ELECTROCARDIOGRAPHIC AND BLOOD ELECTROLYTE CHANGES IN GOATS FOLLOWING SINGLE INTRAVENOUS FUROSEMIDE ADMINISTRATION

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Summary


Fifteen clinically healthy non-pregnant 4-year-old Iranian Najdi does were divided into 3 equal experimental groups (n=5) and received different doses of furosemide intravenously (Group 1: 2.5 mg.kg⁻¹; Group 2: 5 mg.kg⁻¹ and Group 3: 10 mg.kg⁻¹). Electrocardiogram recordings and blood samplings to evaluate serum sodium, potassium, chloride, calcium, magnesium and phosphorus concentrations were performed prior and 1, 2, 3, 4, 5 and 24 hours after furosemide administration. In Group 3, R amplitude at 5th hour was significantly different from other experimental groups (P=0.001) and significantly higher than baseline level (P=0.001). P-R, R-R and S-T intervals in Group 3 at 5th hour were significantly higher than in other groups (P<0.05). These parameters in Group 3 at this time were significantly higher than baseline values (P<0.05). In all 3 experimental groups, serum concentrations of sodium, chloride and potassium at 5th hour were significantly lower than baseline levels at hour zero. It may be suggested that changes of electrocardiographic parameters after furosemide administration are due to alterations of the electrical conduction of action potential in the myocardium.

Key words: blood electrolytes, electrocardiogram, furosemide, Iranian Najdi goat

INTRODUCTION

The electrocardiogram (ECG) is a diagnostic criterion that measures and records heart electrical activity in exquisite details. Base apex lead have been used for large animals and it is shown to be an appropriate lead and ECGs recorded in this lead has clear and large waves and complexes and animal movement has a minimum effect on the recording (Santamarina et al., 2001). The majority of arrhythmias and conduction disturbances can be detected on clinical examination; however, some may be undetected on clinical examinations and could be found only on electrocardiographic examinations (Radostits et al., 2007). There are several literatures on the normal electrocardiographic parameters in cattle (Pourjafar et al., 2012a), camel (Pourjafar et al., 2011a), sheep and goat (Ahmed & Sanyal, 2008), etc. Some of the physiological (Pourjafar et al., 2011b; Pourjafar et al., 2012b) and pathological (Austin et al., 1997; Mir et al., 2007) alterations of the heart electrical activities in large animals are reported by researchers. Varia-
tions in the rate and rhythm can occur in normal animals due to strong or varying autonomic influence but can also be a reflection of primary myocardial disease. Other factors such as acid-base and electrolyte imbalances can influence rate and rhythm (Radostits et al., 2007).

Furosemide inhibits the reabsorption of electrolytes in the ascending limb of the kidney’s loop of Henle. The drug also decreases reabsorption of sodium and chloride and increases potassium excretion in the distal renal tubule and exerts a direct effect on electrolyte transport at the proximal tubule (Bushinsky et al., 1986). Administration of furosemide not only elicits diuresis but is also associated with adverse effects, such as alterations in electrolyte and acid-base homeostasis and imbalance in serum electrolytes is known as an important factor which affects ECG (Greenberg, 2000).

Akita et al. (1998) evaluated the effect of furosemide on ECG and blood electrolyte changes in rats. They mentioned that the furosemide can alter the ECG parameters during electrolyte imbalances mainly via hypokalemia.

Furosemide, is a common diuretic drug in veterinary use, for treatment of pulmonary oedema secondary to congestive heart failure, hepatic and renal diseases, can change acid-base and electrolyte balances (Radostits et al., 2007). Therefore, it may potentially affect the heart rate and rhythm and electrocardiographic parameters.

Thus, the present experimental study was conducted to evaluate the probable alterations of heart electrical activities by ECG recording in clinically healthy Najdi doe following intravenous furosemide administration.

MATERIALS AND METHODS

The present experiment was performed after being approved by the Ethics Committee of School of Veterinary Medicine, Shiraz University. The current study was accomplished in February 2012 on 15 clinically healthy non-pregnant 4-year-old Iranian Najdi does (35±2 kg body weight) in Lamerd (latitude of 27° 20' 4" N and longitude 53° 10' 46" E, 500 m above sea level), Fars province, southwest of Iran. Animals were randomly divided into 3 equal experimental groups (n=5). Goats were grazing in a green pasture with free access to water and shade. The animals were examined prior to ECG recordings and proved to be clinically healthy. None of the goats used in this study had any clinical signs of heart diseases (oedema, jugular distension or pulsation and cardiac murmurs), coughing and exercise intolerance. A 16 gauge, 5.1 cm catheter was secured in the left jugular vein and used for drug infusion and blood samplings. Furosemide (Vetasomide®, Abu-raihan Co., Iran) were infused intravenously at 3 different doses (Group 1: 2.5 mg.kg⁻¹; Group 2: 5 mg.kg⁻¹ and Group 3: 10 mg.kg⁻¹). ECG recordings and blood samplings were performed prior and 1, 2, 3, 4, 5 and 24 hours after furosemide administration. Blood samples were collected from all goats through the fixed catheter in plain tubes. Immediately after blood collections, sera were separated by centrifugation (10 min at 3,000×g) and stored at −22 °C until assayed.

