REVIEW

Primary hyperparathyroidism in the older person

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Abstract

Primary hyperparathyroidism (PHPT) is a common condition which may have few symptoms. One of the principal concerns in the older person with minimally symptomatic PHPT is restoration of bone mineral density and prevention of fracture. Other important considerations are cardiovascular risk and quality of life. Surgery, the traditional treatment of choice, may not always correct these factors. We present a review of the literature and advice of medical therapies which should be of benefit, with emphasis on a multifaceted approach in protecting the patient from PHPT.

Keywords: hyperparathyroidism/surgery, aetiology, drug therapy, diagnosis, parathyroidectomy, hypercalcaemia/drug therapy, elderly

Introduction

Primary hyperparathyroidism (PHPT) is a common condition. The prevalence since the introduction of multichannel analysers is approximately 1:1000, with the older female being the typical patient. PHPT is predominantly a sporadic disorder [1]. However, in the minority (less than 10%) of affected patients, PHPT is associated with a number of distinct hereditary syndromes [2, 3]. More routine testing of calcium means that a greater proportion of patients are being diagnosed at a relatively asymptomatic stage. The clinical presentation originally described by Albright of ‘stones, bones, groans and psychic moans’ is now rarely seen.

Several previous publications have addressed the management of asymptomatic PHPT in the general population [4–6, 7–10]. There is debate as to just how symptom-free an individual needs to be in order to qualify as having ‘asymptomatic’ hyperparathyroidism. Several other studies, including quality of life studies and retrospective reviews have failed to give clear guidance, although these studies generally show a slight advantage in favour of surgery for minimally symptomatic individuals [11–15].

Geriatricians will readily recognise the clinical conundrum of an incidental finding of PHPT in the older patient that was unexpected. Retrospective questioning may identify some pertinent symptoms, but none strong enough on their own to have made the diagnosis obvious prior to testing serum calcium. This group of patients is hard to define and hence there is little published guidance on how to manage the increasingly common clinical scenario of the frail, relatively asymptomatic, older patient with PHPT.

A major concern in this group of patients, who have an increased risk of fracture, is the effective prevention and treatment of associated osteoporosis. The overall fracture risk in patients with PHPT is increased even further by a factor of 1.3 [16]. In addition to the effects on the bones, PHPT can have systemic effects which may be all the more relevant to the frail elderly. For example, PHPT may have an adverse effect on the cardiovascular system, contributing to left ventricular hypertrophy (LVH) [17–20], coronary atherosclerosis [21] and dyslipidaemia [22]. This ‘metabolic syndrome’ may also be characterised by hyperinsulinaemia and hyperuricaemia. Other detrimental effects include renal damage, confusion, dementia and subtle neuro-psychiatric symptoms.

The aim of this article is to review different options for managing minimally symptomatic PHPT with a particular focus on the older patient and bone protection.

Background

Traditional views on hyperparathyroidism have been polarised around two main options – surgery or ‘conservative’ management. Conservative management has often meant careful observation, but little in the way of active
medical management. The accumulating evidence base for medical therapies as well as new emerging surgical options has broadened the scope of treatments available and these various treatment modalities will be appraised below.

The consensus statement from the National Institutes of Health (NIH) 1991, addressed the management of asymptomatic PHPT (Figure 1) [23]. This debate arose to address the change in the population from ‘classical’ hyperparathyroidism to the now dominant ‘asymptomatic’ population, comprising up to 80% of all those with hyperparathyroidism, and how management should reflect this change. This meeting established suggested criteria for surgical intervention. Included in the criteria is ‘age less than 50 years’ reflecting the difficulties of long-term follow-up and perhaps the cost of such an exercise.

The debate was revisited by Silverberg et al. [24], in the light of new evidence – for both surgical and medical therapies. In this paper, the view is presented that surgery is still the only definitive therapy, though may not always be necessary.

If the original NIH criteria are strictly adhered to, up to 50% of asymptomatic individuals will eventually come to surgery. There are few long-term published data on the outcomes of this group, particularly with respect to the elderly. In a 10-year follow-up study of younger patients, Silverberg et al. [24] showed no major detrimental effects in the non-operated compared to the operated group with both symptomatic and asymptomatic hyperparathyroidism.

