Dialysis

Parathyroidectomy Versus Cinacalcet Hydrochloride–Based Medical Therapy in the Management of Hyperparathyroidism in ESRD: A Cost Utility Analysis

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Background: Previously, patients with end-stage renal disease (ESRD) with uncontrolled hyperparathyroidism had few options other than parathyroidectomy, which was reserved for patients refractory to medical therapy. Newer calcimimetic agents, such as cinacalcet, may be an alternative, but raise the possibility of indefinite medical treatment that also would increase costs.

Study Design: Cost utility analysis.

Setting & Population: Base case consisted of prevalent adult US patients with ESRD refractory to management with standard medical therapy. Characteristics were obtained from patients who underwent parathyroidectomy in 2001, and, for purposes of comparison, patients in whom cinacalcet was used were assigned similar characteristics. All data came from preexisting literature and trials or from US Renal Data System analysis files.

Intervention: Use of cinacalcet hydrochloride versus parathyroidectomy.

Perspective & Time Frame: Medicare and societal costs and quality-adjusted life-years from the date of parathyroidectomy or use of cinacalcet followed up for 2 years, respectively.

Model & Outcomes: Primary outcomes were cost (measured in US dollars) and cost utility measured using cost per quality-adjusted life-years.

Results: At base-case surgical and drug costs, surgical and drug success rates, complication rates/costs, and benefit from correction of hyperparathyroidism, parathyroidectomy was found to be both less expensive and more cost-effective at 7.25 $\pm$ 0.25 months. Parathyroidectomy became more cost-effective at 15.28 to 16.32 months at the upper limit of sensitivity analysis, when drug/surgical costs and success/complication rates/costs were maximally weighted to favor cinacalcet-based medical therapy.

Limitations: We assumed current costs of both cinacalcet and parathyroidectomy and assumed cinacalcet use would be indefinite.

Conclusions: For patients with ESRD with uncontrolled hyperparathyroidism who are good candidates for either drug therapy or surgery, cinacalcet hydrochloride is the most cost-effective modality if the patient is to remain on dialysis therapy for 7.25 $\pm$ 0.25 months. Cinacalcet may be more optimal if used in patients who have high risk of mortality or who would expect to receive a kidney transplant quickly. For other subgroups, parathyroidectomy dominated.

Am J Kidney Dis 49:801-813.

INDEX WORDS: Medical decision analysis; cinacalcet hydrochloride; parathyroidectomy; cost-effectiveness; cost utility; hyperparathyroidism; parathyroid hormone (PTH).

Despite the use of phosphate binders and vitamin D analogues, secondary and tertiary hyperparathyroidism lead to derangements in serum calcium, phosphate, and parathyroid hormone (PTH) levels such that the National Kidney Disease-Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines are not met in 29% to 53% of patients on long-term dialysis

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Received August 23, 2006; accepted in revised form March 19, 2007.

Originally published online as doi:10.1053/j.ajkd.2007.03.009 on May 7, 2007.

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Support: None. Potential conflicts of interest: None.

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0272-6386/07/4906-0011$32.00/0

doi:10.1053/j.ajkd.2007.03.009

therapy in the United States.[1-3] This leads to increased risk of mortality and morbidity, hospitalization, bone disease, vascular and soft-tissue calcification, and vascular access failure.[4] Correcting uncontrolled hyperparathyroidism, at least surgically, was associated with improvements in subsequent morbidity and mortality.[5] Surgical parathyroidectomy was well studied in dialysis patients with refractory hyperparathyroidism, with high success rates, low mortality rates, and salutary effects on morbidity and mortality.[5,6]

Newer calcimimetic agents, such as cinacalcet hydrochloride, are now available that act through modulation of the calcium-sensing receptor in parathyroid tissue and inhibit PTH production by mimicking a hypercalcemic state. These agents have become popular and effective in decreasing PTH levels and improving calcium and phosphate metabolism in patients previously refractory to treatment. Cinacalcet was shown to decrease morbidity,[6] although mortality data are not yet available. These effects come at significant additional cost (~$1,000/mo[7,8]). Studies showed an approximately 50% success rate in controlling refractory cases of hyperparathyroidism with cinacalcet, with minimal serious side effects.[8-11]

Because surgical control of parathyroid disease implies primarily 1-time costs, whereas control with cinacalcet implies potentially indefinite costs, it is reasonable to assume that at some point (ie, duration of cinacalcet use), surgery may become more cost-effective than indefinite therapy with cinacalcet. It is unknown when or how significant this break-even point might be given the abbreviated life expectancy of most dialysis patients. Although many patients on dialysis therapy have unacceptably high surgical risk, many patients, such as those on the kidney transplant wait list, often are good candidates for either surgical parathyroidectomy or drug therapy with cinacalcet. Dialysis patients who undergo parathyroidectomy are significantly younger and healthier than dialysis patients in general,[5] although whether such patients receive kidney transplants earlier (and thus have a briefer time on dialysis therapy) than similar patients has not been studied. Circumstances and groups of patients who might benefit best from cinacalcet-based medical therapy versus expeditious parathyroidectomy were not explored previously. We therefore undertook a cost utility analysis of the use of cinacalcet versus surgical parathyroidectomy in patients with end-stage renal disease (ESRD) with hyperparathyroidism refractory to conventional medical therapy.

METHODS

We performed a cost utility analysis using decision tree software by TreeAge Pro 2005 (TreeAge Software Inc, Williamstown, MA) using methods defined by the manual and established in the previous literature.[12]

Case Definition

The population considered was adult (age > 18 years) US patients with ESRD undergoing either hemodialysis or peritoneal dialysis with hyperparathyroidism that was refractory to management with standard medical therapy with phosphate binders and vitamin D analogues. Hyperparathyroidism in this population is defined as PTH levels greater than the KDOQI limit for PTH in patients with ESRD (>300 pg/mL). All data come from preexisting literature and trials. We further restricted our analysis to patients for whom perioperative risk did not exclude them for surgery or who entered the decision analysis already having undergone parathyroidectomy. Similarly, we also excluded patients who could not tolerate cinacalcet because of side effects, which can include up to 8% to 30% of patients.[10]

Decision Analysis Model

Decision analysis is based on a choice between parathyroidectomy and cinacalcet-based medical therapy. A model approximately similar to that previously used for the evaluation of surgery versus medical follow-up in patients with asymptomatic primary hyperparathyroidism was used,[13] with the exception that multiple recursions were not used because of the shorter decision cycle and lack of information on salvage therapy for either parathyroidectomy or especially cinacalcet therapy in patients with hyperparathyroidism of chronic kidney disease. Elements of other decision analyses used in dialysis populations also were emulated when appropriate.[14] The decision tree is shown in Fig 1. In Fig 1, chance nodes are represented by circles, choice nodes (points at which a clinical decision is made) are denoted by squares, and terminal nodes, representing end points in terms of cost in dollars and effectiveness measured in quality-adjusted life-years (QALYs), are represented by triangles.

At the first node, a dialysis patient (peritoneal dialysis or hemodialysis) with uncontrolled hyperparathyroidism refractory to conventional medical therapy either undergoes parathyroidectomy or cinacalcet-based medical therapy. If the patient undergoes surgery, the patient dies, survives, or experiences a serious complication, such as bleeding, vocal cord paralysis, wound infection, seroma, or severe hypocalcemia. Patients who die are given a QALY (effectiveness) score of zero. Because costs associated with death after parathyroidectomy have not been reported, we used data from our extraction of the US Renal Data System (USRDS) database to extract annual Medicare costs stratified by time to death after parathyroidectomy. If the patient survives