Long-term complications in patients with chronic hypoparathyroidism: a cross-sectional study

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Abstract

Objective: Chronic hypoparathyroidism and its treatment may lead to symptoms and complications affecting quality of life. We determined complications in chronic hypoparathyroid patients.

Design: Retrospective cross-sectional study of patients with chronic hypoparathyroidism treated with active vitamin D supplements in a tertiary care centre during the year 2015. Primary outcome parameters were history of kidney stones and seizures and presence of renal and cerebral calcifications on imaging. Secondary outcome parameters were current symptoms of paraesthesia/cramps, hospitalization due to hyper/hypocalcaemia and hypercalciuria.

Subjects: One hundred and seventy patients were included – 143 (84%) with post-surgical hypoparathyroidism (PSHP), 16 (9%) with non-surgical hypoparathyroidism (NSHP) and 11 (7%) with pseudo-hypoparathyroidism (PHP).

Results: History of kidney stones and seizures was present in 15 and 9% of patients, respectively. Renal and cerebral imaging was performed in 51 and 26% of the patients, with 22 and 25% of these patients having renal and cerebral calcifications respectively. Both history of seizures and cerebral calcifications were significantly more in NSHP and PHP than in PSHP patients. No association was observed between seizures and cerebral calcifications. Cramps/paraesthesia were present in 16%, and hospitalization related to hypocalcaemia was reported in 5% of the patients. Calciuria was screened in 47% at the time of consultation, and in 76% of the patients during the past 5 years. In 36% of these patients, calciuria was increased.

Conclusions: Patients with chronic hypoparathyroidism frequently develop ectopic calcifications. Non-surgical patients suffer more from seizures and cerebral calcifications than patients that developed hypoparathyroidism post surgery. There is a need for increased screening of long-term complications, according to the guidelines.

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Introduction

Hypoparathyroidism (HP) is an uncommon endocrinological condition. It is characterized by absent or inappropriately low serum levels of parathyroid hormone (PTH) resulting in hypocalcaemia and hyperphosphataemia (1, 2, 3). Most often, it is an acquired condition after neck surgery. Rare causes are autoimmune conditions, severe magnesium deficiency, infiltrative diseases and genetic abnormalities (4). A distinct form is called pseudo-hypoparathyroidism (PHP) in which there is an end-organ resistance to PTH resulting

in high serum levels of PTH, but low levels of serum calcium (1, 2). In Denmark, post-surgical hypoparathyroidism (PSHP) has a prevalence of 22/100 000 person-years, while non-surgical hypoparathyroidism (NSHP) and PHP forms are much more rare with a prevalence of 2.3/100 000 person-years and 1.1/100 000 person-years respectively (5, 6, 7). In the United States the estimated prevalence of all-cause HP is 37/100 000 person-years (8). The prevalence in Belgium is not known.

HP is one of the few endocrinopathies in which currently the hormonal deficiency is not treated by substitution of the hormone itself. Conventional treatment includes calcium supplements and active vitamin D analogues (1, 2). Additional therapy may consist of non-active vitamin D supplements and anticalciuretic drugs. Despite its different pathogenesis, the management of PHP patients is largely the same as that of patients with HP. In the meantime, recombinant human PTH 1–84 (rhPTH) has been FDA and EMA approved for use in patients with HP that are not well controlled by conventional therapy (9, 10). Goals of HP treatment consist of controlling the symptoms and minimizing short-term and long-term complications (1). Symptoms are generally those of hypocalcaemia that can, depending on the severity and the acuteness of onset, result in paraesthesia, spasms, tetany, cardiac arrhythmias and/or seizures (2, 4). Well-known complications of chronic HP and its treatment are renal insufficiency, ectopic calcifications in the kidneys and the brain, impaired quality of life and higher risk of seizures (3, 4). Recent studies show a higher mortality in patients with HP (11, 12). Since it is a rare disease, studies describing the features and complications of the disease generally suffer from small numbers of patients. Therefore, the recently published management guidelines are mainly based on clinical expertise (9, 13, 14).

Our aim was to study complications in a recent cohort of patients with chronic HP in follow-up in our institution and compare these results with the available data from literature and recent European and US guidelines for the management of patients with chronic HP.