The older patient

The older patient with hyperparathyroidism poses a particular challenge. A multitude of factors will influence his or her overall state of health, other than the radiological and biochemical markers alluded to in the NIH statements.

Concomitant morbidity is much more likely, such as falls, osteoarthritis, pre-existing idiopathic osteoporosis and cognitive impairment, all of which make management more challenging. Polypharmacy can also have an important impact – for example, diuretic and chronic steroid use. Poor nutrition and vitamin deficiencies (particularly vitamin D) will also make the older patient more vulnerable to the deleterious effects of hyperparathyroidism on the skeleton. The high burden of cardiovascular pathology seen in older patients has implications for certain treatment modalities, such as hormone replacement therapy (HRT). Chronic renal impairment (glomerular filtration rates <50 ml/min) can impact upon vitamin D metabolism as well as the pharmacokinetics of various therapies.

In some respects, the increased complexity of managing the older patient strengthens the case for surgery, but this may not be practical (because of co-morbidity and operative or peri-operative risks) nor desirable (patients may not wish to undergo surgery). Furthermore, the evidence for long-term benefit from surgery is not assured.

Diagnosis

Establishing the diagnosis should be relatively straightforward. Inappropriately high parathyroid hormone (PTH) in the presence of hypercalcaemia is the key finding. Serum phosphate is of limited clinical use in the differential diagnosis of hypercalcaemia. Typically, the phosphaturic action of PTH causes hypophosphataemia, but this is not invariable; plasma phosphate concentration may be normal or raised, particularly if there is associated renal damage or age-related decline in the glomerular filtration rate. Plasma alkaline phosphatase is raised, or at least at the upper end of the normal range, in approximately one third of patients. For a detailed overview of the pathophysiology, the reader is referred to the review by Marx [26]. It is well recognised that PHPT may co-exist with hypercalcaemia of malignancy [27] and the PTH should be tested in all patients with hypercalcaemia. Other clues to an underlying malignancy may be found on careful clinical assessment and from other biochemical and haematological markers. Patients taking lithium therapy can have a spuriously high serum calcium and PTH; whilst the majority of these will have PHPT, a firm diagnosis requires that the lithium be withdrawn and then the patient retested.

At the ‘Workshop on Asymptomatic Primary Hyperparathyroidism: A Perspective for the 21st Century’, run by the NIH in April 2002, there were suggestions that the diagnostic criteria for PHPT may be changed. The idea was presented that PHPT should be screened for using

- a corrected serum calcium concentration of >12 mg/dl (3 mmol/l)
- marked hypercalciuria – urinary calcium excretion >400 mg/day (10 mmol/day)
- markedly reduced cortical bone density (z-score for distal 1/3 of radius, < -2)³
- an unexplained cortical bone density
- age of <50 years

Figure 1. Criteria necessitating surgery in an otherwise asymptomatic patient with PHPT, NIH criteria (1991). The z-score reflects the standard deviation from the mean for a sex and age-matched reference population.
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PTH and may be diagnosed by a calcium level in the normal range (as this may be relatively high for the individual tested) with an elevated PTH. In theory, this identifies PHPT at a much earlier stage in the disease process and raises further controversies as to when to intervene.

Once the biochemical diagnosis is established, imaging can localise the parathyroid tissue, although an experienced endocrine surgeon may not require imaging routinely prior to surgery. 99mTc-Sestamibi scanning is the most widely used localisation technique – sensitivity and specificity, 90.7% and 98.8%, respectively, positive predictive value approximately 85% [28]. Occasionally it will be necessary to proceed to selective venous sampling but this is usually reserved for patients who have had previous surgery to the neck, in whom normal anatomical relationships may have been distorted. Other imaging techniques such as ultrasonography, CT and MRI can help to localise the tumour pre-operatively, as ectopic parathyroid tissue may lie anywhere in the midline, as far as the mediastinum.

Management of asymptomatic PHPT

General measures

Traditionally, this would include a reduced calcium intake (<1000 mg/day), good hydration and avoidance of provocative therapy, such as thiazide diuretics which may act as a potent source of PTH stimulation [29]. Renal stones are generally not the major problem in the elderly, but the risk of stones may be reduced by ensuring a good fluid intake and in some cases, a low oxalate diet (though compliance tends to be poor).

