

# Is there a need for an emergency card in hypoparathyroidism?

■ M. C. Astor<sup>1,2</sup> , W. Zhu<sup>1,3</sup>, S. Björnsdóttir<sup>4</sup>, J. Bollerslev<sup>5,6</sup>, O. Kämpe<sup>7</sup> & E. S. Husebye<sup>1,2,7</sup>

From the <sup>1</sup>Department of Medicine, Haukeland University Hospital; <sup>2</sup>Department of Clinical Science and K.G. Jebsen Center for Autoimmune Disorders, University of Bergen, Bergen, Norway; <sup>3</sup>Wellington School of Medicine, University of Otago, Dunedin, New Zealand; <sup>4</sup>Departments of Endocrinology and Molecular Medicine, Karolinska Institutet, Stockholm, Sweden; <sup>5</sup>Department of Endocrinology, Oslo University Hospital; <sup>6</sup>Faculty of Medicine, University of Oslo, Oslo, Norway; and <sup>7</sup>Medicine (Solna), Karolinska Institutet, Stockholm, Sweden

**Abstract.** Astor MC, Zhu W, Björnsdóttir S, Bollerslev J, Kämpe O, Husebye ES (Haukeland University Hospital; University of Bergen, Bergen, Norway; University of Otago, Dunedin, New Zealand; Karolinska Institutet, Stockholm, Sweden; Oslo University Hospital; University of Oslo, Oslo, Norway; Karolinska Institutet, Stockholm, Sweden). Is there a need for an emergency card in hypoparathyroidism? *J Intern Med* 2018; <https://doi.org/10.1111/joim.12865>

**Background.** Patients with hypoparathyroidism are at risk of both hypocalcemic and hypercalcemic crisis. Patients report that health professionals do not always respond adequately in an acute situation. The extent and handling of severe hypo- and hypercalcemia in hypoparathyroidism is unknown.

**Aims.** To outline the need for a medical emergency card for primary hypoparathyroidism.

**Method.** Postal survey amongst Norwegian and Swedish patients with chronic hypoparathyroidism of all causes. Altogether 455 invitations were sent (333 from Norway and 122 from Sweden).

**Results.** Three hundred and thirty-six of 455 (74%) patients responded (253 from Norway and 83 from Sweden). The majority were women (79%), and the main cause was postsurgical hypoparathyroidism (66%). Overall 44% and 16% had been hospitalized at least once for hypo- or hypercalcemia, respectively. Eighty-seven per cent felt that an emergency card would be highly needed or useful. Amongst those hospitalized for hypocalcemia, 95% felt a card was needed compared to 90% amongst those hospitalized for hypercalcemia. Five per cent believed that a card would not be useful.

**Conclusions.** The majority answered that an acute card is highly needed or useful. Hospitalization for acute hypocalcemia was more common (44%) than for acute hypercalcemia (16%). As a result of this survey, an emergency card will be distributed in three European countries to test its utility.

**Keywords:** emergency card, hypoparathyroidism.

## Introduction

Hypoparathyroidism (HP) is a disease characterized by low serum calcium and often increased serum phosphorus as a result of either inadequate secretion of parathyroid hormone (PTH) or resistance to PTH in target organs (pseudoHP). HP is a rare condition, with a prevalence of 102 per million people in Norway [1], 254 per million in Denmark [2–4] and 250 per million in The United States [5].

Hypoparathyroidism is commonly divided into three main groups as follows: surgical, nonsurgical and pseudoHP. Surgical HP is the most common cause, in Scandinavia accounting for 60–88% of all cases [1, 6]. Nonsurgical HP

includes a number of heterogeneous diseases including autoimmune polyglandular syndrome type 1 (APS-1), DiGeorge syndrome, autosomal dominant hypocalcaemia (ADH), mutations in the transcription factor *glial cells missing B* and PTH itself [7]. A large proportion of the nonsurgical patients do not have an identified cause of their disease, collectively referred to as idiopathic HP. Autosomal dominant hypocalcaemia (ADH) types 1 and 2 are genetic diseases leading to increased sensitivity of the calcium receptor and thereby inhibition of PTH secretion. ADH is therefore not true HP, but the consequences are hypocalcaemia and low PTH. In lack of a better classification, it is often included amongst nonsurgical causes of HP.

