Acta vet. scand. 1994, *35*, 283-288.

Influence of Medetomidine on Acid-base Balance and Urine Excretion in Goats

By *M. Raekallio*[1], *M. Hackzell*[2] and *L. Eriksson*[2]

[1]Department of Clinical Sciences and [2]Department of Physiology, College of Veterinary Medicine, Helsinki, Finland.

Raekallio M., M. Hackzell and L. Eriksson: Influence of medetomidine on acid-base balance and urine excretion in goats. Acta vet. scand. 1994, 35, 283-288. – Seven goats were given medetomidine 5 µg/kg as an iv bolus injection. Venous blood samples were taken repeatedly and urine was collected continuously via a catheter up to 7h after the injection.

Medetomidine caused deep clinical sedation. Base excess, pH and PCO_2 in venous blood rose after medetomidine administration. There were no significant changes in plasma concentrations of sodium, calcium, magnesium, creatinine or osmolality, whereas potassium and bicarbonate concentrations increased, and phosphate and chloride decreased. Medetomidine increased plasma glucose concentration, and in 4 of 7 goats glucose could also be detected in urine. Medetomidine did not influence urine flow rate, free water clearance, bicarbonate and phosphate excretion or pH, but renal chloride, sodium, potassium, calcium, magnesium and creatinine excretion were reduced.

The results suggest that the metabolic alkalosis recorded after medetomidine administration is not caused by increased renal acid excretion.

metabolic alkalosis; base excess; bicarbonate.

Introduction

The α_2-adrenoceptor agonist detomidine causes an increase in base excess in horses, which indicates metabolic alkalosis (*Raekallio et al.* 1990). α_2-Adrenoceptor agonists are also known to induce diuresis and natriuresis (*Gellai* 1990), but there seem to be differences between species in the α_2-adrenoceptor modulation of vasopressin action (*Gellai* 1990, Brooks et al. 1991). Renal α_2-adrenoceptors may also influence urinary bicarbonate and chloride excretion and thus affect the acid-base balance.

The purpose of the present study was to determine whether the base excess increases after administration of another α_2-adrenoceptor agonist, medetomidine, in goats and whether increased renal acid excretion is involved in the development of this metabolic alkalosis.

Materials and methods

Seven adult female goats (weight 38-57.5 kg, mean 49.0 kg) were given medetomidine 5 µg/kg iv as a bolus injection. The goats were maintained in metabolic cages during the experiment, and they were supported with slings to keep them in a standing position during sedation.

Venous blood samples were collected from cannulae inserted into both jugular veins. The cannulae were flushed with sodium citrate solution after samplings. Venous blood was taken into heparinized syringes (Arterial

Blood Sampler, QS90™, Radiometer, Copenhagen, Denmark) 30min before and 10, 20, 30 min after treatment, and every 15min until 75min, thereafter every 30min until 6h 45min. The samples were chilled immediately and stored in melting ice until analyzed by an auto-analyzer (ABL 300, Radiometer, Copenhagen, Denmark) within 30min of collection. Venous PCO_2, pH, base excess, and bicarbonate concentration were measured.

Venous blood was also collected into glass tubes containing lithium heparin 30min before administration of medetomidine, 15min after it, and every 30 min thereafter until 6h 45min. The plasma was separated by centrifugation and frozen until sodium, potassium, chloride, calcium, magnesium, phosphate, creatinine and glucose concentrations were analyzed.

The urinary bladder was catheterised with a Foley catheter and emptied 40min before medetomidine injection. Urine was collected continuously into a measuring glass which was emptied 20min before treatment, at the time of treatment, and thereafter every 30min until 7h. Urine pH and volume were measured immediately. The urine was stored at -20°C until determination of sodium, potassium, calcium, magnesium, phosphate, creatinine, and glucose concentrations and osmolality was carried out. In addition, bicarbonate and chloride concentrations were analyzed from the urine samples of four goats. These samples were stored frozen under liquid paraffin until analyzed.

Plasma and urine sodium and potassium concentrations were analyzed by flame photometry (Corning 480 Flame Photometer, Ciba Corning Diagnostics, Halstead, Essex, England), and calcium and magnesium by atomic absorption spectrophotometry (Perkin-Elmer 2380, Perkin-Elmer Corporation, Norwalk, Connecticut, USA). Plasma and urine phosphate concentrations were analyzed by spectrophotometry (*Weissman & Pileggi* 1974; Perkin-Elmer Spectrophotometer Coleman 55, Coleman Instruments, Division of Perkin-Elmer Corporation, Oakbrook, Illinois, USA) and creatinine by Jaffe's reaction (*Fabiny & Ertingshausen* 1971) using an autoanalyzer (Kone Specific Selective Chemistry Analyzer, Kone Corporation, Espoo, Finland). Plasma chloride was analyzed by direct potentiometry (Kone Microlyte, Kone Corporation, Espoo, Finland) and glucose by an autoanalyzer using the enzymatic colorimetric method (Trinder 1969). Test strips (Glukotest, Boehringer Mannheim GmbH, Mannheim, Germany) were used to check urine for glucose. Urine osmolality was measured by the freezing point method (Osmette A, Precision Systems, Inc., Sudbury, Massachusetts, USA). Urine chloride was measured by conductiometric titrating (925 Corning Chloride Analyzer, Corning Medical and Scientific Co., Halstead, Essex, England) and HCO_3 by the carbon dioxide (CARB) method (*Menson et al.* 1974) for the ACA analyzer (Du Pont ACA IV, Du Pont Company, Clinical and Instrument Systems Division, Wilmington, Delaware, USA).

