7 Summary

Practicable determination of the glomerular filtration rate (GFR) in dogs with a “two-step-method”

Introduction

The early determination of renal dysfunction in dogs on the basis of clinical symptoms or laboratory diagnostic tests is difficult. There is thus a need for a simple diagnostic test to determine renal dysfunction in the early state, for instance in incurable and progressive renal failure. Moreover, the establishment of an azotaemia in the dog has been difficult, due to the variability of the upper reference value for the serum creatinine concentration.

Material and methods

A total number of 331 dogs of both genders (male: n = 162 (48.9 %), female: n = 169 (51.1 %)) and median age of 7 (3.0 - 9.1) years were included in the investigation. The dogs belonged to 57 different breeds; mixed-breed dogs (n = 93 (28 %)) were in the majority. For the determination of the creatinine-recovery-rate, the substrate creatinine was analysed either with the kinetic colour test of Jaffé or with the enzyme creatininase. The GFR was determined with the renal function test using the terminal plasma-clearance of exogenous creatinine. For the determination of the limiting value and the qualitative determination of the GFR, the ROC-analysis method was used.

Results

Up to 884 µmol/l (10 mg/dl), the determination rate for creatinine in the serum of dogs was on average 99.2 % for the Jaffé-method and 99.4 % for the enzymatic method. In the range from 804 - 4,420 µmol/l (9.1 - 50 mg/dl), the creatinine concentration was underestimated by about 1 - 2 % with the enzymatic method and overestimated by about 3 - 4 % with the Jaffé-method. If the serum was diluted 1 to 10 with distilled water in the concentration range from 804 - 4,420 µmol/l, there was a determination rate of 87.7 % for the Jaffé method and 97.7 % for the enzymatic method.

The estimated GFR of each dog with the renal function test was compared with 25 different laboratory blood- and urinary parameters (n = 89 dogs). Only when the GFR was reduced to below 40 % of the normal range were there significant changes in some of the laboratory parameter. From all measured parameters, the best correlation was between the endogenous serum-creatinine concentration and the GFR (n = 300 dogs).

These results for GFR in the dogs allowed a new definition for the upper limit of the endogenous serum-creatinine concentration. For GFR of 30% or less of the normal range this was 171 µmol/l. The diagnostic sensitivity was 100% and the specificity 99%. As a compromise between the earliest diagnosis of renal failure and a sufficient diagnostic quality,

a GFR of less than 40% of the reference range was chosen. An upper limit of144 µmol/l for the endogenous serum-creatinine concentration detects this level of renal failure. The diagnostic sensitivity is 89% and the specificity 97%.

The distribution of exogenous creatinine is completed within two hours in both normal and in dogs with renal disease. A simplification of the renal function test to distinguish qualitatively between healthy and diseased dogs using only two blood samples was tested (n = 89 dogs). In the time interval between 2 - 3 h and 3 - 4 h after giving exogenous creatinine, the qualitative differentiation between normal and diseased dogs was impossible. However, the determination of reduced renal function is possible with a satisfactory diagnostic quality at later times of between 6 - 7 h and 7 - 7.5 hours after giving creatinine. With an area under the curve (AUC) of 0,972, the total serum-creatinine concentration showed, in the time interval between 7 - 7.5 h after giving creatinine the greatest diagnostic certainty in the differentiation between healthy and diseased dogs. The total serum-creatinine concentration showed better results than the exogenous serum-creatinine concentration. For this test, a blood sampling before giving creatinine is unnecessary. The estimated upper limit for the total serum-creatinine concentration is 270 µmol/l. In summary, dogs with a total serum-creatinine of over 270 µmol/l in the time interval 7 - 7.5 h after an exactly dosed marker have a GFR ≤ 70 % of the normal range. These dogs have renal disease.

Conclusions

- ◊ With the Jaffé-method, creatinine concentrations up to 2,600 µmol/l (30 mg/dl) can be measured reliably in the serum of dogs
- ◊ Creatinine-concentrations over 2,600 µmol/l should be determined with the enzymatic method; a dilution is not necessary
- ◊ An early diagnosis of renal dysfunction using 25 different laboratory parameters in blood and urine was not possible with a sufficient diagnostic certainty.Such tests cannot be recommended.
- ◊ For the diagnosis of an azotaemia with the GFR ≤ 40 %, the physiological serum-creatinine concentration of 144 µmol/l is recommended as the upper limit. The diagnostic safety is high with a sensitivity of 89 % and a specificity of 97 %.
- ◊ The distribution of the exogenous creatinine is completed within two hours after marker application in both healthy and diseased dogs.
- ◊ To simplify the determination of renal function, the dogs received exogenous creatinine i.v. or s.c. in a dosage of 2 g/m^2 body surface area (BSA) or orally in a dosage of 4 g/m^2 BSA. Only one blood sample for the determination of the total serum-creatinine concentration in the time interval between 7 - 7.5 h is necessary. Dogs with a total serum-creatinine concentration > 270 µmol/l are nephrologically sick (GFR ≤ 70 % of the reference range).