Hypocalcaemia After Total Knee Arthroplasty and its Clinical Significance

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Abstract. *Background: Transient hypocalcaemia is a frequent complication after total knee arthroplasty (TKA). In this study, we investigated the factors associated with the development of hypocalcaemia after TKA in order to explore its clinical significance and treatment. Patients and Methods: A retrospective analysis of the change of serum calcium levels for 40 patients after TKA was performed. We investigated the patients prospectively for age, gender, and amount of bleeding at operation. At 24 hours following the operation, serum calcium of the patients was evaluated and a t-test was performed to analyze the categorical variables. Pearson's correlation analysis was used to determine the risk of hypocalcaemia in univariate analysis. Results: After TKA, the serum calcium level was significantly lower than that before the operation ($p<0.01$); the incidence of postoperative hypocalcaemia was 77.5%, the decline was positively correlated with intraoperative blood loss (Pearson's $r=0.405$, $p=0.01$). Conclusion: Hypocalcaemia occurs frequently after TKA, however, clinical symptoms associated with hypocalcaemia are rare. The calcium ion is an important electrolyte, neurotransmitter and blood coagulation factor. It is suggested that we should routinely monitor calcium ion levels during the perioperative period and deal with hypocalcaemia in a timely fashion.*

In recent years, knee arthroplasty has developed rapidly. It is a major surgery of orthopedics and since most patients are elderly, the perioperative treatment is particularly important. Electrolyte balance during the perioperative period is an important guarantee for the safety of operation and rehabilitation. As an important electrolyte, neurotransmitter and blood coagulation factor, calcium ions actively participate in various processes of metabolism. However, the calcium ion has not attracted as much attention as sodium and potassium ions from clinicians.

The changes in serum calcium levels in the perioperative period of 40 patients who underwent total knee arthroplasty (TKA) were analyzed and the clinical significance explored.

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Patients and Methods

Clinical samples, procedure and sample preparation. The study protocol was approved by the Board of Ethics of Medical Faculty, Yantai Yuhuangding Hospital (2015) 133. Forty patients who had undergone TKA at the Department of Joint Surgery, between October 15, 2007 and October 15, 2008 were included in the study. All operations were managed by the same medical team, the operative time was approximately 65-130 min (average=90±23 min). The patients were assessed prospectively for age, gender, operative time and amount of haemorrhage during operation. The relation of all these factors with hypocalcaemia was assessed. Forty patients were included in the study. Twenty patients were female (50%) and 20 were male (50%), and the mean age was 68.88 years. The mean amount of haemorrhage in these patients was 708.75 ml. The mean calcium level of patients included in the study in the preoperative period was 2.29 mmol/l. The mean postoperative calcium level was 2.03 mmol/l at 24 h after TKA. Patient details are shown in Table I.

Blood samples were taken three days before and 24 h after surgery, these specimens were sent to the clinical laboratory of our hospital to measure serum calcium levels (Ion selective method).

Statistical analysis. Prospective analysis of age, gender, operative time and amount of haemorrhage during the operation in relation to hypocalcaemia was performed. SPSS for windows version 19 software package [IBM software, Bizinsight (Beijing) Information Technology Co., Ltd] was used to perform statistical analysis of the data. A *p*-value of less than 0.05 was accepted as being statistically significant.

Results

After TKA, the incidence of postoperative hypocalcaemia (calcium levels <2.12 mmol/l) was 77.5%. A *t*-test was used to compare the difference in serum calcium levels over the perioperative period. As seen in Table II, the serum calcium

Table I. *The preoperative and postoperative laboratory findings of the patients in this study (n=40).*

		Serum calcium (mmol/l)			
Gender	Mean age, years	Preoperative	Postoperative	Reduction	Blood loss (ml)
Male	70.40	2.28±0.077	2.02±0.13	0.258±0.128	723.37±269.24
Female	67.35	2.31±0.084	2.04±0.11	0.267±0.105	671.43±227.35

Values are mean ± SD.

level post-surgery was significantly lower than that before the operation ($p<0.01$). Similarly, a *t*-test was used to compare the difference in the loss of serum calcium between male and female patients. As can be seen in Table III, no statistical significance was observed between these data ($p<0.05$).

