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Intraoperative Parathyroid Hormone Level Evaluation During Parathyroidectomy
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The parathyroid glands regulate serum calcium and phosphorus levels through the secretion of parathyroid hormone (PTH), a polypeptide of 84 amino acids, which acts opposite calcitonin to raise serum calcium levels while lowering serum phosphorus concentration. The regulation of PTH secretion occurs through a negative feedback loop in which calcium-sensing receptors on the membranes of parathyroid cells trigger decreased PTH production as serum calcium concentrations rise. PTH has a half-life of approximately 4 minutes.[1] There are two known parathyroid hormone receptors, PTH1R and PTH2R, which are members of the transmembrane G protein-coupled family.[2] It is PTH1R that is expressed in high levels in bone and kidney and regulates calcium ion homeostasis through activation of adenylate cyclase and phospholipase C.[3,4]

Primary hyperparathyroidism is the most common form of hyperparathyroidism and represents excessive release of PTH from a benign adenoma of one or more glands. Increased PTH results in hypercalcemia, the signs of which are bone pain, kidney stones, intestinal ileus, and depression.[5] In 80% of patients with hyperparathyroidism, the symptoms of hypercalcemia are mild or are not notable at the time of discovery. However, patients with overtly symptomatic hyperparathyroidism and those with marked hypercalcemia (calcium levels >10.2 mg/dL) must be referred for parathyroidectomy.[6]

Historically, the standard treatment for hyperparathyroidism was a comprehensive bilateral four-gland surgical exploration, which had a success rate of 95% when performed by experienced surgeons. Improvements in imaging technology have allowed surgeons to focus the exploration to the area of the hyperactive gland. The introduction of the rapid intra-operative parathyroid hormone (IOPTH) assay has added the ability to verify adequate resection with a scan-directed, minimally invasive parathyroidectomy. As a result, there is less dissection, less time under anesthesia, lower hospital costs, and similar cure rates when compared with a traditional bilateral neck exploration.[7] In addition to determining the adequacy of resection of parathyroid adenomas, IOPTH may be used to evaluate the function of the remaining parathyroid glands after thyroidectomy.[8]

Rapid intra-operative PTH assays are primarily used to determine whether all hyperfunctioning parathyroid tissue has been removed from the patient. On the day of surgery a baseline rapid PTH level is obtained. Discrepancy in various literature exists as to exactly when the baseline level should be drawn, with some sources indicating before anesthesia and others before incision occurs. Once the surgeon locates and removes the abnormal gland, an adequate amount of time is allowed to pass to allow the circulating PTH to degrade, and then a second PTH level is collected and sent for rapid

analysis. When serum levels of PTH fail to decline promptly after removal of an abnormal parathyroid gland, this indicates either the presence of residual hyperfunctioning parathyroid tissue or that the tissue removed was not the abnormally functioning parathyroid gland. Frozen section may be utilized when there is uncertainty about the identity of the resected tissue. A significant drop in the post-resection PTH levels can give the surgeon confidence that further exploration is unnecessary; however, the literature debates this topic as well. A decline of 50% is thought to be sufficient to determine accurate surgical excision, but reports exist of unknown multi-glandular involvement meeting this benchmark only to later be found that there is residual disease. The percentage of decline should be determined by each surgeon based on their laboratory experience at their institution. Proper planning and execution of intra-operative PTH tests requires communication between the laboratory and the surgeon. The surgeon should inform the laboratory on a daily basis of any changes made to the operating room schedule regarding these procedures.[9]

In summary, IOPTH is an important adjunct to advanced imaging technology in the removal of parathyroid adenomas. Together they have shown an increase in surgical success along with a decrease in surgery time, hospital costs, and patient recovery. Research is still being done to identify the best timeline for baseline and secondary levels; however, all sources agree that IOPTH is an important and necessary tool for the surgeon when performing parathyroidectomy. A decline of 50% is typically considered adequate for determining accurate resection; but this cut-off level should be determined individually at each institution.

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