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Kasuistik aus dem Arbeitskreis Klinische Toxikologie - Case report from the working group Clinical Toxicology

False-positive Paracetamol Results in Hyperbilirubinemic Patients

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A 63-year-old female patient has been transferred to our hospital with acute liver failure for evaluation of liver transplantation. From her medical history it was known that she has taken 21 g paracetamol during the last 3 to 4 days before admittance to our hospital. The laboratory results at entry were bilirubin: 121 µmol/l (<17), ALT: 6207 U7l (< 50), AST: 15136 U/l (<50) and INR: > 4.6 (< 1.2). The concentration of paracetamol was 62 µmol/l and no ethanol was detectable. Due to her chronic abuse of alcohol she did not qualify for liver transplantation and died 6 days after hospitalisation.

During the stay of the patient in the intensive care unit, the determination of paracetamol was repeated several times. First the concentration of paracetamol decreased; afterwards it increased again up to 73 µmol/l. Because the patient was intubated and did not get any paracetamol in the hospital, the reason for the increase of the paracetamol concentration seemed amazing and the accuracy of these measurements had to be questioned. After dilution of the sample (1 + 1) paracetamol was no more detectable. The bilirubin concentration in this patient triplicated between the first and last determination of the analgesic and was therefore suspected to be responsible for the erroneous measurements. The development of these two parameters is shown in Figure 1. The analytical method used in our laboratory for the determination of paracetamol is the enzymatic method on the Cobas Integra (Roche, Basel, Switzerland).

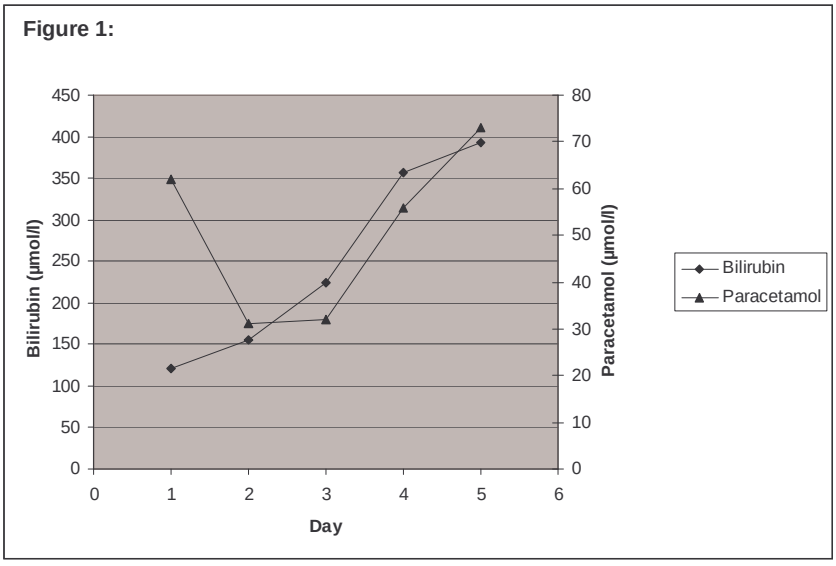

Fig. 1.
Development of the concentration of bilirubin and of the enzymatic paracetamol signal of a 63 year old female patient with acute liver failure.

We tested plasma samples of different other patients with highly elevated bilirubin concentrations (but without paracetamol intake) for the presence of paracetamol and measured the concentrations shown in Figure 2.