Subjects and methods

Patient identification

Patients in follow-up for HP who visited the adult outpatient clinic of endocrinology in the University Hospitals Leuven, Belgium, a tertiary care centre, between 1 January 2015 and 31 December 2015 were studied. Hypoparathyroidism was defined as having hypocalcaemia with inappropriately low/normal levels of PTH at the time of diagnosis, necessitating medical treatment with an active vitamin D analogue. PHP was defined as having hypocalcaemia with elevated PTH levels at time of diagnosis. Patients with other causes of elevated serum PTH such as secondary hyperparathyroidism due to vitamin D deficiency were excluded (1). Patients with HP are evaluated at least once yearly in our centre, which is also a condition for reimbursement of the active vitamin D analogue in

Belgium. Cases were identified using an electronic search query in the clinical file system of the institution using the following keywords: 'hypoparathyroidism', 'pseudo-hypoparathyroidism', '1 alpha leo', 'alfacalcidol', 'rocaltrol' and 'calcitriol', resulting in 319 unique patients. After detailed study of the individual clinical files, 83 patients did not meet the criteria for hypoparathyroidism or PHP and were excluded (for example 'hypoparathyroidism' was mentioned in a differential diagnostic list of hypocalcaemia or a patient was treated with a vitamin D analogue for another disease). Other exclusion criteria were duration of disease less than 1 year (52 patients) and follow-up less than 1 year in our institution (14 patients). Eventually, the studied cohort consisted of 159 patients with 'classical' chronic hypoparathyroidism (post-surgical and non-surgical) and 11 patients with PHP (Fig. 1). The study was approved by the Ethical Committee of the University Hospitals Leuven. Consent has been obtained from each patient after full explanation of the purpose and nature of all procedures used.

Data collection

Patients' characteristics such as age, gender, disease aetiology, disease duration and hypoparathyroidism-related medical treatment (calcium supplements, active vitamin D analogues, vitamin D₃, thiazide diuretics) were retrieved from the clinical files. Disease duration in PHP patients was similar to the patients' age. In NSHP patients, disease duration was also similar to the patients' age in case of a genetic cause of the disease. For autoimmune and idiopathic causes, disease duration was calculated from time of HP diagnosis. Medical history was reviewed in detail for the occurrence of kidney stones, cataracts, seizures and hospitalizations due to hypo- or hypercalcaemia after the diagnosis of HP. The following biochemical parameters were registered: serum creatinine, eGFR and 24-h renal calcium excretion on the day of consultation. The CKD-EPI formula was used to calculate eGFR (15). When a 24-h urine collection was not available on the day of the consultation, the most recent 24-h calciuria result was registered provided that this result was less than 5 years old and post incidence date of the HP diagnosis. Furthermore, any imaging of the kidneys (ultrasound/CT/MRI) and brain (CT/MRI) was registered and screened for the presence of calcifications (nephrocalcinosis, renal stones, intracerebral calcifications), provided that these results were less than 10 years old and post incidence. Finally, data on symptoms of paraesthesia and/or cramps during the month prior to the consultation were registered.

Figure 1

Identification of patients with chronic hypoparathyroidism.

Statistical analysis

The Shapiro–Wilk test was used to verify the assumption of symmetrical distribution of all continuous variables. Symmetrical distributed variables and descriptive data are presented as mean $\pm$ standard deviation (s.d.), whereas asymmetric variables are presented as median (minimum–maximum). For the analysis of symmetrical distributed variables unpaired *t*-tests and one-way ANOVA tests with Bonferroni's multiple test comparison were performed to detect the differences between groups. All non-symmetrical distributed variables were analysed by Mann–Whitney tests and Kruskal–Wallis tests with Dunn's multiple comparisons tests. For continuous categorical data, presented as %(n), the Pearson's χ^2 -test was used. In case of patient numbers ≤ 5 the χ^2 -test with Yates's correction for continuity was used. In case of statistically significant differences between the groups, the Tukey's range test was used for continuous data and Pearson's χ^2 -test for categorical data. A *P* value of <0.05 was considered as statistically significant.

Results

Patient characteristics

Between 1 January 2015 and 31 December 2015, 170 patients with chronic HP or PHP who met the inclusion