Surgical management

Surgery is the treatment of choice in symptomatic individuals and there are a wide variety of techniques now available (Table 1). In minimally symptomatic patients, the role of surgery is less clear.

Newer, less invasive surgical methods are showing promise – such as targeted parathyroidectomy (minimally invasive, under regional anaesthesia or endoscopic) [30–32]. These techniques rely upon intra-operative monitoring of PTH and accurate pre-operative localisation of the culprit adenoma; there is a significant learning curve involved in developing this surgical technique. A fall of 50–70% in the PTH values at 5–10 minutes predicts a successful surgical outcome (the half-life of serum PTH is 3–4 minutes). However, these techniques are not yet widely available and may not be cost-effective as they require a technician to be available in theatre. However, in skilled hands, minimally invasive surgery is a useful addition to the surgical repertoire.

In patients who have had prior surgery for PHPT, there is an increased risk of complications (especially recurrent laryngeal nerve palsy) and an increased failure rate (because of fibrosis and ectopic glands). Recurrent disease is usually due to either hyperplasia, locally recurrent disease or rarely parathyroid cancer (though up to 50% of cancers may initially present as apparently ‘benign’ disease [33]). An open procedure is generally recommended in such cases.

Operative mortality and morbidity

Data from the 1980s on older patients does show a significant rate of peri-operative morbidity and mortality (up to 10% for each category) [34, 35]. Chigot et al. [36] have published results showing mortality rates of 4% in patients over 75 years old, operated upon between 1978 and 1992, though results in the later years were much better. Current published results of surgery, however, are generally very good, with surgical cure rates around 95%, mortality under 1% and complications around 5% [37, 38]. The best results are seen with specialist endocrine surgeons carrying out large numbers of procedures annually [39].

One detailed study from the mid-1990s, looking specifically at the effect of surgery in the ‘old, old’ revealed a worrying level of adverse outcomes [40]. This group of 108 patients with a mean serum calcium of 2.99 mmol/l, consisted of 40% of patients with dementia and nearly 70% with cardiovascular disease. The 30-day mortality was 1.8%, morbidity 8.7%. Perhaps the most worrying figure was that by 4.2 years of follow-up, 60/108 patients had died. Whilst few of these deaths are likely to be causally related to the surgery, we are reminded that the population likely to be coming to surgery are frail and have significant co-morbidity.

Reducing mortality and cardiovascular risk

Only surgical intervention has been shown to reduce any cardiovascular risk associated with PHPT and high calcium levels, including LVH, dyslipidaemia and any proarrhythmic state [41–47]. However, one study specifically looking at the long-term cardiovascular outcomes of surgically treated as opposed to conservatively managed patients showed no significant benefit from surgery [48]. Additional mechanisms explaining the increased cardiovascular mortality might include vascular calcification, increased arterial stiffness, widening pulse pressure and systolic hypertension [49].
It is documented in epidemiological studies that patients with hypercalcaemia (cause unspecified) have an increased risk of death, thought to be related to cardiovascular disease [50, 51]. This risk apparently exists in PHPT and is reduced by surgery [52]. The increased mortality was mainly seen in younger patients (55–70 years) and it correlates with increasing severity of hypercalcaemia. Indeed, data from the Mayo clinic have shown that the mortality ratios in (younger) patients with mild PHPT are normal [53]. It is suggested that in older patients, more traditional cardiovascular risk factors make a greater contribution to the overall risk [54].

Osteoporosis

Several studies have shown that surgery can ameliorate the bone demineralisation seen in PHPT (producing approximately a 20% increase in bone mineral density), at least in the short to medium-term and generally in younger patients (typically 60–70 years old) [55, 56, 57–59]. However, surgery does not guarantee normalisation of bone demineralisation. A small study with a 17-year follow-up also suggests long-term correction of bone demineralisation is not assured [60]. Mole et al. [61] have shown relatively little overall difference in bone mineral density (BMD) between surgically and non-surgically treated patients at 4 years. Silverberg et al. [62] have shown neither changes in bone biochemistry nor BMD in 66 non-operated patients followed-up over 6 years.