Regardless of the cause of HP, the denominators are hypocalcaemia and hyperphosphatemia which can cause tetany, paraesthesia, hyperreflexia, stridor and psychological disturbances [8, 9]. Serious or abrupt hypocalcaemia can cause convulsions and arrhythmias which can be fatal [10, 11]. Typically, patients are managed with a combination of calcium and active vitamin D supplementation, but recently PTH replacement has been introduced as a treatment option [12]. When patients receive excessive amount of calcium and vitamin D, hypercalcemia and/or hypercalciuria can result. This can cause weakness, polyuria and polydipsia, constipation and renal calculi. In severe cases, cardiac arrhythmia, kidney failure and psychological disturbance may occur [13, 14]. The symptoms of hypercalcemia are nonspecific and can easily be misdiagnosed. The symptoms of hypocalcaemia are usually more specific, but in many situations, hypocalcaemia can also be unrecognized or misdiagnosed [15].

Acute illness or other stressful situations can lead to increased requirements of calcium [16–18]. Certain medications such as glucocorticoids and loop diuretics can cause or aggravate hypocalcemia [19]. In these situations, patients with HP are at risk of developing an acute hypo- or hypercalcemic crisis, reflected by an increased rate of hospitalization [20, 21]. Both hyper- and hypocalcemic crises can have a fatal outcome if not treated adequately. An emergency card with information about diagnoses and treatment could lead to quicker diagnosis and treatment in these situations.

Emergency cards for patients with adrenal insufficiency have been used for decades, and recently, a common European card has been issued [22]. Whether the card has led to more prompt treatment in case of adrenal crisis has not been studied. Since almost all patients bring the card with them [23, 24], it probably serves to increase the patients' feeling of security.

As far as we know, an emergency card for HP does not exist. The purpose of an emergency card for HP would be to provide quick and easy information to physicians on acute treatment of hypo- and hypercalcemia. Whether there is an unmet need for such a card in hypoparathyroidism is not known. Therefore, we investigated the patients' opinions.

## Materials and methods

### *Study subjects*

This study was a postal survey amongst Swedish and Norwegian HP patients to ask for their opinion about the need for an emergency card. Invitations to participate were sent to patients registered in the Norwegian national registry ( $n = 243$ ), patients registered at Karolinska hospital in Sweden ( $n = 94$ ), and to all members of the Norwegian ( $n = 90$ ) and Swedish ( $n = 28$ ) hypoparathyroid patient organizations. Altogether 455 invitations were sent (333 from Norway and 122 from Sweden) by mail and by email from the Swedish patient organization. It was also published at the patients' organizations Facebook page. Letters were mailed with a prepaid return envelope, and the responses were anonymous.

### *The postal survey*

The questionnaire contained questions about the need for an emergency card with four response alternatives; 'Highly needed', 'Useful', 'Seldom needed' and 'Not useful'. We asked if they ever had been hospitalized for hypocalcemic or hypercalcemic crises, how much information they had received about their disease, demographics, cause of disease and treatment (Fig 1).

According to the design of the study, an Ethics Committee approval was not needed (confirmed by The Regional Ethics Committee of Western Norway).

### *Statistics*

Patient characteristics and results were reported with descriptive statistics. The hospitalization rate for different subgroups was compared using chi-square test with significance levels of  $P < 0.05$  considered as significant.

