Original Article

Efficacy of an Intravenous Calcium Gluconate Infusion in Controlling Serum Calcium after Parathyroidectomy for Secondary Hyperparathyroidism

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Abstract

Introduction: Intravenous calcium gluconate has been used to prevent postoperative hypocalcaemia (POH) following parathyroidectomy for secondary hyperparathyroidism in chronic kidney disease (CKD). Materials and Methods: Retrospective data were obtained for 36 patients with CKD stage 4 and 5 after parathyroid surgery, correlating albumin-corrected serum calcium with the infusion rate of calcium gluconate. Calcium flux was characterised along with excursions out of the target calcium range of 2 to 3 mmol/L. With this data, an improved titration regimen was constructed. Results: Mean peak efflux rate (PER) from the extracellular calcium pool was 2.97 mmol/h occurring 26.6 hours postoperatively. Peak calcium efflux tended to occur later in cases of severe POH. Eighty-one per cent of patients had excursions outside of the target calcium range of 2 to 3 mmol/L. Mean time of onset for hypocalcaemia was 2 days postoperatively. Hypocalcaemia was transient in 25% and persistent in 11% of patients. Conclusion: A simple titration regimen was constructed in which a 10% calcium gluconate infusion was started at 4.5 mL/h when serum calcium was <2 mmol/L, then increased to 6.5 mL/h and finally to 9.0 mL/h if calcium continued falling. Preoperative oral calcium and calcitriol doses were maintained. Blood testing was done 6-hourly, but when a higher infusion rate was needed, 4-hourly blood testing was preferred. Monitoring was discontinued if no hypocalcaemia developed in the first 4 days after surgery. If hypocalcaemia persisted 6 days after surgery, then the infusion was stopped with further monitoring for 24 hours.

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Introduction

Transient postoperative hypocalcaemia (POH) is often found following parathyroidectomy for secondary hyperparathyroidism (SHP). When the fall in serum calcium is acute, this can cause neuromuscular irritability which may present as numbness, paraesthesia and cramps. When severe, this may result in bronchoconstriction, cardiac arrhythmias, angina, heart failure and seizures.

Clinically, POH is seldom symptomatic unless trough serum calcium (TSC) falls below 2 mmol/L. While symptomatic POH is relatively uncommon following parathyroidectomy for primary hyperparathyroidism (PHP), it may be more problematic following surgery for SHP due in part to higher preoperative parathyroid hormone (PTH) levels.[1]

In hyperparathyroidism, bone turnover is greatly increased under constant PTH stimulation, with high levels of both formation and resorption.[2] During the immediate postoperative period, a number of changes take place that impact on calcium metabolism. There is an initial rapid fall in PTH level on the first postoperative day, followed by a decrease in serum calcium with a trough on the second day.[3,4] Bone resorption falls rapidly, with a steep decline in resorption markers and a virtual disappearance of osteoclast activity. On the other hand, bone formation increases transiently but subsequently declines slowly over time, with corresponding changes in formation markers and osteoblast activity.[5]

Similar changes take place in renal calcium excretion[6,7] and intestinal calcium absorption[8,9] after surgery. The

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complexity of these calcium shifts together with the heterogeneity of the population group and the confounding effect of haemodialysis means that there is very little data available on calcium flux after parathyroidectomy for SHP in chronic kidney disease (CKD).

The problem of postoperative hypocalcaemia can be approached in different ways. Based on expert opinion, the K/DOQI clinical practice guidelines suggest monitoring serum calcium every 4 to 6 hours for the first 48 to 72 hours after surgery, and then twice daily until stable. An intravenous 10% calcium gluconate infusion can be started at a rate of 1 to 2 mg elemental calcium per kilogram body weight per hour if serum calcium falls below normal.[10] Others however feel that an intravenous calcium infusion should be given to all patients after parathyroid adenectomy to reduce the risk of POH.[11]

Our centre at the Kuala Lumpur General Hospital has been treating all postoperative SHP patients with an intravenous 10% calcium gluconate infusion started at 10 mL/h, which is adjusted according to 4-hourly serum calcium levels to keep it between 2 and 3 mmol/L. There is no standard titration regimen, and adjustment of the infusion rate is left to the judgement of the on-call physician.