criteria were seen at the adult outpatient endocrinology clinic in the University Hospitals Leuven. The patient characteristics are summarized in Table 1. The majority of patients were females. Average age was 58 years. The duration of disease varied from 1 year to 68 years, being on average 17 years. PSHP was the aetiology in the majority of the cases. In most cases, a total thyroidectomy (with or without lymph node dissection) was performed. None of the parathyroidectomies was performed due to hyperparathyroidism in the context of end-stage renal disease. Sixteen patients had NSHP, with the following aetiologies: autoimmune hypoparathyroidism in six patients (of which two patients with autoimmune polyendocrine syndrome type I (APS-1)), Di George syndrome in two patients, an activating calcium sensor receptor (CaSR) mutation in two patients, CHARGE (Coloboma of the eye, central nervous system anomalies; heart defects; atresia of the choanae; retardation of growth and/or development; genital and/or urinary defects; ear anomalies and/or deafness) syndrome in one patient and HDR (hypoparathyroidism-deafness-renal disease) syndrome in one patient. In the remaining four patients, the cause of the hypoparathyroidism was not known, and they were classified as having idiopathic HP. Eleven patients were identified as having PHP. Five patients had PHP type Ia with Albright's hereditary osteodystrophy, six patients had PHP type Ib. Genetic confirmation of the disease was available in all PHP and NSHP patients, with the exception

Table 1 Patient characteristics of total cohort. Data are presented as mean $\pm$ s.d. or % (n) for quantitative and categorical data respectively.

	n = 170
Male sex	39.4 (67)
Age (years)	58.11 $\pm$ 15.65
Duration of disease (years)	16.58 $\pm$ 14.65
Aetiology	
Post-surgical hypoparathyroidism	84.1 (143)
Total thyroidectomy	65.0 (93)
Total thyroidectomy + neck dissection	13.3 (19)
Hemithyroidectomy	8.4 (12)
Parathyroidectomy (partial/total)	7.7 (11)
Other types of neck surgery	5.6 (8)
Non-surgical hypoparathyroidism	9.4 (16)
Pseudo-hypoparathyroidism	6.5 (11)
Medical treatment	
Alfacalcidol	95.9 (163)
Mean dose (μ g)	1.31 $\pm$ 0.74
Vitamin D ₃ ($\pm$ calcium supplement)	35.3 (60)
Mean dose (IU)	1067 $\pm$ 692
Calcium supplement ($\pm$ vitamin D ₃)	78.2 (133)
Mean dose (mg)	1035 $\pm$ 507
Vitamin D ₃ + calcium supplement	31.8 (35)
Anticalciuretic	14.1 (24)
eGFR (mL/min/1.73 m ²)	82.9 (141)
Mean	71.94 $\pm$ 20.85

eGFR, estimated glomerular filtration rate.

of the four patients with autoimmune HP without APS-1 and in the four patients with idiopathic HP.

All patients were taking active vitamin D analogues as this was an inclusion criterion. The majority of patients were treated with 1- α -hydroxyvitamin D₃ (alfacalcidol). Only seven patients were taking 1,25- α -hydroxyvitamin D₃ (Rocaltrol). One-third of the patients were also taking vitamin D₃ supplements (cholecalciferol). Almost 80% of patients were taking calcium supplements. Fourteen percent of patients were receiving an anticalciuretic drug (thiazide and/or amiloride).

Long-term complications

As shown in Table 2, 27 out of 170 patients had experienced paraesthesia and/or cramps during the past month. Hospitalization due to severe hypocalcaemia had been necessary in eight cases during the total course of the disease. None of the patients was hospitalized due to a hypercalcaemic event. Cataracts were present in 16 and absent in 12 patients. In the remaining 142 patients the presence or absence of cataract was not mentioned in the clinical file. With regard to renal complications, 14.7% had been diagnosed with kidney stones. For 82.9% of patients

kidney function was measured at time of consultation with a mean eGFR (CKD-EPI) of 71.94 $\pm$ 20.85 mL/min/1.73 m². In the last 5 years, a 24-h urinary calcium excretion was determined in 76% of the patients, of which 46.5% at the time of last consultation. With the upper limit of calciuria for females being 6.5 mmol/24h and for males being 7.5 mmol/24h, 47 out of 129 patients, including patients taking anticalciuretics, exceeded the gender-specific upper limit. Exclusion of patients on thiazide and/or amiloride diuretics resulted in 41 out of 109 patients exceeding the upper limit of 24-h renal calcium excretion. In 51.2% of patients at least one renal imaging in the last 10 years of the disease was performed, of which 21.8% showed kidney stones and/or nephrocalcinosis. Regarding cerebral imaging, which was performed at least once in the last 10 years of the disease in 25.9% of patients, calcifications were observed in 25% of the patients. Finally, 8.8% of patients had a medical history of seizures.

Complications according to disease aetiology

Patients were divided by HP aetiology into three groups: PSHP, NSHP and PHP (Table 3) for comparison of patient characteristics, treatment modality and complications of the disease.