Several cohort studies have pointed towards the fact that much of the bone demineralisation associated with PHPT is seen up to ten years prior to presentation [63]. and may not subsequently change greatly from this baseline, even with surgery [64–65]. It is difficult to be clear whether or not parathyroidectomy can prevent fractures, with current available evidence being contradictory [67–69]. It may be that there is a role for bone densitometry post-operatively to identify and monitor individuals with significant bone loss who may be considered for additional pharmacological bone protection therapy.

Quality of life

The data on quality of life and the more subtle neuropsychiatric symptoms that may be associated with PHPT are difficult to interpret, many of them being retrospective and prone to bias. Additionally, many of the functional tests employed are subject to a 'learning phenomenon' on repeated testing.

Some investigators have postulated that central neurotransmitters may be involved in the symptom complex [70], whereas others have attributed the symptoms to psychological factors [71]. One quality of life study, using the SF-36 questionnaire, compared surgery to medical management and showed improvement in the operative group, suggesting that the more subtle symptoms of hyperparathyroidism may be improved [72]. Several other trials, many without randomisation or controls, have tended to favour surgical intervention [73–78].

Joborn et al. [79] have shown that patients referred for surgery had higher self-reported psychiatric symptoms as compared to those not referred for surgery, who in turn had slightly higher scores than normocalcaemic controls. Perhaps unsurprisingly, the intervention group was shown to benefit from surgery.

These studies raise the important point that the symptoms of PHPT may be subtle and easily overlooked. They suggest that such symptoms may benefit from a surgical intervention, but they have not clearly shown this in the older patient specifically. Furthermore, co-morbidity in the older patient makes it difficult to be sure that surgery will help many of the more non-specific symptoms. Several studies have attempted to show this benefit in the elderly. Chen et al. [80] have shown that patients older than 70 noted improvements in quality of life after surgery and would be prepared to have a further operation if needed; they also showed equivalent outcomes in terms of morbidity, mortality (0%) and length of stay as compared to younger patients. Uden et al. [81], deeming the elderly to be over 60 years old, showed equal benefit in a variety of neuromuscular symptoms from surgery in this group as compared to younger patients.

Neuromuscular function has also been looked at and again, the studies are conflicting. Ljunghall et al. [82] have shown no objective evidence of neuromuscular involvement, using nerve conduction studies. Other investigators have looked at functional assessments of strength and neuromuscular function, without any clear evidence that surgery can help [83–86].

Summary – surgery

Surgical techniques and peri-operative management have advanced considerably since the 1980s, but the frailty and co-morbidity which characterises some older patients remains a significant barrier to successful recovery, though the more widespread introduction of minimally invasive techniques holds promise for the future. Furthermore, bone protection is not always guaranteed. Data on neuropsychiatric outcomes are difficult to interpret and the data on mortality may not be so pertinent in the older patient, in whom traditional risk factors are more important and alternative risk reduction strategies may be employed.

In summary, it is apparent to practising geriatricians that surgery is not an option for all and there is a need for alternative strategies.

Ethanol sclerotherapy

There are several studies and case reports exploring this option in the literature [87]. Karstrup et al. [88] reviewed a group of 32 patients treated with serial, ultrasonically guided ethanol injections. Over a median follow-up period of 45 months, complete or partial responses were
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seen in around 60% of a heterogeneous group. There is no data on long-term bone protection. They acknowledge that the treatment cannot be regarded as definitive, but it does seem to have a role in the medically unifit as well as those reluctant to undergo surgery. It should be noted that this technique can be painful and makes subsequent surgery nearly impossible because of fibrosis. Case reports suggest that radio-frequency ablation may also be an effective modality in selected patients [89].

Medical management

There is an accumulating pool of evidence promoting medical therapy for PHPT, which traditionally, has not been viewed as a satisfactory long-term option.

Acute hypercalcaemia

In the acute setting, severe hypercalcaemia (corrected serum calcium ≥3 mmol/l) can be safely treated with standard therapies such as rehydration, frusemide and intravenous bisphosphonates [90–92, 93, 94]. These measures should buy time during which the patient can be stabilised and the options considered. Anecdotally and intuitively, it appears that the time to the rebound hypercalcaemia seen after the use of bisphosphonates may be a guide to the severity of the hyperparathyroidism. Other predictors of the severity of the disorder include the serum calcium and the PTH levels [95–97].

