Evaluation of Glycopyrrolate as an Anticholinergic in Buffalo Calves (*Bubalus bubalis*)

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**ABSTRACT:** Twelve experimental trials were undertaken on clinically healthy male buffalo calves. Glycopyrrolate was injected @ 0.01 mg/kg, IM. After glycopyrrolate administration, two animals became ataxic. Muzzle, mouth and nostrils became dry after 41.5±3.334 minute of drug administration; the same again became wet at 578.8±19.27 minute. The pulse pressure increased significantly after glycopyrrolate administration without any significant variation in heart rate, mean arterial pressure (MAP) and central venous pressure (CVP).

**Key words:** Atropine, Glycopyrrolate, Anticholinergics, Buffalo.

**INTRODUCTION** - Preanaesthetic drugs are administered to minimize pain, remove apprehension, and facilitate handling of animal and to minimize undesirable sympathetic and parasympathetic reflex activity. Glycopyrrolate blocks cardiac vagus and thus inhibit cardiac inhibitory effect of α₂-adrenoceptor agonists. The study was planned with the objective to evaluate the efficacy and safety of glycopyrrolate as an anticholinergic in buffalo calves.

**MATERIAL AND METHODS** - Twelve experimental trials were undertaken on clinically healthy male buffalo calves of 6 to 18 months of age and weighing 70 to 120 kg. Glycopyrrolate was administered @ 0.01 mg/kg, IM. Each animal was weighed a day before the experiment and had free access to feed and water. Following protocol of experiment was followed:

| Groups (n=no. of animals) | Drugs used | Parameters investigated |
|----------------------------|------------|------------------------|
| I (n=6)                    | Glycopyrrolate | Behavioural changes, rectal temperature, heart rate, respiration rate, haemoglobin (Hb), packed cell volume (PCV), erythrocyte sedimentation rate (ESR), blood/plasma glucose, cholesterol, urea nitrogen, creatinine, total proteins, albumin, calcium, inorganic phosphorus, magnesium, sodium, potassium, chloride, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALKP) and bilirubin |
| II (n=6)                   | Glycopyrrolate | Systolic pressure, diastolic pressure, pulse pressure, mean arterial pressure (MAP), central venous pressure (CVP) and electrocardiogram |
The parameters were investigated at various time intervals after administration of drug as shown in different tables. The statistical analysis of data was done by one-way-analysis of variance and Duncan’s multiple range test (Duncan, 1955).

**RESULTS AND CONCLUSIONS** - Ataxia was observed in two animals only at about 23 minute of drug administration. Only one calf went to sternal recumbency. Five animals showed urination and defaecation. After 41.5±3.334 minute of drug administration, muzzle, mouth and nostrils became dry which again became wet at 578.8±19.27 minute. There was no cutaneous analgesia. Complete recovery was observed at 110±6.324 minute with heart rate within normal range. The effect of glycopyrrolate administration on mean values of rectal temperature and respiration rate in buffalo calves are shown in table 1.

Respiration rate was elevated at peak effect of drug (26±2 per minute) as compared to the base value (21±2 per minute) but this increase was of no statistical or clinical significance. However, in dogs respiration remained unaffected after glycopyrrolate administration (Thurmon *et al.*, 1996). No significant variations were observed in rectal temperature, the values being within the normal range throughout the period of observation.

The effects of glycopyrrolate administration on haematological parameters are shown in table 2. Haemoglobin, ESR and PCV values did not show any significant change.

### Table 1. Effects of IM administration of glycopyrrolate on rectal temperature and respiration rate. Table showing arithmetic mean of values obtained before and at various intervals after its administration in buffalo calves. Mean values are presented here with (±) their respective standard errors (n=6).

| Parameters (Units) | Before administration of drug | At its peak effect | At recovery from effect of drug | 24 hours after administration of drug |
|-------------------|-------------------------------|-------------------|-------------------------------|--------------------------------------|
| Rectal temperature (°C) | 38.02±0.340 ^a^ | 38.15±0.292 ^a^ | 38.27±0.271 ^a^ | 38.10±0.254 ^a^ |
| Respiration rate (per minute) | 21±2 ^ab^ | 26±2 ^a^ | 19±2 ^b^ | 19±1 ^b^ |

Means with different superscript vary significantly (p<0.05).