The ECGs were recorded on a bipolar base apex lead, using limb lead I. Animals were kept standing without any sedation and minimum restraint. When animals got calm (decreasing of panting behaviour and muscle tremors), the ECGs were recorded, using alligator-type electrodes.
which were attached to skin after cleaning it with ethanol and applying electrocardiographic jelly to improve skin contact. The positive electrode (left arm) was placed over cardiac apex on the 5th left intercostal space at the level of the elbow, the negative electrode (right arm) was placed on the left jugular furrow at the top of heart base, and the ground was placed on the dorsal spine or another site away from the heart (Radostits et al., 2007). All ECGs were obtained in a single channel electrocardiographic machine (Kenz-line EKG 110, Suzuken Co., Ltd., Japan) with paper speed of 25 mm/sec and calibration of 10 mm equal to 1 mV. The precision of duration was 0.02 s, the amplitude – 0.05 mV.

Sera were assayed for sodium, potassium, chloride, calcium, magnesium and phosphorus concentrations. Serum chloride and phosphorus were analysed using routine biochemical procedures (Burtis & Ashwood, 1994). The serum concentrations of sodium and potassium were measured by the flame photometry (Flame Photometer, FLM, Ontario, Canada). The samples were also analysed for magnesium and calcium by atomic absorption spectroscopy (Shimadzo AA-670, Pourjafar, M., A. Chalmeh, Kh. Badiei, S. M. Mehdi Heidari & A. Sanati, Japan).

Data were expressed as mean ± standard error of mean (SEM). Statistical analysis was performed using one-way ANOVA with LSD post-hoc test to compare mean concentrations of different electrocardiographic parameters and serological factors within similar hours among different experimental groups. Repeated measures ANOVA was also used in order to study the changes in pattern of different electrocardiographic parameters and serological factors in each group, statistically. Paired samples t-test was used to determine differences between two different times in each experimental group using SPSS software (SPSS for Windows, version 11.5, SPSS Inc, Chicago, Illinois). The level of significance was set at P<0.05.

RESULTS

The occurring ECG changes are presented on Fig. 1, 2, 3 and 4. In Group 3, R amplitude at 5th hour was significantly different from other experimental groups (P=0.001) and significantly higher than baseline level (P=0.001; Fig. 2B). The results of repeated measures ANOVA showed that changes in pattern of this parameter were significant in Group 3. There were no significant differences among other recorded amplitudes at similar times.
Electrocardiographic and blood electrolyte changes in goats following single intravenous furosemide...

Fig. 2. Effects of intravenous furosemide administration on amplitudes (Mean±SEM) of electrocardiographic waves of Iranian Najdi goats receiving different doses of furosemide (--- ● --- 2.5 mg.kg⁻¹; — ● — 5 mg.kg⁻¹ and - - - - • - - 10 mg.kg⁻¹).
A: P amplitude; B: R amplitude; C: S amplitude; D: T amplitude. Different letters (a,b) show significant differences in similar hours among groups (P<0.05).

Cardiac hours in all experimental groups (P>0.05). P-R, R-R and S-T intervals in Group 3 at 5th hour were significantly higher than other groups (P<0.05; Fig. 3A, B and D). The results of paired samples t-test showed that these parameters in Group 3, at this time, were significantly higher than baseline values (P<0.05). P durations at 5th hour were significantly different among all 3 experimental groups and this factor in Group 3 at this time was significantly higher than that in other groups (P<0.05; Fig. 4A).

Serum concentrations of calcium, magnesium and phosphorus showed no significant changes patterns due to intravenous furosemide administration in all experimental groups. The results of one-way ANOVA revealed no significant differences among these parameters at similar hours in 3 groups (P>0.05; Fig. 5). In all 3 experimental groups, serum concentrations of sodium, chloride and potassium at 5th hour were significantly lower than baseline levels at hour zero. There were no significant differences among sodium concentrations at similar hours in all 3 groups (P>0.05; Fig. 6A). Serum concentrations of chloride and potassium in Group 3 at 4th and 5th hours were significantly lower than Groups 1 and 2 (Fig. 6B, C). There were no significant differences between values of chloride and potassium at similar hours in Groups 1 and 2 (P>0.05; Fig. 6B, C).

DISCUSSION
According to our findings, there were no significant changes and differences in calcium, magnesium and phosphorus concentrations in each group and also among all experimental groups (P>0.05; Fig. 5). Sodium, chloride and potassium
concentrations at 5th hour in Group 3 were significantly lower than their baseline values and chloride and potassium concentrations in Group 3 were significantly lower than other experimental groups (P<0.05; Fig. 6).