As the consequences of POH are potentially serious, it would be useful to assess our current infusion regimen to see if it is effective in preventing significant hypocalcaemia in postoperative SHP patients. In addition, we would like to identify problems with the existing infusion regimen, and see if a standard titration regimen can be devised based on data that we obtain from this study.

In a parallel study, the authors found a strong correlation between preoperative serum alkaline phosphatase (ALP) and the magnitude of postoperative hypocalcaemia in PHP. It would be useful to see if a similar relationship exists in SHP.[12]

Study Objectives

The first objective of the study was to characterise calcium flux in patients during the immediate postoperative period. The second objective was to ascertain the proportion of time that patients spent out of the target serum calcium range of 2 to 3 mmol/L during the treatment period. The third objective was to determine the time course of hypocalcaemia in patients who develop it. The fourth objective was to examine the study data to see if a standard titration regimen can be constructed that could improve on the performance of the current regimen.

Materials and Methods

Inclusion and Exclusion Criteria

Only patients diagnosed with SHP of renal origin (ICD-9 Code 588.81) who underwent parathyroidectomy with auto-transplantation were included. In addition, they had to be started on an intravenous calcium gluconate infusion after surgery. Patients younger than 16 years and pregnant women were excluded as physiological differences in skeletal metabolism would make the study data difficult to interpret. Treatment with bisphosphonates, calcitriol and calcium supplementation did not exclude patients from the study. However, usage within the 6 months prior to surgery and during the immediate postoperative period was noted.

Data Collection

This study was done with prior ethics approval from the Malaysian Ministry of Health in accordance with current guidelines on Good Clinical Practice, the Declaration of Helsinki, and subsequent relevant versions. Data were collected retrospectively based on patient records. As this was done anonymously, informed consent was not required by the ethics review board. The study population consisted

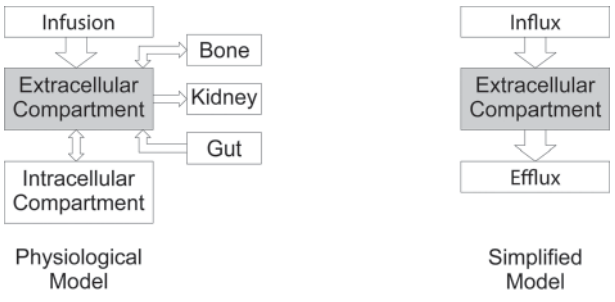

Fig. 1. Physiological and simplified model of calcium flux.

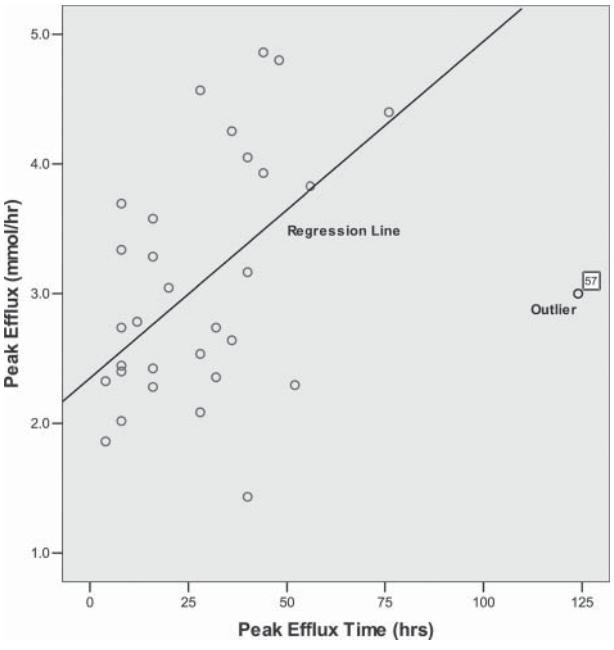

Fig. 2. Scatterplot of peak efflux rate against peak efflux time.

of patients operated for SHP at a single tertiary institution (Kuala Lumpur General Hospital, Malaysia) over the period from 2004 to 2007.

