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DOI: 10.1373/clinchem.2006.083667

Use of Intraoperative Samples to Optimize Efficacy of Central Laboratory Parathyroid Hormone Analyses

To the Editor:

Intact (1-84) parathyroid hormone (PTH) has a short half-life and can be monitored during surgery to confirm the removal of all hyperfunctioning parathyroid tissue, but exact criteria for timing of sample collection and number of samples that best indicate a surgical cure are still to be perfected *(1)*. We report the degree of accuracy of our protocol of performing only 2 intraoperative PTH tests in patients undergoing parathyroidectomy.

Sixty patients (43 women, 17 men; mean age 59.8 years, range 22–79 years), without renal failure, who underwent a minimally invasive surgical operation for sporadic primary hyperparathyroidism, participated in the study. Blood was collected from a peripheral vein before skin incision (basal or t-0) and 10 min after parathyroidectomy (t-10). The removal of the hyperfunctioning gland(s) was considered effective when the PTH decrease was ≥50% from the t-0 value *(2)*. We measured the t-0 concentration before skin incision because physical manipulation of the parathyroid glands during surgery often leads to false increases in PTH concentrations. Thus baseline PTH obtained after incision may be falsely increased, and PTH may show a misleading decrease and appear to meet cutoff criteria compared with the t-10 concentration, which might actually represent the true baseline PTH *(3)*. When t-10 PTH did not decrease, we collected another blood sample, generally 35 min after parathyroidectomy (t-35). While awaiting the result of the last sample, we performed bilateral neck exploration and removed any enlarged glands. A subtotal parathyroidectomy was performed if the last sample did not show a PTH decrease or no other adenomas were found.

We measured PTH with an electrochemiluminescence immunoassay (Roche Diagnostics) performed on an Elecsys-2010 (Roche Diagnostics). The PTH assay detection limit was 1.2 ng/L, the assay analytical range was 1.2–5000 ng/L, and the reference interval was 15–65 ng/L. The total imprecision values (n = 12) were 5.9% and 4.3% at PTH concentrations of 1.8 ng/L and 11.7 ng/L, respectively. The definition of operative success was eucalcemia for 6 months or longer after parathyroidectomy *(4)*.

With a considerable decrease of PTH concentration of ≥50% at t-10, the procedure had 1 (1.5%) false positive, 5 (8%) false negatives, 8 (13%) true negatives, and 46 (77%) true positives with 90% sensitivity, 89% specificity, 98% positive predictive value, 62% negative predictive value, and 90% overall accuracy. For the false positive result, the PTH decrease was 72%, and for the false negatives, true negatives, and true positives, respectively, the median (range) PTH decreases were 27% (5%–42%), 16% (5%–33%), and 82% (53%–92%). Considering the decrease at t-35, for the patients without a PTH decrease of ≥50%, the procedure had 1 (1.5%) false positive, 0 false negative, 0 true negative, and 59 (98.5%) true positives. The median (range) PTH decrease was 81% (53%–94%) for the true positives. In 59 of 60 patients the presented protocol led to correct prediction of postoperative eucalcemia with 100% sensitivity, 98.5% positive predictive value, and 98.5% overall accuracy. Thus the rapid PTH assay correctly identified all but 1 case of solitary adenoma and of multigland disease, including 3 cases of hyperplasia.

Because the last sample must be collected 10 min after excision and transport of samples to the laboratory took 5 min, the average total waiting time after parathyroidectomy was ~35 min.

The cost of 2 intraoperative PTH determinations was $13.28 on the Elecsys-2010 already in use in the laboratory. The cost with a STAT-IntraOperative-System (Future Diagnostics), was $1035.51 (2 samples and 6 calibrators plus 2 controls, all performed in duplicate) with 15 min of processing time making a total of 25 min after the parathyroidectomy. Thus, the overall costs for a paired intraoperative PTH assay were $89.86 ($13.28 for the reagents and $76.58 for the operating room, allowing for an additional 10 min awaiting laboratory results) and $1059.94 ($1035.51 for the reagents and $24.43 for 2 h of technician time) when performed in the laboratory and in the operating theater, respectively. If the intervention lasted until t-35, the overall costs for 3 intraoperative PTH assays was $96.49 ($19.91 for the reagents and $76.58 for 10 min use of the operating room) and $1194.63 ($1164.10 for the reagents and $30.53 for 2.5 h of technician time) when performed in the laboratory and in the operating theater, respectively.

The suggested procedure with only 2 intraoperative PTH tests performed in the laboratory seems the most appropriate to obtain the highest quality results at the lowest cost if the laboratory is in close proximity to the surgical site (transport time of 5 min).

