Comparison of calcium levels in patients with *benign paroxysmal positional vertigo* and the other type of vertigo

Perbandingan kadar kalsium pada penderita *benign paroxysmal positional vertigo* dan jenis vertigo lainnya

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ABSTRACT
Introduction: *Benign paroxysmal positional vertigo* (BPPV) is commonly found in older women; caused by the presence of otoconia in semicircular canals, which will stimulate the ampulla. Degeneration of otoconia and abnormal calcium metabolism could contribute to BPPV. This study aims to find a difference in serum calcium levels between idiopathic BPPV and non-BPPV vertigo patients. **Methods**: Cross-sectional study was held in Wahidin Sudirohusodo hospital in Makassar from August to October 2019. Subjects who fulfilled the criteria were divided into two groups (BPPV and non-BPPV). Venous blood was taken to obtain serum calcium levels. Statistical analysis was performed with SPSS software version 21. Chi-square and Mann-Whitney tests were used to determine the relationship between variables. **Result**: As many as 45 subjects were grouped into BPPV (n=30) and non-BPPV (n=15). Majority of subjects were female (n=30). Mean serum calcium level was significantly lower in BPPV group (8.51±0.67 vs 8.9±0.63; p=0.023). Area under curve of serum calcium level according to vertigo type was 22.4% (p<0.05). Optimal cut-off point for serum calcium level was 8.55 (p=0.024). **Discussion**: Majority of subjects in this study were females between 40-60 years old. Patients with BPPV tend to have lower serum calcium levels. Possible underlying mechanisms include estrogen deficiency, otoconial degeneration, vitamin D deficiency, lack of sunlight, and abnormal calcium metabolism. Examination of serum calcium level and calcium supplementation could be considered for these patients. Some factors that affect serum calcium level were not considered in this study. It was concluded that examination of serum calcium level and calcium supplementation could be considered for patients with BPPV.
Keywords: benign paroxysmal positional vertigo, serum calcium level, vertigo

ABSTRAK
Pendahuluan: *Benign paroxysmal positional vertigo* (BPPV) banyak ditemukan pada wanita usia lanjut; disebabkan oleh adanya otokonia pada kanalis semisirkularis yang akan merangsang ampula. Degenerasi otokonia dan metabolisme kalsium yang abnormal dapat berkontribusi pada BPPV. Penelitian ini bertujuan untuk mengetahui perbedaan kadar kalsium serum antara pasien vertigo BPPV idiopatik dan non-BPPV. **Metode**: Studi *cross-sectional* dilaksanakan di RS Wahidin Sudirohusodo Makassar pada bulan Agustus sampai Oktober 2019. Subjek yang memenuhi kriteria dibagi menjadi kelompok BPPV dan kelompok non-BPPV. Darah vena diambil untuk mendapatkan kadar kalsium serum. Data dianalisis dengan software SPSS versi 21. Uji *Chi-square* dan *Mann-Whitney* digunakan untuk menentukan hubungan antar variabel. **Hasil**: Sebanyak 45 subjek dikelompokkan menjadi BPPV (n=30) dan non-BPPV (n=15). Mayoritas subjek berjenis kelamin perempuan (n=30). Rerata kadar kalsium serum secara signifikan lebih rendah pada kelompok BPPV (8,51±0,67 vs 8,9±0,63, p=0,023). *Area under curve* kadar kalsium serum menurut tipe vertigo adalah 22,4% (p<0,05). *Cut-off point* optimal untuk kadar kalsium serum adalah 8,55 (p=0,024). **Pembahasan**: Mayoritas subjek adalah perempuan berusia antara 40-60 tahun. Pasien dengan BPPV cenderung memiliki kadar kalsium serum yang lebih rendah. Kemungkinan mekanisme yang mendasarinya termasuk defisiensi estrogen, degenerasi otoconial, defisiensi vitamin D, kekurangan sinar matahari, dan metabolisme kalsium yang abnormal. Pemeriksaan kadar kalsium serum dan suplementasi kalsium dapat dipertimbangkan untuk pasien ini. Beberapa faktor yang mempengaruhi kadar kalsium serum tidak dipertimbangkan dalam penelitian ini. Disimpulkan bahwa pemeriksaan kadar kalsium serum dan suplementasi kalsium dapat dipertimbangkan untuk pasien dengan BPPV.
Kata kunci: *benign paroxysmal positional vertigo*, kadar kalsium serum, vertigo
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INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is a type of peripheral vertigo characterized by short duration (<1 minute), usually recurrent, and triggered by a change in head position. The prevalence of this disorder is 10.7-64.0 in 100,000 people. It is found more often in women dan in the elderly.[1,2] Vertigo was the third most common symptom found in outpatient clinic of Wahidin Sudirohusodo hospital between 2006 and 2007.

The BPPV occurs when the otoconia are released from utricle and enter the semicircular canals. The movement of otoconia inside semicircular canals will trigger endolymphatic fluid movement and eventually stimulate the ampulla of corresponding semicircular canals.[1–7]

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Otoconia is made of calcium carbonate, which is denser than endolymphatic fluid. Otoconial dysfunction is thought to play a role in BPPV. This process depends on calcium and protein inside the endolymphatic fluid. Otoconial degeneration occurs in crystal fragmentation, filament bond damage, and structural change of otolithic membrane. Degeneration can occur naturally (genetic factor and age) or triggered by certain conditions (infection, trauma, drugs, and impaired calcium homeostasis).[1-7]

Calcium is needed to form and stabilize otoconia and maintain otolithic turnover. It also has roles in the pathophysiology of BPPV through vitamin D metabolism. Calcium channels TRPV5 and TRPV6 regulate calcium level inside the endolymphatic space. BPPV is associated with the homeostasis of calcium. Abnormal calcium metabolism leads to otoconial remodeling failure. It was also thought to be important in the crystal formation process in the endolymphatic fluid and adhesion to the cupula.[2,3,6,8–10] This study aims to find a difference in serum calcium levels between idiopathic BPPV and non-BPPV vertigo patients.