Normally, the interior of cardiac cells is more negative than the exterior due to the distribution of the main intra and extracellular electrolytes such as sodium, potassium and chloride. In myocardial cells, the interior is maintained more negative than the exterior by the extrusion of 3 sodium ions for every 2 potassium ions pumped in by the sodium/potassium ATPase pump. Movement of electrolytes across the impermeable cell membrane is through a number of channels (sodium and potassium channels, e.g.) that permit or prevent the movement of ions depending upon transmembrane voltage.

Whereas calcium is the main electrolyte responsible for pacemaker cell depolarisation, sodium is the main electrolyte responsible for depolarisation of myocardial cells and cells dedicated to conduction of impulses (Fisch, 1984).

In humans, hypokalemia is known to produce typical changes in the T wave, in particular decreased amplitude and the appearance of a U wave (Surawicz et al., 1957). Similar changes have been observed in hypokalemic dogs (Felkai, 1985). In the study of Hanton et al. (2007) hypokalaemia was also associated with decreasing amplitude of the T wave and with morphological changes in tracings recorded in CV5RL. In the present study, using ECG recordings by base apex lead, R amplitude at 5th hour in Group 3 was significantly higher than its baseline value and also statistically sig-

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![Graph](image)

**Fig. 3.** Effects of intravenous furosemide administration on intervals (Mean±SEM) of electrocardiographic waves of Iranian Najdi goats receiving different doses of furosemide (- - - - - 2.5 mg.kg⁻¹; - - - - - 5 mg.kg⁻¹ and - - - - - 10 mg.kg⁻¹). A: P-R interval; B: R-R interval; C: Q-T interval; D: S-T interval. Different letters (a,b) show significant differences in similar hours among groups (P<0.05).
Potassium plays a key role in electrophysiological phenomena and, in particular, in the repolarisation of the ventricular cells (Gadsby et al., 1995). Hypokalemia increases the duration of cardiac action potential and, consequently, prolongs QT interval. The inhibition of cardiac repolarisation associated with decrease in extracellular potassium is assumed to be related to faster inactivation of potassium channels responsible for delayed potassium outflow and consequent inhibition of repolarisation currents (Yang et al., 1997). The P-R interval can be prolonged along with an increase in the amplitude of the P wave (Drighil et al., 2007). In the present experimental study, P-R, R-R and S-T intervals at 5th hour in Group 3 were significantly higher than their baseline values and these parameters in Group 3 were significantly higher than other experimental groups (P<0.05; Fig. 3A, B and D).

Akita et al. (1998) demonstrated that the ECG changes that are induced by hypokalemia in the rat, included suppression of conduction in most parts of the heart, prolongation of the Q-T interval, and de-
crease of the amplitude of all waves except P waves. A prolonged Q-T interval is also a typical ECG manifestation of hypokalemia. A low extracellular potassium concentration produced a prolonged action potential and increased the time of diastolic depolarisation (Gettes & Sura-witz, 1968).

In humans, the cardiac effect of hypokalemia is well documented. Decreases in potassium plasma levels may occur in different pathological states and may be produced by a number of drugs (Cohen et al., 2002). Hypokalemia may have a major effect on cardiac repolarisation and ECG durations (Yelamanchi et al., 2001). Hyponatremia would have a Q-T prolongation effect similar to that of hypokalemia (Yelamanchi et al., 2001). However, sodium produces electrophysiological abnormalities only at a concentration well outside the physiological range (Surawicz, 1995). Theoretically, reduction of the extracellular concentration of sodium should slow cardiac pacemaker activity. In animal models, wide QRS complexes, either through hyperkalemia or quinidine administration have been documented (Surawicz, 1995). Hyponatremia plays a role in the pathogenesis of the cardiac conduction defect.

In the current study, P duration at 5th hour in Group 3 was significantly higher than its baseline value and this parameter in Group 3 was significantly higher than in other experimental groups (P<0.05; Fig. 4A). An increase in durations occurred simultaneously with the decrease in plasma potassium level following the effect of a potent diuretic. A number of publications report high values of durations in dogs with severe hypokalemia (Weissenburger et al., 1991).

In conclusion, in the present experiment, we have shown that furosemide, as a potent diuretic, affects ECG parameters after its intravenous administration in Najdi goat. According to our findings, ECG abnormalities may be categorised as furosemide side effects and furosemide induced its side effects in a dose dependent manner. It may be also suggested that changes of ECG parameters are due to alterations of the electrical conduction of

![Fig. 6. Effects of intravenous furosemide administration on serum electrolyte changes (mmol/l: Mean±SEM) of Iranian Najdi goats receiving different doses of furosemide (--- - 2.5 mg.kg⁻¹; --- 5 mg.kg⁻¹ and - - - - 10 mg.kg⁻¹). A: Sodium; B: Chloride; C: Potassium. Different letters (a, b) show significant differences in similar hours among groups (P<0.05).](image-url)
action potential in the myocardium. Furthermore, based on the observed changes, furosemide affects normal cardiac activities in goats and it should be stated that handling the animals after furosemide application requires caution in order to prevent the risk of cardiac accidents.

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