of regurgitation. In view of the above, present study was conducted with the objective to determine the clinical effects and manifestations and the extent of skeletal muscle relaxation obtained in buffaloes after the administration of Vecuronium.

MATERIALS AND METHODS

The study was done on five clinically healthy adult buffalo bulls (3-4 years). The dose of Vecuronium was standardized before actual experiment was undertaken. The animals were fasted for 24 hours before the experiment and then comfortably secured in standing position and Vecuronium @ 40 µg/kg was injected in the jugular vein. The parameters observed included: behavioral changes, heart rate, rectal temperature, respiratory rate, haemoglobin, packed cell volume, total erythrocyte count, total leucocyte count, platelet count, differential leucocyte count, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, blood/plasma glucose, urea nitrogen, creatinine, bilirubin, cortisol, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, total plasma proteins, albumin, alanine amino transferase, aspartate amino transferase, lactate dehydrogenase, gamma glutamyl transferase, alkaline phosphatase, calcium, phosphorus, sodium, potassium and chloride. Recording of various parameters and collection of blood samples were done at varying time intervals. Statistical analysis of data was done by Students' 't' test at 5% level of significance. The study was conducted after taking necessary permission from institutional animal ethical committee.

RESULTS AND DISCUSSION

A decrease in spontaneous activity with ataxia was seen in all the animals at 1.11±0.02 min. of Vecuronium administration and animals became recumbent at 1.28±0.04 min. (Table 1). This may be due to blocking of the effectiveness of the endogenous neurotransmitter acetylcholine (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 leads to skeletal muscle paralysis and muscular relaxation (Kita and Goodkin, 2000).The onset of action was rapid similar to other species such as cats (Bencini *et al.*, 1983), dogs (Jones and Young, 1991) and horses (Fantoni *et al.*, 1998). Muscle paralysis proceeds at different rate in different

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body regions after administration of a myoneural blocking agent. Usually head and neck muscles are affected first; often within 0.25-1 min. after injection. The tail is usually affected with head and neck (Hall and Clarke, 1991). Subsequently muscle of limbs are paralysed and then the muscle of larynx, abdomen, intercostal and diaphragm. Recovery usually proceeds in reverse of this sequence (Hall and Clarke, 1991) and the diaphragm usually is first to regain function. In the present study, this typical pattern of paralysis was observed (Table 2). The fore limbs (2.03±0.13 min.) were relaxed earlier than the hind limbs (2.05±0.13min.). Apnoea was not seen in any of the animals. However, apnoea has been observed in horses at doses of 0.1mg/kg (Fantoni *et al.*, 1998). Corneal reflex and palpebral reflex were intact in all the animals throughout the experiments. Pin pricks in the region of abdomen and thorax showed the presence of cutaneous reflex because the muscle relaxants do not have analgesic property (Meleger, 2006). Peak time of the drug effect with profound relaxation of jaw muscles was observed at 3.02±0.56 min. Intubation was done after moderate relaxation of jaw at 5.10 ± 0.39 min. and extubation was done at 27.32 ± 0.81 min. The early signs of recovery i.e. spontaneous movement of tail were noticed at 19.77±1.94 min. All the animals returned to sternal recumbency at 27.77 ± 0.77 min. All the animals stood up by their own and walked with ataxia at 28.17±0.79 and ataxia disappeared at 30.10±0.75 min. of administration of Vecuronium to ensue complete recovery.

There was a significant increase in heart rate (85.00 ± 5.53 beats/min.) at 5 min. of Vecuronium administration as compared to the base value (49.40 ± 3.94 beats/min.) which may be due to the Vecuronium blocking (Table 3) the noradrenaline re-uptake (Narita *et al.*, 1992). Vecuronium has been shown to be remarkably free of action on the cardiovascular system in animals (Marshall *et al.*, 1980) and in man (Fahey *et al.*, 1981) and does not appear to liberate histamine (Basta *et al.*, 1983).

There was a significant decrease in respiratory rate (Table 3) at 15 min. of Vecuronium administration (9.00 ± 1.97 breaths/min.), which remained significant lower till 30 min. of Vecuronium with a minimum value (6.40 ± 0.87 breaths/min.) at 20 min. of Vecuronium as compared to the base value (18.00 ± 3.35 breaths/min.). Vecuronium causes respiratory depression in dogs (Jones and Young, 1991) and horses (Fantoni *et al.*, 1998).

There was significant increase in hemoglobin, total erythrocyte count (TEC) at peak effect of drug and significant increase in mean corpuscular haemoglobin concentration (MCHC) at recovery but the values remain within the normal physiological limit so does not affect any system in the body (Table 4). Other parameters remained within the normal physiological limits. Jones and Young (1991) found no significant variations in any of the haematological parameters after Vecuronium administration in dogs (Kumar *et al.*, 2018).