Pearson's correlation analysis was used to detect any relationship between age and reduction of serum calcium; there was no statistical significance ($p>0.05$). Pearson's correlation analysis was also used to detect any relationship between blood loss and reduction of serum calcium. The decline in serum calcium was found to positively correlate with intraoperative blood loss (r=0.405, $p=0.01$) (Figure 1).

Table II. *Change of serum calcium during the perioperative period (n=40, mean±s).*

	Serum calcium (mmol/l)
Time-point Preoperative	2.29±0.081
Postoperative	2.03±0.099*
Reduction	0.026±0.12

*$p<0.01$ *vs.* Preoperative value. Values are mean ± SD.

Table III. *Reduction of serum calcium in male and female patients (n=40, mean±s).*

Gender	Reduction of serum calcium (mmol/l)
Male	0.258±0.128
Female	0.267±0.105

$p>0.05$. Values are mean ± SD.

Discussion

Calcium is considered one of the most abundant electrolytes in the body. Most calcium (almost 99%) is deposited in the bones and teeth. The remaining calcium is left circulating in the blood (1, 2). Calcium in the blood exists in three primary states: bound to proteins (mainly albumin), bound to anions such as phosphate and citrate, and as free (unbound) ionized calcium. About 40% of the calcium in the blood is attached to albumin, whereas the 15% is bound to phosphates, sulphates, citrate, and lactate. The remaining 45% circulates in the body in its biologically active form or ionized form (3). Only ionized calcium is physiologically active. Normal blood calcium levels are between 8.5 to 10.5 mg/dl (2.12 to 2.62 mmol/l) and that of ionized calcium is 4.65 to 5.25 mg/dl (1.16 to 1.31 mmol/l). Levels are highly regulated by vitamin D and the parathyroid hormone (4, 5). The extracellular calcium-sensitive receptors are known to play a vital role in calcium homeostasis. These receptors allow the regulation of calcium by the parathyroid gland and other tissues. Calcium levels are also influenced by hormones, such as calcitonin, and other electrolytes, such as phosphorus and magnesium (6). Common causes of hypocalcaemia include hypoparathyroidism, vitamin D deficiency, and chronic kidney disease. Symptoms of hypocalcaemia include neuromuscular irritability (including tetany as manifested by Chvostek's sign or Trousseau's sign, bronchospasm), electrocardiographic changes, and seizures (7).

After TKA, we found that the serum calcium level of the patients were significantly lower than those before the operation. The mechanism accounting for this may be: (i) Gastrointestinal dysfunction, caused by trauma following surgery, may lead to the reduction of calcium intake and absorption. (ii) Inhibitory effects on parathyroid function, caused by hypoxia during anaesthesia, may also bring about hypocalcaemia. At the same time, throughout the operation, some toxins may directly damage the cell membrane, increasing the permeability of calcium ions, combined with a decreased efficacy of the calcium pump brought about by hypoxia resulting in enhanced internal calcium concentrations. (iii) Under surgical stress, thyroid C cells secrete more calcitonin, which reduces the plasma calcium level; meanwhile, owing to the stress, the capillary vascular permeability of the whole body increases, exacerbating the extravascular leakage of calcium. (iv) Calcium loss is caused by blood loss during the operation. At the same time, the fluid replacement therapy dilutes serum calcium concentrations, which explains why the decline of serum calcium was positively correlated with intraoperative blood loss.