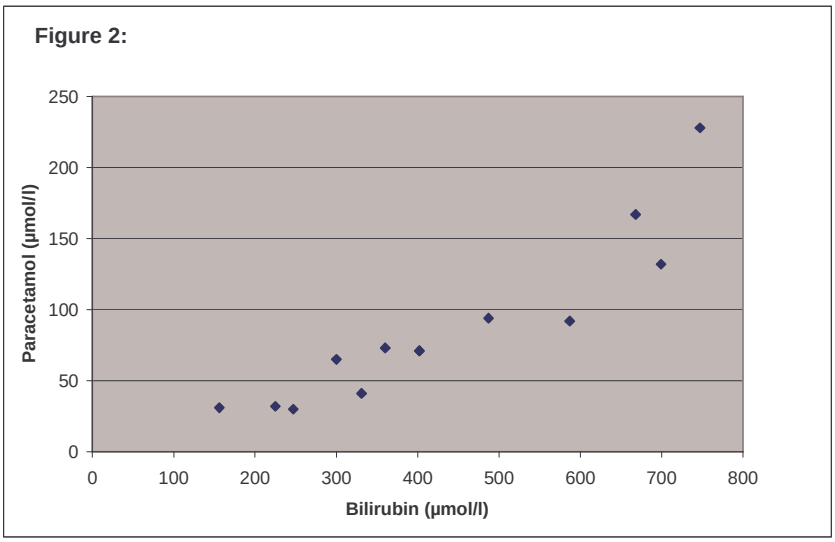

Fig. 2.
False positive paracetamol signals in patients with highly elevated bilirubin concentrations but no paracetamol intake.

After studying the literature, a case report was found [1] describing a similar situation in a 17-year-old child with severe hyperbilirubinemia. The authors showed that the interference disappears immediately when paracetamol is present in the hyperbilirubinemic sample. A possible explanation of this phenomenon is the reaction of periodate with bilirubin in the indicator reaction of the enzymatic assay to produce a product that absorbs more strongly at 600 nm than does unreacted bilirubin. The comparatively favourable kinetics of the p-aminophenol/periodate reaction explains the absence of this interference in the presence of paracetamol. When using an immunological assay (e.g. on the Axsym analyser) the interference does not appear whereas the concentration of paracetamol could be verified in samples containing the drug (Figure 3).

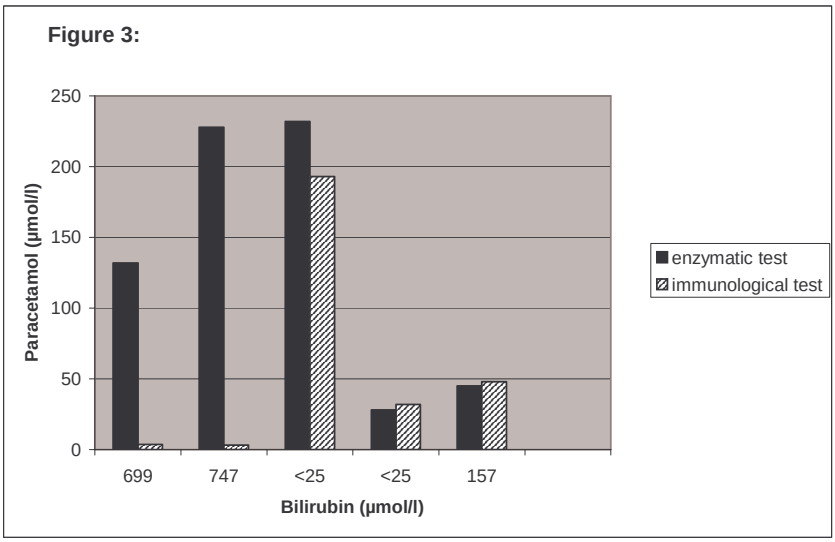

Fig. 3.
Comparison of paracetamol concentrations from enzymatic and immunological test

As a consequence of this interference, enzymatically determined therapeutic or subtherapeutic paracetamol concentrations in hyperbilirubinemic patients have to be interpreted very carefully and an interference of bilirubin has to be considered. Whenever possible, these results should be verified by an immunological or chromatographic method.

Reference

[1] Bertholf RL, Johannsen LM, Bazooband A, Mansouri V. False-positive acetaminophen results in a hyperbilirubinemic patient. Clin Chem 49: 695 (2003)