## Results

The survey was conducted between May and October 2017. Overall 336 patients responded (253 from Norway and 83 from Sweden). The response rates were 76% in Norway and 68% in Sweden, altogether 74%. The majority were women (79%) and above 40 years of age. Sixty-six per cent had a surgical cause of HP. Duration of disease

## Survey Questions

## Gender

- ☐ Male  
☐ Female

## Age

- ☐ < 20 years  
☐ 20-40 years  
☐ 41-60 years  
☐ >60 years

## Hypoparathyroidism

## Year of diagnosis

## Diagnosed Cause

- ☐ Complication to surgery or radiation  
☐ Autoimmune  
☐ DiGeorge syndrome  
☐ Autosomal dominant hypocalcemia  
☐ Pseudohypoparathyroidism  
☐ Unknown cause  
☐ Other: \_\_\_\_\_

## Have you ever been hospitalized for acute hypocalcaemia (low calcium) with seizure (tetany)?

- ☐ Yes  
☐ No

## If yes, how many times?

- ☐ Once  
☐ 2-3  
☐ >3

## Have you ever been hospitalized for hypercalcemia (high calcium)?

- ☐ Yes  
☐ No

## If yes, how many times?

- ☐ Once  
☐ 2-3  
☐ >3

## In your opinion, how useful would a medical alert card for hypoparathyroidism be?

- ☐ Highly needed  
☐ Useful  
☐ Seldom needed  
☐ Not useful

## Do you feel you have received adequate information about the symptoms and treatment of low and high calcium levels?

- ☐ Yes  
☐ No  
☐ I am uncertain

## Treatment (several answers possible)

- ☐ Vitamin D analogue (Etalpa, Rocaltrol)  
☐ Calcium supplement  
☐ Other vitamin D preparations  
☐ Magnesium supplement  
☐ Parathyroid Hormone (PTH)  
☐ Diuretics (Thiazide)  
☐ Other: \_\_\_\_\_

**Fig. 1** The questionnaire used for the survey (English translation).

ranged from one to 61 years (mean 20 (SD 14), Table 1).

Most of the patients were treated with active vitamin D (90%) and calcium (69%), whereas 10% used PTH. Fifty per cent reported that they had been hospitalized for hypo- or hypercalcemia, 44% for acute hypocalcaemia and 16% for acute hypercalcemia. Thirty-five patients (10%) had been hospitalized for *both* hypo- and hypercalcemia. Of those hospitalized, about half had been admitted for an acute crisis more than once. Amongst surgical patients ( $n = 213$ ), 83 (39%) had been hospitalized for acute hypocalcaemia and 34 patients (16%) for acute hypercalcemia. Amongst

nonsurgical patients ( $n = 93$ ), forty-eight (53%) had been hospitalized for acute hypocalcaemia and seventeen (18%) for acute hypercalcemia. Amongst pseudoHP patients ( $n = 18$ ), nine (50%) had been hospitalized for hypocalcaemia and one for hypercalcemia (6%).

There was a tendency to more frequent hospitalization amongst PTH users compared to non-PTH users, both due to hypocalcemia (58% vs. 42%,  $P = 0.06$ ) and hypercalcemia (27% vs. 15%,  $P = 0.07$ ). The PTH-treated group had more post-surgical HP compared to the non-PTH-treated patients ( $n = 28$ , 88% vs.  $n = 184$ , 61%,  $P = 0.001$ ).

**Table 1** Demographics of 336 patients with hypoparathyroidism

Female, <i>n</i> (%)	264 (79)
Male, <i>n</i> (%)	70 (21)
Age in years, <i>n</i> (%)	
<20	6 (1.8)
20–40	50 (15)
41–60	147 (44)
>60	131 (39)
Mean duration of disease, years (SD)	20 (14)
Surgical	23
Nonsurgical and PseudoHP	17
HP aetiology	
Surgical, <i>n</i> (%)	213 (66)
Nonsurgical, <i>n</i> (%)	93 (29)
Autoimmune (APS1), <i>n</i>	31
DiGeorge, <i>n</i>	6
ADH, <i>n</i>	4
Idiopathic, <i>n</i>	35
Other/na, <i>n</i>	29
Not answered	12
PseudoHP, <i>n</i> (%)	18 (6)
Treatment, <i>n</i> (%)	
Active vitamin D	301 (90)
Calcium	233 (69)
Other vitamin D supplementation	129 (38)
Magnesium	161 (48)
PTH	33 (10)
Diuretics	26 (8)