The data were analyzed using the analysis of variance for repeated measurements. If differences were observed, Dunnett's 2-tailed t-test was used to compare individual time points with pretreatment levels. Statistical significance was considered at $P<0.05$.

Results

All the goats showed signs of deep clinical sedation after administration of medetomidine. They stood up 25 to 95min after the injection. Base excess and blood pH increased significantly, the average of both reaching their maximums 60min after medetomidine injection (Fig. 1). Venous PCO2 was significantly

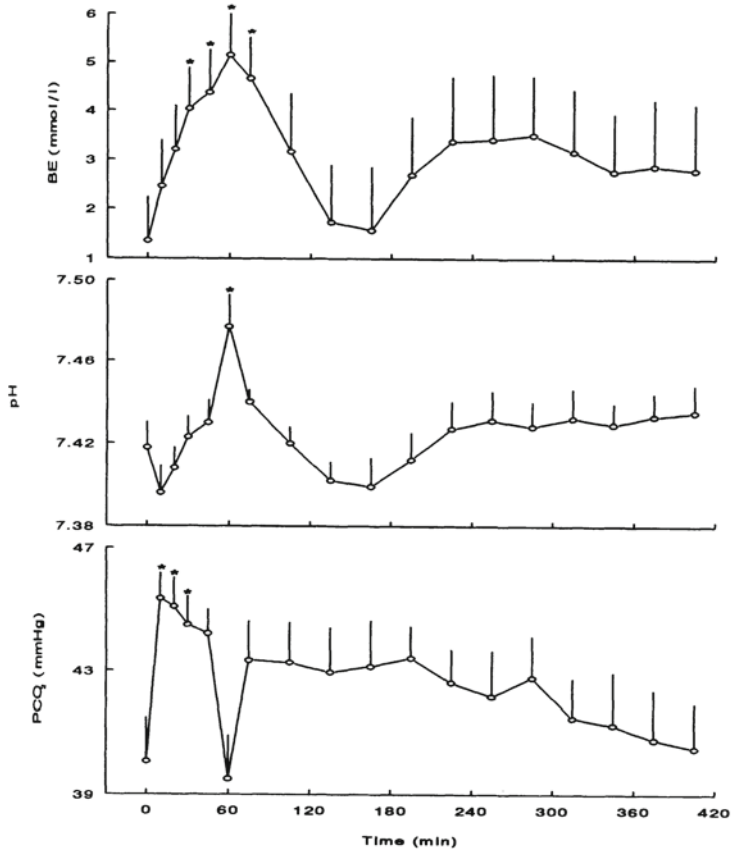

Figure 1. Means ± SEM of venous base excess (BE, mmol/l), pH and partial carbon dioxide pressure (PCO_2, mmHg) in goats (n=7) after iv administration of medetomidine (5 µg/kg).
* significantly different from baseline ($p<0.05$).

higher than before medication in samples taken 10 to 30min after medetomidine administration (Fig. 1), and venous bicarbonate concentration was increased 20 to 75 and 285min after medetomidine.

Medetomidine did not influence significantly urine pH, bicarbonate or phosphate excretion. Renal chloride excretion was significantly decreased 135min after medetomidine injection (Fig. 2). Medetomidine reduced also renal sodium, potassium, calcium, magnesium and creatinine excretion, but flow rate and free water clearance were not altered.