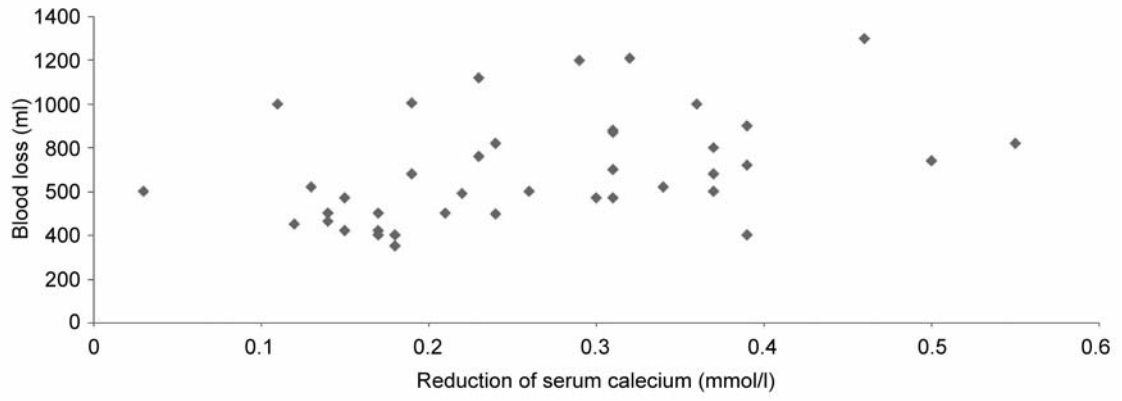

Figure 1. *Relationship between blood loss and reduction of calcium.*

In our study, we also found that the serum calcium level of the perioperative period varied. Hypocalcaemia occurred in most of our patients, however, clinical symptoms associated with hypocalcaemia were rare. This may be due to the following reasons: (i) Drainage following TKA fluctuates with changes due to many reasons. The physical condition of the patients and the intervention to the soft tissue intraoperatively are usually key factors, which may explain why hypocalcaemia may cause blood coagulation dysfunction, nevertheless, postoperative blood loss was less affected. (ii) Cardiac arrhythmia events may have occurred with no patient discomfort, low blood calcium levels did not reach the threshold to induce a convulsion and therefore was unlikely to trigger symptoms. Quiros *et al*. once reported that the lowest threshold of serum calcium required to trigger symptoms was 1.65 mmol/l (8). (iii) Cardiac contractility and electrical activity can be seriously agitated by long-standing hypocalcaemia (9), in our study, once hypocalcaemia was detected, we gave calcium chloride and calcitriol to correct the serum ion concentration, which improved cardiac function and electrical activity avoiding the emergence of cardiac arrhythmia events.

Above all, we believe that hypocalcaemia frequently occurs after TKA. Intraoperative bleeding may be the main reason for the low serum calcium levels. Although postoperative hypocalcaemia related to clinical symptoms is rare, we still recommend that serum calcium be re-assessed in the first 24 h following TKA, and that hypocalcaemia be dealt with promptly.

References

1 National Institutes of Health (US). Dietary Supplement Fact Sheet: calcium [Internet]. Bethesda (MD): National Institutes of Health. Available from http://ods.od.nih.gov/factsheets/Calcium/HealthProfessional/ [Last accessed August 23, 2014].

2 Institute of Medicine Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (US). Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, VitaminD, and Fluoride. Washington, D.C.: National Academies Press, 1997.

3 Longmore M, Wilkinson I and Rajagopalan S: Calcium: physiology. Oxford Handbook of Clinical Medicine, 2004.

4 Bushinsky DA and Monk RD: Electrolyte quintet: Calcium. Lancet *352*: 306-311, 1998.

5 Cooper MS and Gittoes NJ: Diagnosis and management of hypocalcaemia. Br Med J *336*: 1298-1302, 2008.

6 Egbuna OI and Brown EM: Hypercalcaemic and hypocalcaemic conditions due to calcium-sensing receptor mutations. Best Pract Res Clin Rheumatol *22*: 129-148, 2008.

7 Signs of Hypocalcaemia - Chvostek's and Trousseau's signs: Urbano, FL (Editor), Review of clinical signs: Hospital Physician (2000).

8 Quiros RM, Pesce CE, Wilhelm SM, Djuricin G, and Prinz RA: Intraoperative parathyroid hormone levels in thyroid surgery are predictive of postoperative hypoparathyroidism and need for vitamin D supplementation. Am J Surg *189*: 306-309, 2005.

9 Yang YC, Shen FR, and Lu YQ: Hypocalcemia: a reversible cause of T-wave alterationsand heart failure. J Zhejiang Univ Sci B *15*: 598-600, 2014.

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