Fifty-three per cent felt that they had got adequate information about symptoms and treatment of hypoparathyroidism, whilst 21% answered that they had not received adequate information. Some additional comments from the respondents were that they had been inadequately informed by their general physician and that healthcare providers lacked such knowledge. A higher proportion of PTH users than non-PTH users (79% vs. 50%,  $P < 0.001$ ) felt that they had received adequate information (Table 2).

The majority (87%) felt that an emergency card would be highly needed or useful. Amongst those hospitalized for an acute hypocalcemia, as many as 95% thought that an emergency card would be

**Table 2** Results of the survey in 336 patients with hypoparathyroidism

Hospitalization for acute hypocalcemia	
Yes	146 (44)
No	188 (56)
Times hospitalization acute hypocalcemia	
Once	69 (47)
2–3 times	37 (25)
More than 3 times	40 (27)
Hospitalization for acute hypercalcemia	
Yes	54 (16)
No	275 (84)
Times hospitalization acute hypercalcemia	
Once	31 (57)
2–3 times	15 (28)
More than 3 times	8 (15)
Usefulness of card	
Highly needed	108 (34)
Useful	169 (53)
Seldom needed	28 (9)
Not useful	16 (5)
Received adequate information about HP	
Yes	173 (53)
No	69 (21)
Uncertain	85 (26)

highly needed (49%) or useful (46%), compared with 90% of those hospitalized for hypercalcemia. PTH users were more likely to find the card highly needed (52% vs. 30%,  $P = 0.015$ ) than non-PTH users.

## Discussion

In recent years, the burden of illness in HP has been clearly demonstrated [1, 6, 20, 21, 25]. In addition to reduced health-related quality of life [1, 26–28] and self-reported symptoms including fatigue, paraesthesia, brain fog and memory loss [21], the studies have also shown increased risk of kidney failure, infections and psychiatric disorders [20]. In accordance with these studies, we found that a large proportion of HP patients have been hospitalized due to a crisis, most commonly due to hypocalcaemia, whilst hospitalizations for acute hypercalcemia are relatively rare. Surprisingly, a higher percentage of nonsurgical and pseudoHP patients



had been hospitalized for acute hypocalcaemia compared with surgical patients (51% vs. 39%,  $P = 0.024$ ). In our experience, it can sometimes be very challenging to stabilize calcium levels amongst some surgical patients without measurable PTH. The increased hospitalization rate amongst nonsurgical patients might be explained by longer duration of the disease (nonsurgical patients 23 years compared to surgical patients 18 years,  $P = 0.005$ ). PTH-treated patients had more hospitalizations, which could explain why they are treated with PTH. However, we do not know whether hospitalization rates were increased before or after they started PTH treatment.

The majority of the patients felt that an emergency card would be useful, and nearly, all patients who had been hospitalized for an acute hypocalcaemia felt so. Patients who were hospitalized were more likely to say that an emergency card would be useful which may reflect their experiences with health professionals in the acute setting. Health professionals may not encounter the condition or presentation often enough to be able to effectively diagnose and treat it.