METHODS

A cross-sectional study was held in outpatient clinic of Wahidin Sudirohusodo hospital in Makassar from August to October 2019. Subjects were taken according to the order of admission (consecutive sampling). Inclusion criteria include patients who were diagnosed with vertigo. The exclusion was applied to patients with labyrinthitis history, ear trauma, ototoxic drugs usage, tumor, hyperparathyroidism, and Meniere's disease. Informed consent was obtained from all subjects.

Eligible subjects were divided into two groups, that is (BPPV and non-BPPV). All subjects were examined for calcium levels taken within 48 hours after the diagnosis was made. Subjects with a positive Dix-Hallpike or Supine-Roll test were included in the BPPV group. This study's normal serum calcium levels were 8,3-10.6 mg/dL.

Statistical analysis was performed with SPSS software version 21. Chi-square and Mann-Whitney tests were used to determine the relationship between variables. Receiver operating characteristics (ROC) determined the cut-off point of serum calcium level for vertigo was determined by ROC, and *a p*-value less than 0,05 was considered statistically significant. The Ethics Committee has approved this study of the Faculty of Medicine at Hasanuddin University.

RESULTS

As many as 45 subjects were diagnosed with vertigo, further divided into BPPV (n=30) and non-BPPV (n=15). Most subjects were female, either in the BPPV group (n=22) or the non-BPPV group (n=8). The serum calcium level of both groups was declared in mean± standard deviation.

Table 1 Demography of subjects

Demography		Serum Calcium Level (%) Low	Normal	*p*-value[1]
Age (years)	<40	3 (50)	3 (50)	0,628
	40-60	5 (25)	15 (15)	
	>60	6 (31,6)	13 (13)	
Sex	Male	3 (20,0)	12 (80,0)	0,260
	Female	11 (36,7)	19 (63,3)	

[1]Chi-Square test

Table 2 Serum calcium levels in BPPV and non-BPPV groups

Serum Calcium Level		Groups BPPV	Non-BPPV	*p*-value[1]
Low	n (%)	13 (92,9)	1 (7,1)	0,012*
Normal	n (%)	17 (54,8)	14 (45,2)	

[1]Chi-Square test

Table 3 Mean serum calcium levels in BPPV and non-BPPV groups

Groups	Mean±SD	*p*-value[1]
BPPV	8,51±0,67	0,023*
Non-BPPV	8,90±0,63	

[1]Mann-Whitney test

No significant difference was observed between serum calcium level with age (p=0.628) and sex (p=0.260) (table 1). Significant difference of serum calcium level was discovered between both groups (p=0.012) (table 2). Mean serum calcium level was significantly lower in BPPV group (8.51±0.67 vs 8.90±0.63, p=0.023) (table 3). Area under curve of serum calcium level according to vertigo type was 22.4% (p<0.05). Optimal cut-off point for serum calcium level was 8.55 (p=0.024).

DISCUSSION

Majority of subjects in this study were females between 40-60 years old. This finding is similar to previous studies. There is a correlation between serum calcium level and BPPV rate, as confirmed by the result of this study. Patients with BPPV tend to have lower serum calcium levels.[6,11,12]

The causa of idiopathic BPPV is still unknown. Possible underlying mechanisms include estrogen deficiency and otoconial degeneration. Menopausal women with BPPV have a higher prevalence of osteopenia or osteoporosis. On the other hand, women with osteopenia or osteoporosis have a higher rate of BPPV. The biochemical marker of bone turnover was associated with BPPV.[6,13] Otokonia is a deposit of calcium carbonate. Low calcium serum levels may be related to low density of otoconia renders it more susceptible to be cracked and detached from the otoconia membrane of the macu-

la. Debris of otokoni move from macula utriculus to semicircular canals (canalithiasis) or be embedded in the cupula (cupulolithiasis). In the event of head motion, the presence of these fragments provokes asymmetrical signals from endolymphatic fluid and cupula, which is delivered through the vestibular nerve to the central vestibular, causing BPPV.[1,4,10,14–16]

This study implied that calcium's effects on BPPV are indirect (through vitamin D metabolism). Kahraman et al. reported that vitamin D deficiency and decreased ionized calcium might be some risks for developing BPPV in all patients.[8]

The results of this study are according to Buki et al and Talaat et al. Both studies reported that patients with BPPV tend to have osteopenia or osteoporosis and lower mineral density compared to control group.[17,18] These findings suggest that otoconial release in parallel with bone demineralization.[3,13]

This study follows Lips, and Riggs et al. Lips reported that vitamin D deficiency often occurs in the elderly, especially those who did not get enough sunlight. Riggs et al. mentioned that lack of estrogen could cause hypocalcemia. Lower serum calcium level is often found in older women because of significant estrogen decrease.[11,12]

It was concluded that examination of serum calcium level and calcium supplementation could be considered for patients with BPPV; but this study did not consider factors that can affect serum calcium levels in older people, such as diet and hormones.

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