There was no difference of gender distribution between the different groups, but PSHP patients were older compared to PHP patients. The disease duration was significantly longer in the PHP group compared to the PSHP group. The median dose of active vitamin D analogues was similar. More PHP patients took non-active vitamin D₃ supplements compared to the other two groups, but the amount of substitution did not differ. The proportion of patients taking calcium supplementation did not differ between the different groups, but the amount of substitution was higher in the PSHP group compared to the NSHP group. Recent complaints of paraesthesia and/or cramps were similar, and there was no difference in hospitalization due to hypocalcaemia.

Regarding renal complications, there was no difference in history of kidney stones. The average kidney function, expressed as eGFR, was lower in PSHP patients as compared to NSHP and PHP patients. Median renal calcium excretion was significantly lower in PHP compared to PSHP patients. No difference was observed regarding the performance of renal imaging or the presence of renal calcifications. Cerebral imaging was more often performed in NSHP and PHP patients. Calcifications were visualized in 75 and 60% of patients with NSHP and patients with PHP with cerebral imaging respectively, in contrast with

Table 2 Complications in the total cohort. Data are presented as mean $\pm$ S.D. or % (n) for quantitative and categorical data, respectively.

	n = 170
Paraesthesia and/or cramps	15.9 (27)
Urinary calcium excretion	75.9 (129)
Mean renal calcium excretion (mmol/24 h)	6.20 $\pm$ 3.79
Exceeding upper limit	36.4 (47)
History of seizures	8.8 (15)
History of kidney stones	14.7 (25)
Hospitalization due to hypocalcaemia	4.7 (8)
Renal imaging	51.2 (87)
Nephrocalcinosis and/or stones	21.8 (19)
Cerebral imaging	25.9 (44)
Intracerebral calcifications	25.0 (11)

calcifications being present in only 6.5% of imaging in PSHP patients. History of seizures was present in 45.5% of patients with PHP and in 25% of patients with NSHP, which statistically differs from the 4.2% in patients with PSHP ($P < 0.001$ and $P < 0.01$).

Seizures and cerebral calcifications

Patients with a history of seizures were younger and their disease duration was longer compared to patients without seizures, and more cerebral imaging was performed in this group (Table 4). However, there was no difference in presence of intracerebral calcifications on imaging.

Cerebral imaging was performed in 44 patients of the total cohort, of which 11 patients were diagnosed with intracerebral calcifications (Table 5). Patients with intracerebral calcifications were younger and had a longer disease duration than patients without intracerebral calcifications. There was no difference in seizures in their past medical history.

Discussion

This cross-sectional study analyses complications in a cohort of patients with chronic hypoparathyroidism in follow-up at a tertiary endocrine outpatient clinic in Belgium, with particular focus on the role of disease aetiology, risk of renal and cerebral calcifications and risk of seizures. The majority of the patients was female, consistent with other cohorts described in literature (16, 17). A substantial proportion of patients had already long-lasting disease. Neck surgery was the aetiology in more than 80% of patients, which is in agreement with other studies (1, 2, 4).

A substantial part experienced symptoms of the disease. Complaints of paraesthesia and/or cramps in the past month were present in 3 out of 20 cases. Well-being was not being assessed in this study, but previous data showed failure to restore well-being in patients with HP with standard therapy of calcium and vitamin D (18, 19). Therapy with rhPTH 1–84 may help to improve the quality of life in these patients (20). Hospitalization due to hypocalcaemia was rather rare in this study, having occurred in 5% of the cohort, with 75% of the hospitalizations occurring at the time of HP diagnosis and not during follow-up. In 84% of patients the presence or absence of cataracts could not be retrieved from the patient's file. There is certainly a need for increased screening for this complication in chronic HP patients.

In our cohort in 21.8% of the available renal imaging kidney stones and/or renal calcifications were present. Mitchell *et al.* described renal calcifications being present in 31% of patients with hypoparathyroidism (16). Of note, mean daily dose of calcium supplements in the latter study was almost two times higher than that in our study (2048 mg vs 1035 mg), which could explain the difference in the prevalence of renal calcification. Postoperative patients are at increased risk (up to five times more) of developing kidney stones and renal calcifications compared to healthy individuals (5, 16).

Results of a 24-h urine collection of the last 5 years were present in three out of four patients with less than half of these collections at time of the consultation. Nevertheless, one out of three patients exceeded the gender-specific upper limit for mean renal calcium excretion, indicating underuse of calciuria screening in the chronic follow-up of HP patients. Hence, the reported frequency of calcifications and hypercalciuria is a minimum estimate. Lopes *et al.* found no correlation between urinary levels of calcium and presence of calcifications, but 24-h urinary calcium excretion was significantly higher in patients with kidney calcifications compared to patients without calcifications (2, 17).