Plasma sodium, calcium, magnesium, and creatinine concentrations and osmolality did not change significantly. Plasma potassium concentration was significantly increased 45min after medetomidine injection (Fig. 3), but the initial concentration was lower than the normal reference values (*Kaneko* 1989), and the highest concentrations did not exceed them. Plasma phosphate concentration was

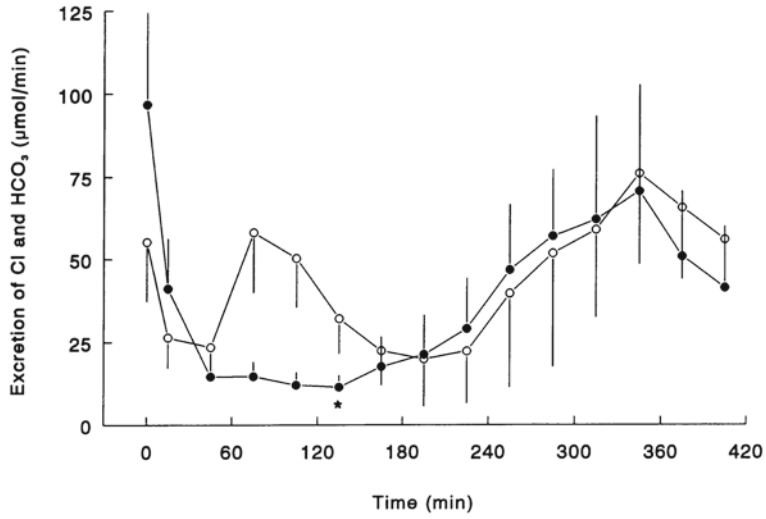

Figure 2. Means ± SEM of excretion of chloride (●) and bicarbonate (o) (µmol/min), in goats (n=4) after iv administration of medetomidine (5 µg/kg).
* significantly different from baseline ($p<0.05$).

significantly reduced at 135min, and plasma chloride concentration at 105min after medetomidine injection (Fig. 3).

Plasma glucose concentration increased significantly from 3.6±0.5 to 8.9±1.9 mmol/l; peak concentration was reached 75 min after medetomidine injection. In 4 of 7 goats glucose could also be detected in urine during the high plasma concentrations.

Discussion

In many species, α_2-adrenoceptor agonists have been found to induce water diuresis and natriuresis (*Gasthuys et al.* 1987, *Gellai* 1990, *Brooks et al.* 1991). Our findings in goats did not agree with these reports. Instead, a decrease was observed in renal sodium and potassium excretion, which confirmed the antinatriuretic effect of medetomidine reported earlier in this species (*Kokkonen* 1992). The detectable urine glucose concentrations in several goats and the marked hyperglycaemia caused by medetomidine were analogous to the findings in horses after detomidine administration (*Gasthuys et al.* 1987).

In the present study, the goats had relatively high urine bicarbonate concentrations both before and after drug administration. The alkaline urine, high in bicarbonate, is typical of herbivores due to the accumulation of bicarbonate ions when organic salts of feed are metabolized (*Houpt* 1993). In humans, ammonia and phosphate are the two basic urinary buffers, and bicarbonate is not detected in the urine in notable quantities before the blood bicarbonate concentration is around 26 mmol/l (*Sabatini & Kurtzman* 1989).

Acidosis was not observed after administration of medetomidine in spite of the increased venous PCO_2. On the contrary, medetomidine increased base excess and elevated blood pH in goats as detomidine did in horses (*Raekal-*

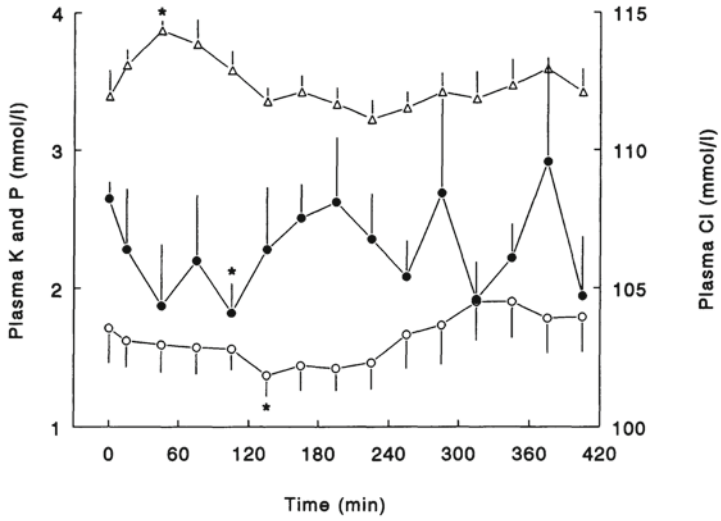

Figure 3. Means ± SEM of plasma potassium (△), phosphate (○) and chloride (●) concentrations (mmol/l) in goats (n=7) after iv administration of medetomidine (5 μg/kg).
* significantly different from baseline ($p<0.05$).

lio et al. 1990), indicating metabolic alkalosis. However, no changes were detected in urine pH or bicarbonate excretion. Therefore, changes in renal function are not a likely reason for the medetomidine induced alkalosis.