Long-term medical therapies

Parfitt and colleagues [98] argued strongly for medical treatment ahead of surgery, at least in women. They advocated the use of oestrogens or bisphosphonates in those women unable to take HRT. In a review of older patients with PHPT, Pearson [99] also suggested a conservative (non-operative) approach had outcomes similar to operative intervention. Several other studies have also shown no major detrimental outcomes in asymptomatic PHPT, though outcomes varied between studies [100–105]. However, medical therapy cannot be regarded as definitive treatment for PHPT.

In addition to symptom control, for which there is relatively little evidence to support medical therapy alone, the main area of concern, particularly with regards to the older patient, is that of osteoporosis and prevention of bone injury. Plain X-rays do not assess osteoporosis adequately and consequently, one has to rely on bone densitometry. The NIH guidelines (1990) suggest that BMD is assessed every 6–12 months, though few centres in the UK would have such ready access to densitometry and this may well be impractical. Furthermore, the co-efficient of variation of densitometry may be higher than the expected changes in bone density over such a relatively short period. The recommended NIH lower limit for surgical intervention in otherwise asymptomatic individuals with PHPT, is a z-score of <−2 at the radius. Whether the z- or T-score is the appropriate parameter to use in the elderly, is still under debate. Indeed, BMD scores alone are not the sole predictors of future fracture in osteopaenic older individuals, in whom previous fracture, low body mass index, and falls amongst others should be considered in assessing overall risk for an individual. Westerdahl et al. [106] suggested that elevated collagen telopeptide is a marker of future fracture, even over BMD. More recent work from the same group has identified 25-hydroxyvitamin D3 and PTH levels as predictors of fracture [107]. Nakaoka and colleagues [108] studied 44 patients, using pre- and post-operative bone densitometry (at one year) and showed that alkaline phosphatase and the severity of cortical bone mass reduction are clinically useful for predicting the changes in lumbar BMD after surgery. Such indices are useful for identifying high-risk patients and targeting treatment accordingly.

Bisphosphonates and calcitonin

Whilst bisphosphonates have a useful role in the acute control of hypercalcaemia, results have generally been mixed in the long-term, with rebound hypercalcaemia as the main problem [109, 110]. However, small studies have shown successful control of hypercalcaemia for up to 3 months [111]. Two studies have demonstrated that alendronate can safely improve BMD compared to placebo at up to 24 months [112, 113]. The second of these two studies, by Rossini et al. [113] was particularly useful, as it looked at post-menopausal women aged 67–81 years. They showed a transient fall in serum calcium, accompanied by a rise in PTH and after 2 years, statistically significant increases in BMD in the intervention group. In the only published randomised control trial comparing bisphosphonates to parathyroidectomy, Horiguchi et al. [114] have shown that etidronate improves lumbar spine BMD by 10% over 1 year compared to a 20% increase with surgery (but no difference for total BMD). The study was relatively small (22 patients) and did not show any difference in fracture rates, but remains interesting none the less.

Several small trials have shown some evidence that salmon calcitonin is useful in short-term control of hypercalcaemia [115–117]. Bisphosphonates and calcitonin reduce bone resorption and are established as long-term therapy for primary osteoporosis [118]; it would seem reasonable to consider them for use in those patients with proven osteoporosis and asymptomatic PHPT; in the meantime further studies are awaited.

Hormone replacement therapy

The general preponderance of women over men (3:1) in the hyperparathyroid population lends itself to the use of HRT. Traditionally, HRT has been seen as an effective and safe treatment for osteoporosis in women. However,
several recent trials using HRT in the prevention of osteoporosis and heart disease have raised concerns [119, 120].

HRT – the evidence for use in hyperparathyroidism

Marcus et al. [121, 122, 123] have shown that high-dose HRT may modulate hypercalcaemia and the effect of PTH on the bones, but not the secretion of PTH, at least in the short-term. Similar results have been demonstrated by Selby and Peacock [124].