### Table 2. Effects of IM administration of glycopyrrolate of haematological parameters. Table showing arithmetic mean of values obtained before and at various intervals after its administration in buffalo calves. Mean values are presented here with (±) their respective standard errors (n=6).

| Parameters (Units) | Before administration | At its peak effect | At recovery from effect of drug | 24 hours after administration of drug |
|-------------------|-----------------------|--------------------|-------------------------------|--------------------------------------|
| Haemoglobin (g/dl) | 9.83±1.07 ^a^ | 8.91±0.995 ^a^ | 8.41±1.05 ^a^ | 9.25±1.12 ^a^ |
| Erythrocyte sedimentation rate (mm per hour) | 55±5.559 ^a^ | 58±5.375 ^a^ | 62±4.707 ^a^ | 61±5.821 ^a^ |
| Packed cell volume (%) | 29±3.809 ^a^ | 27±3.618 ^a^ | 26±3.296 ^a^ | 27±3.693 ^a^ |

Means with different superscript vary significantly (p<0.05).
The effects of glycopyrrolate administration on blood glucose, total plasma proteins, BUN, plasma creatinine, plasma cholesterol, albumin, calcium, phosphorus, magnesium, sodium, potassium, chloride, bilirubin, SGOT, SGPT and alkaline phosphatase are shown in table 3. There was no significant variation in any of the blood bio-chemical parameters.

### Table 3: Effects of IM administration of glycopyrrolate on blood biochemical parameters. Table showing arithmetic mean of values obtained before and at various intervals after its administration in buffalo calves. Mean values are presented here with (±) their respective standard errors (n=6).

| Parameters (Units)       | Before administration | At its peak effect | At recovery from effect of drug | 24 hours after administration of drug |
|--------------------------|-----------------------|--------------------|---------------------------------|---------------------------------------|
| Blood glucose (mg/dl)    | 46.56a±4.499          | 51.61a±6.222       | 55.98a±8.166                    | 47.93a±8.488                          |
| Cholesterol (mg/dl)      | 39.30a±6.808          | 37.33a±5.082       | 38.95a±4.577                    | 38.76a±5.096                          |
| BUN (mg/dl)              | 24.09a±0.838          | 24.89a±0.633       | 24.40a±0.607                    | 23.95a±0.751                          |
| Creatinine (mg/dl)       | 2.01a±0.242           | 2.15a±0.151        | 1.91a±0.215                     | 1.95a±0.243                           |
| Total proteins (g/dl)    | 5.05a±0.438           | 4.56a±0.707        | 5.10a±0.204                     | 5.90a±0.567                           |
| Albumin (g/dl)           | 3.33a±0.175           | 3.26a±0.082        | 3.34a±0.134                     | 3.33a±0.181                           |
| Calcium (mg/dl)          | 6.79a±0.606           | 6.02a±0.236        | 6.68a±0.471                     | 6.34a±0.647                           |
| Phosphorus (mg/dl)       | 4.98ab±0.424          | 4.29ab±0.289       | 3.78b±0.301                     | 5.35a±0.768                           |
| Magnesium (mg/dl)        | 2.45a±0.120           | 2.583a±0.100       | 2.48a±0.045                     | 2.49a±0.096                           |
| Sodium (mmol/l)          | 107.11a±7.134         | 99.33a±3.997       | 100.05a±2.468                   | 28.81a±2.964                          |
| Potassium (mmol/l)       | 3.68a±0.244           | 3.93a±0.344        | 3.53a±0.352                     | 3.71a±0.137                           |
| Chloride (mmol/l)        | 94.23a±1.506          | 94.91a±0.965       | 98.30a±3.086                    | 95.21a±1.279                          |
| Bilirubin (mg/dl)        | 0.10a±0.055           | 0.09a±0.050        | 0.11a±0.063                     | 0.19a±0.148                           |
| SGOT (U/l)               | 31.07a±2.721          | 34.11a±3.093       | 34.76a±1.713                    | 36.76a±1.280                          |
| SGPT (U/l)               | 22.87a±1.032          | 24.67a±1.892       | 22.59a±0.891                    | 23.39a±0.716                          |
| ALKP (U/l)               | 89.66a±4.580          | 90.83a±4.643       | 90.33a±5.213                    | 90.83a±4.805                          |

Means with different superscript vary significantly (p<0.05).