Table 1
Behavioural characteristics induced by administration of Vecuronium in male buffaloes

Parameters	Mean ±SE (Min.)
Weak time	1.11±0.02
Down time	1.22±0.04
Chin on ground	1.23±0.04
Turning of neck	1.26±0.04
Lateral recumbency	1.28±0.04
Paddling of limbs	2.25±0.08
Salivation	2.70±0.20
Mouth gag application	4.17±0.35
Intubation	5.10±0.39
Extubation	27.32±0.81
Urination	16.74±2.87
Regaining of sternal recumbency	27.77±0.77
Standing with ataxia	27.86±0.76
Walking with ataxia	28.17±0.79
Walking without ataxia	30.10±0.75

Table 2
Reflexes induced by administration of Vecuronium in male buffaloes

Reflex	Loss Mean ±SE (Min.)	Gain Mean ±SE (Min.)
Tail tone	2.39±0.17	19.77±1.94
Fore limb tone	2.03±0.13	24.47±0.93
Hind limb tone	2.05±0.13	23.84±0.83
Prepuce tone	3.24±0.31	16.12±3.04
Scrotal tone	8.96±0.33	24.95±1.79
Jaw tone	3.02±0.56	27.23±0.85
Muzzle dryness	18.57±0.55	28.98±0.58

There was a significant increase in glucose at peak effect of drug which may be due to increase in cortisol level in the blood (Table 5). Cortisol counters insulin by encouraging higher blood sugar and stimulating gluconeogenesis (Toshihiko *et al.*, 1996). There was a significant increase in potassium at peak effect of drug which may be because during hypoxia, the concentration of intracellular ATP in skeletal muscles might be lowered sufficiently to activate the opening of an ATP-sensitive K+ channel (Woll *et al.*, 1989). Other biochemical parameters

Table 3
Effects of Vecuroniumon rectal temperature, heart rate and respiratory rate in male buffaloes (Mean ± S.E., n=5)

Parameters (Units)	Before drug admn.	At 5 min.	At 10 min.	At 15 min.	At 20 min.	At 25 min.	At 30 min.	At recovery	At 24 hrs. of recovery
Ambient temperature (°C)	25.20^{a} ±0.37	25.20^{a} ±0.37	25.20^{a} ±0.37	25.20^{a} ±0.37	25.20^{a} ±0.37	25.20^{a} ±0.37	26.00^{a} ±0.00	25.20^{a} ±0.37	24.90^{a} ±0.46
Rectal temperature (°C)	37.78^{a} ±0.29	37.86^{a} ±0.29	37.74^{a} ±0.24	37.76^{a} ±0.25	37.68^{a} ±0.24	37.72^{a} ±0.24	37.20^{a} ±0.00	37.66^{a} ±0.21	37.70^{a} ±0.22
Heart rate (beats /min.)	49.40^{b} ±3.94	85.00^{a} ±5.53	55.00^{b} ±2.72	49.60^{b} ±3.06	58.00^{b} ±10.64	49.00^{b} ±2.65	60.00^{b} ±0.00	48.20^{b} ±3.75	49.80^{b} ±3.58
Respiratory rate (breaths/min.)	18.00^{a} ±3.35	10.60^{ab} ±2.16	10.40^{ab} ±2.46	9.00^{b} ±1.97	6.40^{b} ±0.87	7.20^{b} ±1.77	9.00^{b} ±0.00	11.60^{ab} ±1.33	18.20^{a} ±3.06

Means with different superscripts vary significantly ($p<0.05$)

Table 4
Effects of Vecuroniumon haematological parameters in male buffaloes (Mean±S.E., n=5)

Parameters (Units)	Before Drug admn.	At peak effect of drug	At recovery	At 24 hrs. of recovery
Haemoglobin (g/dl)	8.64^{b} ± 0.23	10.12^{a} ± 0.32	8.48^{b} ± 0.20	8.70^{b} ± 0.23
Packed cell volume (%)	30.42^{ab} ± 0.83	34.48^{a} ± 1.73	28.90^{b} ± 2.48	29.32^{b} ± 1.15
TEC (x10v /mm^{3})	6.54^{b} ± 0.07	7.43^{a} ± 0.32	6.59^{ab} ± 0.39	6.24^{b} ± 0.29
TLC (x10^{3}/mm^{3})	9.88^{a} ± 0.60	11.15^{a} ± 0.72	11.54^{a} ± 1.00	9.43^{a} ± 1.18
Total platelets count (x10^{3}/mm^{3})	220.20^{a}± 23.53	253.80^{a} ± 35.45	231.40^{a} ± 27.25	197.00^{a} ± 21.95
Lymphocytes (%)	50.20^{a} ± 5.17	52.80^{a} ± 5.12	54.20^{a} ± 3.89	49.60^{a} ± 4.61
Monocytes (%)	2.60^{ab} ± 0.24	1.60^{b} ± 0.40	2.20^{ab} ± 0.37	3.00^{a} ± 0.70
Granulocytes (%)	47.20^{a} ± 4.93	45.60^{a} ± 4.75	43.60^{a} ± 3.57	47.40^{a} ± 4.22
MCV (fl)	46.66^{a} ± 0.92	47.22^{a} ± 1.04	46.46^{a} ± 0.86	46.72^{a} ± 0.79
MCH (pg)	13.16^{a} ± 0.25	13.82^{a} ± 0.37	13.74^{a} ± 0.16	13.36^{a}± 0.19
MCHC (%)	28.30^{b} ± 0.50	29.42^{ab} ± 0.67	29.74^{a} ± 0.24	28.80^{ab} ± 0.17