McDermott et al. [125] reported a cross sectional study in which 59 women with mild asymptomatic PHPT were contrasted between those on HRT and those not taking HRT. They found that the HRT treated group \( (n = 16) \) had higher BMD than those not taking HRT, both in the PHPT group and the control group.

Diamond et al. [126] reported a study in which 15 frail, elderly ladies with osteoporosis and PHPT were divided into two groups, those treated with HRT \( (n = 5) \) and a surgically treated group \( (n = 10) \).Whilst the surgical treatment was more successful in reducing serum PTH levels, there were no significant differences in BMD between the two arms (although BMD was non-significantly increased in both groups). Orr-Walker et al. [127] carried out a placebo controlled trial using HRT to treat PHPT associated osteopaenia in 11 women \( (\text{versus} \ 12 \text{controls}) \). They showed a 7–8% increase in bone density in the intervention group as well as a slight fall in PTH levels, with no significant difference in fracture rates between the two groups. Drawing on these and other studies, Parttiff makes a strong case for the use of HRT as first line therapy in asymptomatic women [128].

Safety profile of HRT

Recently, concerns regarding the safety profile of combined HRT have been raised. Traditionally, it has been thought that HRT conferred a degree of cardiovascular protection, through an observed reduction in LDL-cholesterol and an increase in HDL-cholesterol. The Heart and Estrogen/Progesterin Replacement Study (HERS) [77] and the recently halted Women’s Health Initiative (WHI) [78] studies have both shown an increased risk of adverse outcomes [coronary heart disease (CHD), breast cancer, stroke and pulmonary embolus (PE)] in primary prevention. However, it is important to note that the absolute adverse risks incurred were still very small. Over 1 year, 10 000 women taking oestrogen plus progesterin compared with placebo (WHI study) might experience 7 more CHD events, 8 more strokes, 8 more PEs and 8 more invasive breast cancers. Moreover, there are also benefits – 6 fewer colorectal cancers, and 5 fewer hip fractures.

It should be recognised however, that these were trials of primary or secondary prevention of ischaemic heart disease, in a relatively young (50–79 years) cohort of women who were otherwise healthy. This is quite a different cohort to the patients that we are targeting in this article.

In our opinion, women in whom an increased risk of fracture has been demonstrated, the benefits of HRT (over 5 years or less) may well outweigh the potential risks. The evidence for bisphosphonates is less strong than that for HRT in PHPT; tolerability is also an issue with bisphosphonates. It should be emphasised that the absolute risk of any adverse effects from HRT remains small, but it would seem sensible to exercise caution when prescribing HRT for women with a heightened risk of breast cancer or cardiovascular disease – based on risk factor analysis and/or a family history. Furthermore, there is a significant mortality and morbidity associated with osteoporotic fractures, especially fractured neck of femur (20% mortality, 50% lose independence at 1 year).

Interestingly, in the HERS study, subgroup analysis of those women taking a statin as well as HRT, showed a marked protective effect with respect to cardiovascular disease and venous thromboembolism [129]. This negated any initial increased risk seen in those not taking a statin. The Estrogen Replacement and Atherosclerosis trial [130] has shown that some women may benefit more from HRT than others in reducing cardiovascular risk. Specifically, variance in the oestrogen-receptor \( \alpha \)-gene predicted an increase in HDL-cholesterol with HRT.

If there is still evidence of osteoporosis after 5 years of HRT, other modalities, such as bisphosphonates or raloxifene may be considered (see below).

Raloxifene

Raloxifene is a relatively new agent, originally designed for use in breast cancer, which has a partial agonist action on the oestrogen receptor. It has been shown to be beneficial in the prevention of osteoporosis and may have benefits on the cardiac risk profile, as well as reducing the incidence of newly diagnosed breast cancer (Raloxifene Use for the Heart – trial in progress). Initial results from the Multiple Outcomes of Raloxifene Evaluation study (MORE), looking at the role of raloxifene in prevention of IHD are encouraging [131]. One small study (three patients) has looked to see if osteoporosis due to hyperparathyroidism can be prevented using raloxifene, in women not undergoing surgery or declining HRT, with encouraging short-term results [132]. They showed a small but significant increase in BMD at 1 year. Clearly, more work on the role of raloxifene in PHPT is required, but given the controversy surrounding HRT, it appears an attractive option.
Other medical therapies