The intestinal secretions contain high concentrations of bicarbonate. An α_2-adrenergic mechanism is involved in the inhibition of acid-induced duodenal bicarbonate secretion in rats, although it is not known whether the neurogenic mechanism acts directly on the secreting epithelial cells or on enteric secretomotor neurons (*Jönson et al.* 1991). Thus a change in intestinal bicarbonate secretion might be a contributory factor of the metabolic alkalosis seen after administration of medetomidine in goats. In addition, α_2-adrenergic stimulation of intestinal epithelial cells is known to promote fluid and electrolyte absorption (*Fedorak et al.* 1985), which might influence also bicarbonate absorption.

It is concluded that the metabolic alkalosis detected after medetomidine administration is not likely to be caused by increased urinary acid excretion.

Acknowledgements

This study was supported by the Finnish National Research Council for Medical Sciences (Project No 1091008).

References

Brooks DP, Gellai M, DePalma PD, Edwards RM: Modulation of vasopressin antidiuretic action by α_2-adrenoceptors is species specific. Amer. J. Physiol. 1991, *261,* R1242-R1246.

Fabiny DL, Ertingshausen G: Automated reaction-rate method for determination of serum creatinine with the CentrifiChem. Clin. Chem. 1971, *17,* 696-700.

Fedorak RN, Field M, Chang EB: Treatment of diabetic diarrhea with clonidine. Ann. Int. Med. 1985, *102,* 197-199.

Gasthuys F, Terpstra P, van den Hende C, De Moor A: Hyperglycaemia and diuresis during sedation with detomidine in the horse. J. vet. Med. 1987, A *34,* 641-648.

Gellai M: Modulation of vasopressin antidiuretic action by renal α_2-adrenoceptors. Amer. J. physiol. 1990, 259, F1-F8.

Houpt TR: Acid-base balance. In: (Eds) Swenson MJ, Reece WO: Dukes' Physiology of Domestic Animals, 11th ed. Comstock Publishing Associates, Ithaca. 1993, pp. 604-615.

Jönson C, Hamlet A, Fändriks L: Hypovolemia inhibits acid-induced alkaline transport in the rat duodenum via an alpha-2 adrenergic mechanism. Acta physiol. scand. 1991, *142,* 367-373.

Kaneko JJ: Appendixes. In: (Ed) Kaneko JJ: Clinical Biochemistry of Domestic Animals, 4th edn. Academic Press Inc., San Diego. Ed Kaneko JJ. 1989, pp. 877-901.

Kokkonen U-M: Renal action of medetomidine, an alpha-2-agonist, and atipamezole, an alpha-2-antagonist, in the goat. Acta physiol. scand. 1992, *146,* Suppl. 608, 188.

Menson RC, Narayanswamy V, Bussian RW, Adams TH: A kinetic method for determination of CO_2 in biological fluids. Clin. Chem. 1974, *20,* 872.

Raekallio M, Vainio O, Karjalainen J: The influence of atipamezole on the cardiovascular effects of detomidine in horses. J. Ass. vet. Anaesth. 1990, *17,* 50-53.

Sabatini S, Kurtzman NA: Overall acid-base regulation by the kidney. In: (Eds) Seldin DW & Giebisch G. The regulation of acid-base balance, Raven Press, New York. 1989, pp. 185-210.

Trinder P: Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann. Clin. biochem. 1969, *6,* 24-27.

Weissman N, Pileggi VJ: Determination of Inorganic Phosphorus. In: (Eds) Henry RJ, Cannon DC, Winkelman JW. Clinical Chemistry, Principles and Technics, 2nd ed. Harper & Row, Publishers, Inc., Maryland. 1974, pp. 723-727.

Sammanfattning

Effekten av medetomidin på syra-basbalans och urinutsöndring hos get.

Medetomidin gavs till sju getter som intravenös engångsdos av 5 µg/kg. Venösa blodprov togs upprepande gånger och urin samlades kontinuerligt via kateter ända till 7 timmar efter injektionen.

Medetomidin framkallade djup klinisk sedation. Basöverflöd, pH och PCO_2 i venöst blod ökade efter medetomidin injektionen. Plasmans koncentration av natrium, kalcium, magnesium, kreatinin samt osmolalitet ändrade sig inte signifikant, medan koncentration av kalium och bikarbonat ökade och fosfat och klorid minskade. Medetomidin ökade plasmans glukoskoncentration och i fyra av de sju getterna kunde glukos upptäckas även i urin. Medetomidin inverkade inte på urinflöde, »fritt vatten-clearance«, utsöndring av bikarbonat och fosfat eller pH, men utsöndring av klorid, natrium, kalium, kalcium, magnesium och kreatinin minskade.

Resultaten tyder på, att den observerade metaboliska alkalosen efter medetomidin injektionen med all sannolikhet inte förorsakades av ökad syra-utsöndring i urin.

(Received April 6, 1994; accepted June 9, 1994).

Reprints may be requested from: M. Raekallio, Department of Clinical Sciences, College of Veterinary Medicine, P. O. Box 6, SF-00581 Helsinki, Finland.