The effect of glycopyrrolate on heart rate, pulse pressure, mean arterial pressure and central venous pressure are shown in table 4.

Heart rate was elevated after glycopyrrolate administration but this increase was not statistically significant. Excellent cardiovascular stability after glycopyrrolate administration was also observed causing little change in heart rate (Hall and Clark, 1991). There was no significant variation in MAP during entire period of observation. Arterial blood pressure and heart rate remained unaffected in dogs at intravenous dose of 0.005-0.01 mg/kg (Thurmon et al., 1996). The pulse pressure which increased significantly at 5 minute of drug administration (9.00±0.447 mm Hg) as compared to base value (6.33±0.802 mm Hg). No significant variation was observed in CVP during the experiment. No variation in time and
voltage function of ECG was observed after glycopyrrolate administration. Primary T-wave changes can be related to variation in cardiac contractibility and myocardial oxygenation that usually occurs in such circumstances as animals were not on a ventilator.
From the present study, it was concluded that glycopyrrolate induced tachycardia and anti-sialagogic activity in buffalo calves.

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| Parameters (Units) | Base | After atropine administration |
|-------------------|------|------------------------------|
|                   |      | 5 min | 10 min | 15 min | 30 min | 45 min | 60 min |
| Heart rate (beats per minute) | 57\(^a\) | 57\(^a\) | 59\(^a\) | 61\(^a\) | 67\(^a\) | 65\(^a\) | 66\(^a\) |
| ±4                | ±5   | ±5    | ±4    | ±5    | ±1    | ±2    |
| Systolic pressure (mm Hg)    | 156.00\(^a\) | 159.66\(^a\) | 157.33\(^a\) | 152.33\(^a\) | 151.66\(^a\) | 151.66\(^a\) | 140.00\(^a\) |
| ±8.594            | ±8.394 | ±7.111 | ±6.955 | ±8.056 | ±7.181 | ±8.422 |
| Diastolic pressure (mm Hg)  | 149.66\(^a\) | 150.66\(^a\) | 150.66\(^a\) | 146.33\(^a\) | 145.00\(^a\) | 146.00\(^a\) | 135.00\(^a\) |
| ±8.754            | ±8.604 | ±6.666 | ±7.437 | ±8.242 | ±7.676 | ±8.481 |
| Pulse pressure (mm Hg)     | 6.33\(^b\) | 9.00\(^a\) | 6.66\(^b\) | 5.66\(^b\) | 6.66\(^b\) | 6.00\(^b\) | 5.00\(^b\) |
| ±0.802            | ±0.447 | ±0.666 | ±0.333 | ±0.421 | ±0.516 | ±0.447 |
| Mean arterial pressure (mm Hg) | 152.00\(^a\) | 153.66\(^a\) | 153.33\(^a\) | 148.66\(^a\) | 147.33\(^a\) | 148.33\(^a\) | 137.33\(^a\) |
| ±8.160            | ±8.394 | ±6.545 | ±7.369 | ±8.240 | ±7.164 | ±8.480 |
| Central venous pressure (cm water) | 5.15\(^ab\) | 3.18\(^b\) | 8.00\(^a\) | 8.03\(^a\) | 3.60\(^b\) | 5.11\(^ab\) | 4.233\(^b\) |
| ±1.338            | ±0.415 | ±1.755 | ±1.365 | ±0.629 | ±1.309 | ±0.891 |

Means with different superscript vary significantly (p<0.05).