**Vitamin D**

Vitamin D insufficiency (as opposed to deficiency*) is common and perhaps under-recognised in PHPT. Such patients have a higher than expected PTH concentration and worse bone disease [133]. The addition of vitamin D in patients with mild PHPT and low vitamin D levels has been studied. Oral doses between 1 and 2 µg of 1α-(OH)-vitamin D3 daily have been used over 6–12 months, without any adverse effect, however, we would suggest smaller doses should be considered in the elderly [134]. Other authors have safely used oral calciferol 1000 IU per day in an older patient [135]. Vitamin D has a beneficial effect upon the diastolic blood pressure, reducing it by approximately 7 mmHg [136, 137]. Additionally, vitamin D has a beneficial effect upon stretch receptors in muscles and may reduce falls in certain subjects [138]. Supplementation with vitamin D in PHPT, particularly in the elderly in whom vitamin D deficiency is common, may have significant benefits. However, supplementation does risk slight worsening hypercalcaemia in the short-term and requires close monitoring.

PTH inhibitors (somatostatin, propranolol and cimebidine) have thus far been disappointing, with either negative or conflicting outcomes [139, 140]. Calcimimetic agents increase the sensitivity of G-protein linked calcium receptors on parathyroid cells, thus reducing PTH secretion and lowering serum calcium levels. Silverberg et al. [141] studied a calcimimetic agent ‘R 568’ in patients not qualifying for or declining surgery and showed good initial results, but there are not yet published outcome data on as bone and renal complications long term. Further trials are underway. AMG 073 is another calcimimetic agent, which has been shown to reduce PTH and calcium levels in PHPT [142]. At 24 weeks, there was no significant change in BMD and further data are awaited.

**A global approach**

Of essential importance, is the practice of adopting a global approach to the treatment of the older patient. Hyperparathyroidism is about more than just serum calcium levels and bone damage. Falls intervention schemes, including medication reviews, physiotherapy, occupational therapy and hip protectors all have an important role to play. The recently published joint American/European falls guidelines provide a synopsis of how falls may be reduced [143].

In addition to balancing the risks and benefits of HRT as regards cardiovascular risk, we need to be aware of the increased cardiovascular risk seen in patients with PHPT and address cardiovascular risk factors on their own merit.

The traditionally recognised neuropsychiatric manifestations of PHPT have been shown to respond to surgical therapy, but thus far there is no evidence that any of the non-operative approaches can help in this respect specifically. However, dementia (which may be a feature of PHPT) is very common in the elderly and it would be difficult to justify surgery on every demented patient with hyperparathyroidism. It may be reasonable to subject such individuals to a trial of bisphosphonates to determine if there is any reversible component to their mental state relating to hypercalcaemia (which may be mild [144]) prior to committing them to surgery.

**Conclusion**

The geriatrician with his or her multidisciplinary team and expanding therapeutic options is ideally placed to take a central role in the management of the older patient with hyperparathyroidism. A wide variety of medical therapies are available which should reduce the cardiovascular and fracture risks associated with hyperparathyroidism and may complement or even obviate the need for surgery. There is some hesitancy, even amongst surgeons, that surgery is always the best choice for the older patient [145]. It could well be that in the first instance, the older patient with hyperparathyroidism should be referred to a geriatrician rather than surgeon.

**Key points**

- PHPT is common in the older patient and may have few overt symptoms.
- The prime concern in minimally symptomatic PHPT is prevention of osteopaenia, but additionally there is an associated metabolic syndrome, both of which are amenable to medical therapy.
- Surgery alone may not be sufficient treatment to prevent bone complications.
- Proven effective medical therapies include bisphosphonates and HRT; of probable benefit – raloxifene and for the future calcimimetics.
- It is important to view the patient holistically – addressing falls, co-morbidity, poly-pharmacy and vascular risk factors.

**References**

The very long list of references supporting this review has meant that only the most important are listed here and are represented by **bold type** throughout the text. The full list of references is available on our website: [http://ageing.oupjournals.org](http://ageing.oupjournals.org)


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