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DOI: 10.1373/clinchem.2006.080796

Monitoring Blood Glucose with Microdialysis of Interstitial Fluid in Critically Ill Children

To the Editor:

Hyperglycemia, a common feature in critically ill patients, was traditionally perceived as an adequate stress response reflecting the severity of the disease state and was treated only if glycemia exceeded 11–13.5 mmol/L. In recent studies in intensive care patients, we showed that tight glycemic control (TGC) with intensive insulin therapy (IIT) reduced the risk of organ failure and death *(1)*. In critically ill children, peak blood glucose (BG) and duration of hyperglycemia are associated with risk of mortality *(2)*. Implementing TGC and avoiding hypoglycemia with intensive insulin therapy requires frequent BG sampling. Microdialysis of interstitial fluid (ISF) is a promising approach to reduce diagnostic blood loss. Continuously sampling dialyzed ISF and converting the ISF glucose concentration (IFG) to a BG value is a promising new method for glucose monitoring in diabetes patients. We conducted a prospective clinical trial in critically ill children to evaluate the feasibility of prolonged subcutaneous microdialysis and the correlation between BG and IFG.

The study was approved by the Institutional Ethical Review Board. Twenty children were enrolled after written informed consent was obtained from the parents. A CMA 60 microdialysis catheter (CMA Microdialysis) was inserted subcutaneously. This catheter has a dialyzing membrane with a molecular cutoff of 20 kDa and was continuously perfused with a 5% mannitol solution at a flow rate of 1 μL/min. BG was determined on an ABL 715 blood gas analyzer (Radiometer) and dialysate glucose (DG) values with a Cobas Mira Analyzer (Roche). Both techniques use the enzyme glucose dehydrogenase. Because of the used flow rate of 1 μL/min, the concentration in the dialysate reaches only partial equilibration and thus does not reflect the absolute concentration in the extracellular fluid. Therefore, IFG was calculated using the ionic reference technique *(3)*. This technique is based on the simultaneous measurement of glucose and ions in the samples. The ionic recovery can be calculated as the ratio of sodium in the sample to the sodium concentration in plasma, using an ion-free perfusate. Assuming that recovery rates of glucose and sodium were the same, we calculated the glucose concentration of the ISF as IFG = dialysate glucose × plasma sodium/dialysate sodium. Thus, the relative recovery of a particular substance is the concentration of this substance in the dialysate expressed as percentage of the concentration of this substance in the surrounding tissues. Mean age and body weight were 3.4 years and 14.5 kg. No complications with the technique occurred. Median microdialysis recovery rate was 89% ($^{P25–75:}$79–94%).

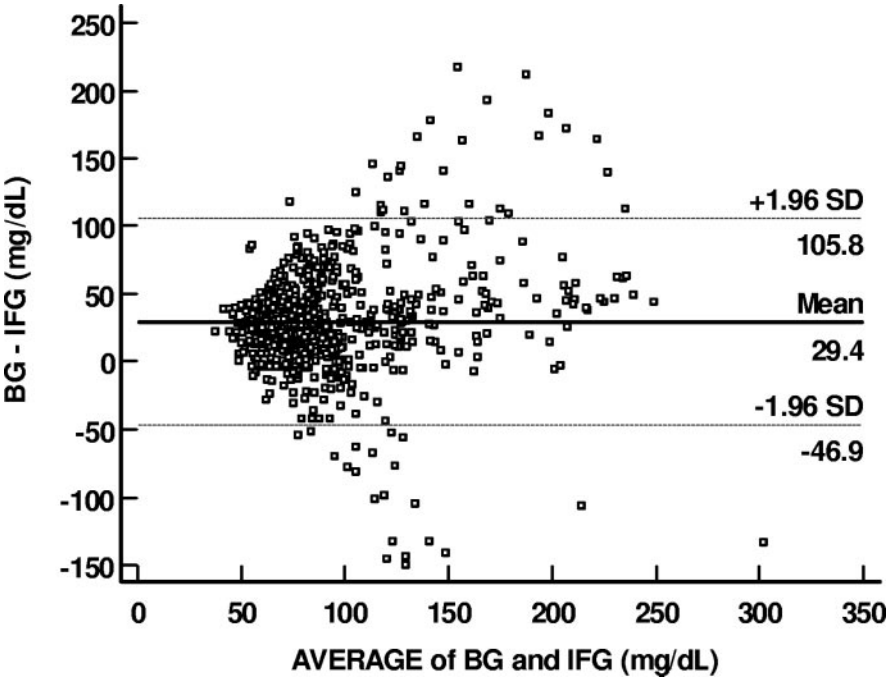

Fig. 1. Bland–Altman analysis.

The bias is 29.4 mg/dL (1.6 mmol/L). This bias represents the mean of the systematic distribution of the values. To achieve TGC, this bias of 29.4 mg/dL is inaccurate for safe clinical implementation in ICU. Bias SD (1.96) represents the limits of agreement. A potential difference reaching between 105.8 and −46.9 mg/dL (5.9 and −2.6 mmol/L) is unacceptable for clinical use in ICU-settings applying TGC.