Cerebral imaging was available in one out of four HP patients, with calcifications observed in one out of four patients. In the study of Mitchell *et al.* intracerebral calcifications were present in one out of two cases. (16) A possible explanation is the difference in aetiology of the HP, with 84.1% being post-surgical in our study compared to only 66% in the study of Mitchell *et al.* In this study history of seizures was present in 8.8% of patients. This result is consistent with the 8% incidence of seizures in the cohort of Mitchell *et al.* (16).

Clinical Study	K David and others	Complications of hypoparathyroidism	180:1	76
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Table 3 Patient characteristics and complications according to disease aetiology. Data are presented as % (n) for categorical data. Quantitative data are presented as mean $\pm$ s.d. or median (minimum–maximum) for symmetrical and non-symmetrical distributed variables respectively.

	Hypoparathyroidism			P value
	Post-surgical (n = 143)	Non-surgical (n = 16)	Pseudo (n = 11)	
Male sex	36.4 (52)	56.3 (9)	54.5 (6)	0.3308
Age (years)	60.7 (24.8–88.5)	52.4 (19.9–83.3)	42.7 (23.3–68.2) ^c	<0.001
Duration of disease (years)	9.4 (1.0–57.5)	20.1 (1.6–56.9)	42.7 (23.3–68.2) ^c	<0.001
Medical treatment				
Alfacalcidol	95.8 (137)	100 (16)	90.9 (10)	0.9777
Median dose (μ g)	1.3 (0.3–6.0)	1.3 (0.5–3.3)	1.0 (0.5–2.5)	0.5848
Vitamin D ₃ ($\pm$ calcium suppl.)	33.6 (48)	31.3 (5) ^b	63.6 (7) ^c	<0.001
Median dose (IU)	833 (400–3571)	833 (800–1760)	833 (833–1786)	0.7075
Calcium suppl. ($\pm$ vitamin D ₃)	79.7 (114)	81.3 (13)	54.5 (6)	0.2900
Median dose (mg)	1000 (500–3000) ^a	1000 (500–3000)	1000 (500–2000)	<0.05
Vitamin D ₃ + calcium suppl.	32.2 (46)	31.3 (5)	27.3 (3)	0.9999
Anticalciuretic	14.0 (20)	18.8 (3)	9.1 (1)	0.9841
Paraesthesia and/or cramps	16.8 (24)	25 (4)	9.1 (1)	0.7411
Hospitalisation due to hypocalcaemia	3.5 (5)	6.3 (1)	18.2 (2)	0.3342
History of seizures	4.2 (6) ^a	25 (4)	45.5 (5) ^c	<0.001
History of kidney stones	15.4 (22)	12.5 (2)	9.1 (1)	0.9889
eGFR (mL/min/1.73 m ²)	83.9 (120)	87.5 (14)	63.6 (7)	0.4155
Mean	69.9 $\pm$ 19.79	82.2 $\pm$ 26.93	85.9 $\pm$ 10.86	<0.05
Urine analysis	75.5 (108)	75.0 (12)	81.8 (9)	0.9942
Median renal calcium excretion (mmol/24 h)	6.2 (0.7–17.6)	3.2 (0.9–14.6)	2.4 (0.4–5.4) ^c	<0.01
Imaging				
Renal	47.6 (68)	75.0 (12)	63.6 (7)	0.0793
Calcinosis and/or stones	27.9 (19)	6.3 (1)	14.3 (1)	0.5312
Cerebral	21.7 (31)	50.0 (8)	45.5 (5)	<0.05
Calcifications	6.5 (2) ^a	75 (6)	60 (3) ^c	<0.001

Statistical significant differences ($P < 0.05$) between two different groups separately are illustrated by ^{a,b} and ^c.

^aPSHP vs NSHP; ^bNSHP vs PHP; ^cPSHP vs PHP.

eGFR, estimated glomerular filtration rate.

According to the HP aetiology, several differences were observed. Not unsurprisingly, PHP patients were younger than PSHP patients and had a longer disease duration. So post-surgical patients are generally older at the time of diagnosis, which is consistent with the fact that PSHP is an acquired condition, while PHP is a congenital disease.