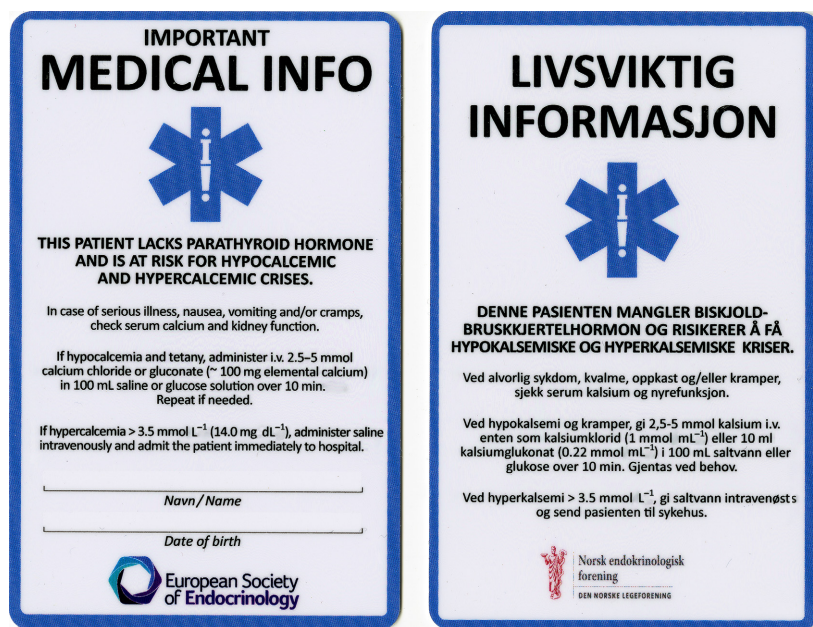
Twenty-one per cent of the patients reported they had not received adequate information about their disease. We consider patient education important for treatment and increased patient knowledge will hopefully reduce the prevalence of acute

emergencies in the future. In the countries participating in this study, no formal training/patient education courses for HP exist. The rare and heterogeneous nature of HP makes education challenging, but it is still warranted. Education of healthcare professionals is also needed and such programmes are in planning in the Scandinavian countries. A higher proportion of PTH-treated patients reported that they had received adequate information, which probably reflects a more frequent contact with endocrinologists with special interest and knowledge in parathyroid disease.

The large number of patients and high response rate is a strength of the study. A limitation is that hospitalization rates are self-reported, which could possibly imply over-reporting. On the other hand, hospitalization rates in this study are somewhat lower than found by Hadker [21], but higher than found by Mitchell [25]. Another limitation could be that patients who have been hospitalized for an acute crisis are more likely to respond, possibly overrating the usefulness of the card. The majority of the respondents were women. This reflects the sex distribution of the disease and is not considered a confounding effect.

The benefit of an emergency card is expected to be prompt management of the acutely ill patient with HP, especially when symptoms are severe, psychological disturbance occurs or patient knowledge is lacking.

**Fig. 2** Emergency card for hypoparathyroidism endorsed by the European Endocrine Society. The cards are bilingual with the English language on one side and another language on the other (in this example Norwegian).



HP is a rare condition and would not be a likely differential diagnosis if the healthcare worker was unaware of their illness. Finally, print in English and national languages makes the card useful for travel abroad, where health professionals often are unaware of the patient's history and language may be a barrier.

## Conclusion

The majority of HP patients report that an acute card will be very useful or useful to facilitate treatment of hypo- and hypercalcemia. Hospitalization for acute hypocalcaemia is common, and most of these patients find an emergency card useful. As a result of the clear message from the patients, an emergency card will soon be distributed amongst Norwegian, Swedish and German patients (Fig. 2).

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## Conflict of interest statement

Wendy Zhu has no declaration. Marianne Astor, Eystein Husebye, Jens Bollerslev and Sigridur Bjornsdottir have received consulting fee from Shire.

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## Author contributions

ESH, JB and OK planned the study including drafting the questionnaire and the emergency card. WZ, MCA and SB performed the study. All authors contributed to writing and review of the paper.

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*Correspondence:* Marianne Catharina Astor MD, Department of Clinical Science, University of Bergen at Haukeland University Hospital, Jonas Lies vei 65, 5021 Bergen, Norway.  
(fax: +47 559 75890; e-mail: [marianne.astor@helse-bergen.no](mailto:marianne.astor@helse-bergen.no)). ■