Hyperparathyroidism: Medical or Surgical Treatment?

Secondary hyperparathyroidism (sHPT) is commonly encountered in conjunction with chronic kidney disease (CKD). It is believed that over the course of their severe renal insufficiency more than 90% of dialysis patients develop sHPT – although to varying degrees [1]. An elevated serum level of parathyroid hormone (PTH) is the characteristic feature of this condition. The clinical manifestations of sHPT are not inconsiderable: It may lead to osteodystrophia, a condition that entails bone pain and increased fracture risk. However, the cardiovascular complications are far more serious: Elevated levels of PTH are associated with vascular calcification and with an increased risk of cardiovascular events [2] – and therefore also with increased mortality [3].

For many years parathyroidectomy, the surgical removal of one or more parathyroid glands, or the therapy with active vitamin D (VDRA) had been the only treatment alternatives. Latter has been commonly used to treat sHPT, because it inhibits the production of PTH and PTH levels return to normal in response to calcitriol or alfacalcidol therapy. However, a limiting factor with this therapy is that serum calcium and serum phosphorus levels may increase markedly, a phenomenon that is associated with the risk of vascular calcification.

For some years now, a new treatment alternative belonging to the group of PTH antagonists has been available for PTH lowering: Cinacalcet is an allosteric modulator of the calcium-sensing receptor (CaSR). It increases the sensitivity of the calcium receptors in the parathyroid glands and thus effectively inhibits the excessive production of PTH.

As part of the COSMOS study (Current management of secondary hyperparathyroidism: A multicentre observational study), a 3-year observational study conducted in 6,251 HD patients, Cannata-Andia performed a prospective evaluation of parathyroidectomy versus Cinacalcet therapy. In the study, the use of cinacalcet was associated with a better survival (the addition of VDRAs to Cinacalcet lead to an additional survival benefit). But, of course, there is always the risk of bias and confounding in observational studies; therefore the authors emphasize that for answering the question, which treatment option – surgical or medical – is associated with a better outcome, a randomized controlled study is needed.
Impact Of Parathyroidectomy And Cinacalcet Use On Survival In Chronic Hemodialysis Patients: The Cosmos Study.

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INTRODUCTION AND AIMS: Secondary hyperparathyroidism is a common complication of chronic kidney disease leading to increased risk for cardiovascular and all-cause mortality. Different therapeutic strategies are currently used to manage this problem. In the present study, we analyzed the association between the use of parathyroidectomy or cinacalcet and survival in COSMOS (Current management Of Secondary hyperparathyroidism-a Multicenter Observational Study).

METHODS: COSMOS is a multicentre, open-cohort, 3-year prospective study, designed to evaluate CKD-MBD management in 20 European countries. Forty two variables with 304 items including demographics, comorbidities, routine biochemical laboratory parameters and concomitant therapies were collected from 227 European haemodialysis centres every 6 months during three years. In the present analysis, 6251 haemodialysis patients were included, 4285 randomly recruited at baseline plus 1966 (31.5%) included to replace patients who died, were transplanted, switched to peritoneal dialysis or lost to follow-up. Three additive multivariate Cox’s regression models including 20 variables were used to assess the association of parathyroidectomy or prescription of cinacalcet with all-cause mortality.

The relative risk of mortality was assessed by using four different approaches: 1) the full cohort (N=6251) was included and the exposure was parathyroidectomy or cinacalcet (additional analyses assessed the combination of cinacalcet plus VDRAs); 2) only patients not prescribed cinacalcet at any time (N=5087, 251 patients parathyroidectomized at baseline) were included and the exposure was parathyroidectomy; 3) only patients not parathyroidectomized at any time (N=5460, 353 patients prescribed cinacalcet at baseline) were included: the exposure was cinacalcet; 4) only patients either parathyroidectomized or initiating treatment with cinacalcet during 3-year follow-up were included (N=620) and cinacalcet use vs. parathyroidectomy was compared. In approaches 1, 2 & 3 the exposures were considered as time-varying variables. In addition, in approaches 2, 3 & 4 propensity score matching was performed. In
approach 4, time 0 was the time of parathyroidectomy or initiation of cinacalcet prescription.

RESULTS: Approach 1 showed after full adjustments that the use of cinacalcet (independently of the use of VDRAs) was associated to lower relative risk of mortality (HR: 0.74[0.59-0.94]), meanwhile parathyroidectomy was not. The combination of cinacalcet with VDRAs improved the association (HR: 0.65[0.48-0.87]). Approaches 2, 3 and 4 showed that the prescription of cinacalcet but not parathyroidectomy was associated with a significantly lower relative risk of mortality. Specifically, in approach 3(not PTX but cinacalcet), the HR was 0.75[0.59-0.95] with full adjustments and 0.57[0.33-0.99] after propensity score matching.

CONCLUSIONS: In COSMOS, the use of cinacalcet was associated with better survival compared with parathyroidectomy. The addition of VDRAs to cinacalcet exerted additional benefits. These findings strongly suggest the need for randomized controlled trials comparing the effect of medical vs. surgical treatment in the management of the CKD secondary hyperparathyroidism.

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