The majority of the patients took alfacalcidol (21, 22, 23). The median dose of active vitamin D analogues did not differ between the three groups. PHP patients did however more often combine with non-active vitamin D₃ than the other two groups. One might hypothesize that this reflects the prescriber's reasoning that due to high levels of PTH in patients with PHP, there is a higher potential for conversion into active vitamin D. Streeten *et al.* found less morbidity from hypocalcaemia treated with vitamin D₂ than with calcitriol (24). Combination treatment with rhPTH 1–84 allows for dose reduction of calcium and active vitamin D analogue while maintaining a stable serum calcium level (25, 26, 27).

There was no difference in history of kidney stones or nephrocalcinosis at renal imaging according to HP disease aetiology. There was also no difference in eGFR between the groups, although NSHP patients and PHP patients had the tendency to have higher eGFR than PSHP patients. This is probably due to the aforementioned differences in age between the three groups. It is known that patients with NSHP and PSHP have an increased risk of developing renal insufficiency, while risk of renal disorders in PHP patients is not increased (5, 6, 7). PHP patients also had significant less calciuria than PSHP patients, which is an expected finding as sensitivity to PTH in the tubular and collecting duct of the nephron is intact in PHP (7, 28).

Cerebral imaging was performed in half of the patients with NSHP and PHP. A probable explanation for this finding is the fact that these patients also had a higher incidence of seizures, with cerebral imaging being standard of care in the work-up. The proportion of brain calcifications was also higher in these two groups compared with PSHP patients.

Table 4 Seizures. Data are presented as % (n) for categorical data. Quantitative data are presented as mean $\pm$ s.d. or median (minimum–maximum) for symmetrical and non-symmetrical distributed variables respectively.

	History of seizures		P value
	Present (n = 15)	Absent (n = 155)	
Male sex	46.7 (7)	39.7 (60)	0.5471
Age (years)	49.29 $\pm$ 18.49	58.96 $\pm$ 15.08	<0.05
Duration of disease (years)	23.67 (2.08–54.42)	10.08 (1.00–68.17)	<0.01
Cerebral imaging	66.7 (10)	21.9 (34)	<0.001
Calcifications	20.0 (2)	26.5 (9)	1.000

Underbjerg *et al.* reported similar occurrence of seizures in patients with PSHP (3.8%) and NSHP (23.3%); however, the rate in PHP (16.6%) patients was much lower (5, 6, 7). We found no correlation between a history of seizures and the presence of intracerebral calcifications. Basal ganglia calcifications were present in 73.8% of the 145 NSHP patients reported by Goswami *et al.* (29), and these authors did find a correlation between cerebral calcifications and seizures. Aggarwal *et al.* found intracerebral calcifications in 88.7% out of the 62 patients with NSHP (30). However, they could not find a correlation between neuropsychological dysfunctions – present in up to one-third of NSHP patients – and intracerebral calcifications. The clinical significance of cerebral calcifications remains unclear.

The strength of this study lies in the number of patients studied in detail, and the analysis according to different HP aetiologies, shedding light on the risk of complications and on the current clinical management of long-standing HP. The limitation of this study is its retrospective, single-centre, cross-sectional design. All patients were treated with active vitamin D analogues (inclusion criterion) which implicates that this cohort includes patients at the more severe side of the spectrum of hypoparathyroidism, excluding patients with mild hypoparathyroidism that are sufficiently controlled with calcium and non-active vitamin D.

Table 5 Intracerebral calcifications. Data are presented as % (n) for categorical data. Quantitative data are presented as mean $\pm$ s.d. or median (minimum–maximum) for symmetrical and non-symmetrical distributed variables respectively.

	Cerebral calcifications		P value
	Present (n = 11)	Absent (n = 33)	
Male sex	54.5 (6)	45.5 (15)	0.6011
Age (years)	48.08 (19.92–68.42)	68.17 (23.33–87.75)	<0.01
Duration of disease (years)	35.17 (7.83–53.5)	9.92 (1.08–43.25)	<0.01
Seizures	18.2 (2)	24.2 (8)	1.000

Conclusion

Patients with chronic HP frequently experience complications. Non-surgical and pseudo-HP patients have more seizures and cerebral calcifications than post-surgical HP patients. No correlation was found between seizures and cerebral calcifications. There is a need for increased screening for long-term complications of HP. Undoubtedly, the recently published guidelines will be of help in the clinical management of chronic hypoparathyroidism patients. Whether treatment with recombinant PTH will decrease the long-term complications of chronic HP remains to be discussed.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this study.

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