As a marker of tubular disruption, urine CST3 concentrations can be measured in hospitalized patients as well as in emergency situations in which acute renal failure is suspected. In the latter cases, collection of 24-h urine is impossible because physicians need rapid laboratory results for immediate patient staging.

The absence of a circadian rhythm for CST3 allows its quantification in a single urine sample. As its automatic measurement allows a result in less than 1 h, both plasma/serum and urine CST3 could be used as standard markers for assessment of renal function.

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References


Marc Conti1*
Mokhtar Zater1
Karim Lallali1
Antoine Durrbach2
Stéphane Moutereau3
Philippe Manivet4
Pascal Eschwe`ge5,6
Sylvain Loric3

1 Biochemistry Laboratory
2 Nephrology Department
3 Biochemistry & Genetics Department
AP-HP Mondor University Hospital
Créteil, France
4 Biochemistry Laboratory
AP-HP Lariboisière University Hospital
Paris, France
5 Urology Department
Antony Private Hospital
Antony, France
6 Urology Department
AP-HP Bicêtre University Hospital
Le Kremlin-Bicêtre, France

*Address correspondence to this author at: Laboratoire de Biochimie CHU de Bicêtre, 78 avenue du Général Leclerc, 94270 Le Kremlin-Bicêtre, France. Fax 33-1-4521-3574; e-mail marc.conti@bct.aph-op-paris.fr.

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Pseudoparaproteinemia after Iopamidol Infusion for Coronary Angiography

To the Editor:

Automated capillary zone electrophoresis (CZE) is increasingly used for separation of serum proteins in routine clinical laboratories (1). Detection of proteins is based on the absorbance of peptide bonds at 214 nm, in contrast to older, gel-based methods, which use dye binding.

A 62-year-old man with ischemic heart disease, type II diabetes, and chronic renal failure underwent coronary angiography and received 62 g (100 mL) of iopamidol (Jopamiron®; Bracco s.p.a) intraarterially during the procedure. Blood was taken ~6 h after angiography for serum protein electrophoresis (SPE). Analysis by CZE (Paragon CZE® 2000; Beckman Coulter®) showed a defined peak of “5.2 g/L” in the cathodal end of the α2-globulin region. Immunofixation on the same instrument failed to confirm this peak as an immunoglobulin, and assays for apoprotein-B100, haptoglobin, and ceruloplasmin were within reference values. Repeat CZE after 2 and 5 days showed a progressive decrease in peak size. This relatively rapid clearance suggested a nonprotein compound, which was confirmed by the absence of an abnormal band on agarose gel electrophoresis (AGE; Paragon® SPE Kit; Beckman Coulter).

To confirm the interference of iopamidol in the CZE analysis, we added iopamidol to serum aliquots to give concentrations comparable to

![Fig. 1. CZE electropherograms (top) and AGE gels (bottom) of pooled serum before (A) and after (B) addition of 6.12 g/L iopamidol. The iopamidol peak is indicated by the arrow.](image-url)
those expected during angiography. A well-defined peak was obtained in the same zone of the α2 region in a dose-dependent fashion. Appearance on AGE was unaffected by the additions (Fig. 1). Iopamidol diluted in CZE buffer solution displayed an absorbance maximum of 242 nm as described previously (2). The absorbance of iopamidol at 214 nm was 75% of the peak value, accounting for its interference in the CZE analysis.

Interference of iodinated radio-opaque contrast agents in CZE analysis of serum proteins has been described, with abnormal peaks in the α2, β, and prealbumin regions (2,3). Radio-opaque agents are usually cleared rapidly from the serum; in this case, clearance of iopamidol was retarded by renal failure.

Clinicians may not be familiar with the potential interference of radio-opaque contrast agents in CZE. This may lead to diagnostic confusion in instances where blood for SPE by CZE is taken soon after an imaging procedure or in patients in whom renal clearance of contrast agent is defective. With the widespread use of CZE, this phenomenon may be encountered more frequently, and laboratories are urged not to discard AGE methods entirely because they have value in validating abnormal peaks on CZE.

References

George van der Watt*
Peter Berman

Division of Chemical Pathology
Groote Schuur Hospital
University of Cape Town
Observatory
Cape Town, South Africa 7925

*Author for correspondence. Fax 027-12-4044105; e-mail georgev@chempath.uct.ac.za.

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Concentrations of Circulating Gelatinases (Matrix Metalloproteinase-2 and -9) Are Dependent on the Conditions of Blood Collection

To the Editor:
Matrix metalloproteinases (MMPs) are a family of zinc endopeptidases collectively capable of degrading essentially all components of the extracellular matrix. They are involved in many physiologic and pathologic processes, such as wound healing, angiogenesis, embryo implantation, cancer progression, and metastasis. Several studies have measured circulating MMP-2 and -9 in cancer patients, but the results have been contradictory, specially for MMP-9, for which very large patient-to-patient variability was observed (1,2). This could be caused by different preanalytical conditions in blood sampling, as suggested by recent studies (3–6).

We studied the impact of blood sampling conditions on the measurement of immunoreactive MMP-2 and -9 in plasma by ELISA of MMP-2 and -9. This study was accepted by our Institutional Review Board, and written informed consent was obtained from all volunteers participating in the study.

In our first study, we collected venous blood samples from 12 healthy volunteers into Vacutainer® tubes containing clot activator (SST), lithium heparinate (LH), dipotassium EDTA, or sodium citrate. The tubes were either centrifuged immediately (t0) or after 0.5, 2, or 24 h. Tubes were left at room temperature, except for the tubes that sat for 24 h, which were kept at 4°C. Measurements were performed within 5 days of sampling, and plasma and sera were stored at 4°C until assayed.

In our second study, we collected venous blood samples from four healthy volunteers as described above (except for serum). Cells and plasma were immediately separated by centrifugation and aspiration. Cells were then transferred to clean plastic tubes containing a volume of sterile saline equal to that of the original plasma. Plasma and cells were incubated for 0.5 h, 2 h (room temperature) and 24 h (4°C). After incubation, plasma and cell supernatants were stored at −20°C until assayed.

MMP-2 and -9 concentrations were measured in plasma and serum samples by our own enzyme immunoassays (EIAs) (7). Results were confirmed by commercially available assays (Biotrak; Amersham). Gelatinolytic activity was measured by zymography as described previously (8).

Statistical analyses were performed by ANOVA using the Fisher test. P <0.05 was considered as representing a statistically significant difference.

In the first study, with the exception of citrate plasma, the concentration of immunoreactive MMP-9 increased with the time between sampling and centrifugation (Fig. 1A). The effect of time was dependent on the type of anticoagulant, however, being much more marked in heparin plasma and serum compared with EDTA plasma. Furthermore, the mean (SE) measured concentration of MMP-9 in EDTA plasma [55.4 (8.1 μg/L)] was significantly higher than in citrate plasma [19.4 (3.5 μg/L); P = 0.0003], heparin plasma [27.4 (3.1 μg/L]; P = 0.0002], or serum [32.6 (1.2) μg/L; P = 0.0094].

We obtained similar results when we measured the gelatinolytic activity of MMP-9 by zymography (results not shown), except that MMP-9 activity was significantly increased after 2 h only in heparin plasma and serum.

In sharp contrast to MMP-9, the concentration of immunoreactive MMP-2 did not increase with time between sampling and centrifugation; in fact, it was decreased in EDTA plasma after 2 and 24 h. The measured concentrations of MMP-2 were significantly lower...