**Introduction**

- Primary hyperparathyroidism (PHPT) can be asymptomatic in many patients; however, a cohort of patients may develop complications such as renal stones, osteoporosis and risk of fragility fracture and more commonly symptomless hypercalcaemia. (Bilazikjian 2014 J Clin Endocrinol Metab)
- Surgical removal of the culprit parathyroid adenoma offers the best option for cure of PHPT; a substantial number of patients may not be eligible for this definitive treatment due to comorbidities, surgical fitness, patient choice or absence of end organ damage.
- Cinacalcet is an allosteric modulator of CaSR gene, thereby increasing sensitivity of the parathyroid gland to circulating calcium, and hence downregulating PTH production.
- Cinacalcet is known to reduce calcium levels consistently in >50% of the patients and also to normalize PTH levels, though not very predictably. (Luque-Fernandez 2013 Thor Adv Endocrinol Metab)
- The calcium reducing capacity of cinacalcet is noted across various cohorts of patients such as post-operative recurrent hypercalcemia, intractable hypercalcemia in PHPT and mild PHPT (Peacock 2011 J Clin Endocrinol Metab, Marcocci 2009 J Clin Endocrinol Metab)
- Cinacalcet is licensed by EMA for PHPT; in the UK, cinacalcet is licensed for use in secondary HPT or parathyroid cancer.
- The process of prescribing cinacalcet for patients with PHPT varies regionally. The regional medicines management committee have restrictions in using it in primary care. Therefore the responsibility of prescribing and continuing the treatment lies with tertiary care centres.

**Aim**

The aim of our study was to assess the usefulness of cinacalcet in PHPT in reducing serum calcium and benefits in admission avoidance

**Methods**

- Retrospective clinical observational analysis
- Patients with PHPT treated with cinacalcet included
- Baseline serum calcium, PTH collated
- Latest calcium levels were used to assess treatment response; also serum calcium at approximately 6 and 12 months (if completed) was collected
- Number of hospital admissions preceding the initiation of cinacalcet and since collated (data restricted since 2012 due to lack of computerized data preceding this)
- Hospital admissions included admission to MAU or to endocrine unit for IV fluids ± pamidronate infusion

**Results**

- N=14 (men 2 and women 12)
- Mean age 81.6 years (59-99)
- Mean duration of treatment 22 months (2-69)
- Initial parameters:
  - Calcium 3.1 mmol/L (2.92-3.2) [normal range 2.2-2.6]
  - PTH 21.1 pmol/L (7.7-58.1) [normal range 0-8.5]
  - Vitamin D 74 nmol/L (21.4 to 152.9) [normal range >50]
  - Calcium improvement 3.02 vs 2.52 ; p<0.005
  - Calcium improvement 3.05 vs 2.63 ; p<0.0001
- Hospital episodes 15 (10 patients, mean 1.1 admission/patient)
- Patients assessment at 6 months of treatment
  - N=12
  - Calcium improvement 3.05 vs 2.63 ; p<0.0001
  - Patients assessment at 12 months of treatment
  - N=8
  - Calcium improvement 3.02 vs 2.52 ; p<0.005
- Hospital admission avoidance pre and post cinacalcet
  - Hospital episodes 15 (10 patients, mean 1.1 admission/patient) Vs 2 episodes (2 patients, mean 0.2 admission/patient) p = 0.001
- Tolerability
  - One patient had to reduce dose due to side effects
  - One patient developed biochemical hypocalcaemia that required dose adjustment

**Discussion**

- Our study shows the potential of Cinacalcet in lowering calcium levels quite effectively and the effect to be sustained
- The incidence and prevalence of PHPT is increasing; the prevalence increases with age and therefore the need for use of cinacalcet is likely to keep increasing (Yeh 2013 J Clin Endocrinol Metab)
- Cinacalcet can reduce calcium fairly rapidly (though not as fast as bisphosphonates) and sustain the calcium lowering effect for a significantly longer period of time (Leere et al 2017 Front Endocrinol)
- There is no data to support the role of cinacalcet with bone mineral density or prevention of fragility fractures (Leere et al 2017 Front Endocrinol)
- Cinacalcet is known to be an effective treatment option in patients who refuse surgery or are unfit for definite treatment options (Abusahmin 2018 Indian J Endocrinol Metab)
- Long term treatment with Cinacalcet is shown to be sustainable, reduces PTH levels and maintains stability but lacks data on any changes to BMD (Peacock 2009 J Clin Endocrinol Metab)
- Pamidronate IV infusion given periodically is an alternate choice of therapy. Though this is cheap, it is time consuming, requires admission to a medical area or endocrine unit as a day case, needs clinical observation during treatment and more frequent blood tests to monitor the response.
- Pamidronate may have the additional advantage of offering some protection to BMD; cinacalcet may have some benefits in reducing the risk of nephrolithiasis

**Conclusion**

- Cinacalcet offers an effective and sustainable treatment option for medical management for primary hyperparathyroidism
- It can significantly reduce hospital admissions for hypercalcemia and keep calcium levels under safe control
- Regional / national guidelines are required to facilitate use of cinacalcet across the health care regions, with agreed shared care pathways, so that the treatment can be safely continued in primary care under consultant monitoring