Means with different superscripts vary significantly ($p<0.05$)

Table 5
Effects of Vecuroniumon blood biochemical parameters in male buffaloes (Mean±S.E., n=5)

Parameters (Units)	Before Drug admn.	At peak effect of drug	At recovery	At 24 hrs. of recovery
Glucose (mg/dL)	61.14^{b} ± 4.39	152.64^{a} ± 10.12	149.94^{a} ± 6.42	68.84^{b} ± 19.29
Triglycerides (mg/dL)	12.60^{bc} ± 1.32	15.60^{ab} ± 1.28	18.20^{a} ± 2.31	10.60^{c} ± 1.03
Total cholesterol (mg/dL)	77.60^{a} ± 2.37	80.60^{a} ± 2.01	72.40^{a} ± 3.66	72.20^{a} ± 4.07
HDLC (mg/dL)	37.30^{a} ± 1.56	37.88^{a} ± 1.59	33.92^{a} ± 1.96	35.36^{a} ± 4.14
LDLC (mg/dL)	18.87^{ab} ± 1.19	20.37^{a} ± 0.72	17.33^{b} ± 0.81	17.36^{b} ± 0.66
Cortisol (ng/L)	103.23^{a} ± 27.57	175.38^{a} ± 64.41	172.63^{a} ± 64.25	100.51^{a} ± 29.52
LDH (IU/L)	446.94^{a} ± 30.67	468.62^{a} ± 30.30	459.48^{a} ± 31.29	453.04^{a} ± 31.43
ALT/SGPT (IU/L)	28.58^{a} ± 2.34	34.92^{a} ± 2.26	31.94^{a} ± 2.10	29.20^{a} ± 1.89
AST/SGOT (IU/L)	47.88^{a} ± 2.97	53.00^{a} ± 3.02	50.30^{a} ± 3.48	48.42^{a} ± 3.80
ALP (IU/L)	79.20^{a} ± 5.96	74.80^{a} ± 4.51	71.80^{a} ± 6.47	81.20^{a} ± 7.44
GGT (IU/L)	21.46^{a} ± 0.68	21.66^{a} ± 0.69	20.44^{a} ± 1.22	20.54^{a} ± 0.75
Bilirubin Direct (mg/dL)	0.14^{a} ± 0.01	0.13^{a} ± 0.01	0.13^{a} ± 0.02	0.11^{a} ± 0.02
Total protein (g/dL)	9.22^{a} ± 0.91	8.51^{a} ± 0.35	8.28^{a} ± 0.45	9.35^{a} ± 0.40
Albumin (g/dL)	3.51^{ab} ± 0.10	3.61^{a} ± 0.06	3.23^{b} ± 0.10	3.33^{ab} ± 0.11
Globulin (g/dL)	5.71^{a} ± 0.93	4.90^{a} ± 0.40	5.05^{a} ± 0.37	6.02^{a} ± 0.46
A:G ratio	0.73^{a} ± 0.18	0.76^{a}±0.09	0.64^{a} ± 0.03	0.56^{a} ± 0.05
BUN (mg/dL)	55.32^{a} ± 2.60	53.98^{a}± 4.25	53.14^{a} ± 1.17	45.80^{a} ± 6.23
Creatinine (mg/dL)	0.10^{ab} ± 0.01	0.08^{b} ± 0.01	0.12^{a} ± 0.00	0.10^{ab} ± 0.00
Sodium (mmol/L)	140.00^{a} ± 2.13	142.62^{a} ± 2.34	136.08^{a} ± 2.74	141.12^{a} ± 3.70
Potassium (mmol/L)	4.09^{b} ± 0.20	5.88^{a} ± 0.55	3.93^{b} ± 0.17	4.14^{b} ± 0.12
Chloride (mmol/L)	106.40^{a} ± 2.39	108.92^{a} ± 2.67	93.44^{a} ± 11.08	105.68^{a} ± 1.61
Calcium (mg/dL)	8.72^{a} ± 0.57	9.42^{a} ± 0.59	8.86^{a} ± 0.47	8.64^{a} ± 0.61
Phosphorus (mg/dL)	4.72^{a} ± 0.66	5.53^{a} ± 0.50	4.04^{a} ± 0.47	5.67^{a} ± 0.63

Means with different superscripts vary significantly ($p<0.05$)

did not vary significantly. A non-significant increase in cortisol level was 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 vecuronium (Brunt and Ganong, 1963). On the basis of findings of this study, it can be concluded that Vecuronium (40 µg/kg IV) is a safer and better muscle relaxant in terms of early onset of action, rapid and smooth recovery and cardiovascular stability.

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