Serum calcium (reference interval: 2.00-2.60 mmol/L, Roche-Hitachi 747, Roche Diagnostics, Basel, Switzerland) was corrected for albumin level (reference interval: 35 to 50 g/L, Roche-Hitachi 747) according to the formula by Payne et al.[13] All postoperative 4-hourly serum calcium values were charted together with the corresponding intravenous calcium gluconate infusion rates (mL/h). Missing serum calcium values were replaced with the most recent valid reading. Charting was continued until 24 hours after the infusion was stopped.

Data for patient age at operation, gender, ethnicity, CKD stage, ALP, PTH (reference interval: 0.5 to 5.1 pmol/L, Elecsys 1010 analyser, Roche Diagnostics), peak preoperative serum calcium corrected for albumin, and parathyroid gland volume on ultrasonography were also collected.

Analysis

Objective 1: Calcium Flux

It is assumed that prior to surgery, extracellular calcium flux in patients is in a steady state. The rapid fall in PTH after surgery upsets this balance, leading to overall efflux of calcium from the extracellular pool which is balanced by replacement influx from the calcium gluconate infusion (Fig. 1).

The calcium influx (mmol/h) is calculated by multiplying the infusion rate (mL/h) with the conversion factor (0.2325 mmol/mL), given that 1 mL 10% calcium gluconate contains 0.2325 mmol elemental calcium. The rate of change in the extracellular pool (mmol/h) is calculated by taking the difference in serum calcium (mmol/L) between 2 consecutive readings divided by the time difference (4 hours) and multiplied by total extracellular fluid (ECF) volume (15 L in a normal adult). The calculated efflux (mmol/h) is thus the difference between the rate of change in the extracellular calcium pool and influx rate. The peak efflux rate (PER) and timing are obtained for each subject, ignoring readings immediately after dialysis sessions. Scatterplots of PER against time, and PER against preoperative ALP are then charted to see if a relationship exists between these variables. In addition, the 90th, 99th and 99.99th percentiles are calculated for the rate of decline in serum calcium (mmol/L/h), excluding readings taken after dialysis.

Objective 2: Excursions

The proportion of the treatment duration period where serum calcium goes below 2 mmol/L and above 3 mmol/L is charted, along with corresponding trough and peak serum calcium.

Objective 3: Time course of Hypocalcaemia

The times of onset and recovery from hypocalcaemia with serum calcium below 2 mmol/L are charted, along with the duration of treatment with calcium gluconate. For patients with persistent hypocalcaemia at the end of the treatment period, the average calcium efflux from the extracellular pool is calculated for the last 6 readings (24 hours), and is deemed to be significant if it could potentially deplete the extracellular calcium pool by more than 10% per hour. The 10% threshold is calculated by multiplying serum calcium at the start of the 24 hour period by 0.0625 (10% multiplied by ECF volume divided by 24 hours). The 90th percentile for the time of onset and recovery from hypocalcaemia are also calculated.

Objective 4: Titration Regimen

To construct a titration regimen, a scale for the calcium gluconate infusion along with appropriate time intervals for blood testing needs to be determined so that serum calcium can be maintained in the set target range. The infusion rate should be sufficient to replace losses from the extracellular pool, while avoiding over-replacement and consequent hypercalcaemia. The time interval for blood testing should be short enough to allow adjustment of the infusion rate to compensate for changes in serum calcium. The duration of intensive monitoring should be specified, along with criteria for stopping the infusion.

The target range for serum calcium is between 2 and 3 mmol/L as patients are usually asymptomatic within this range. When serum calcium falls below 2 mmol/L, a calcium gluconate infusion should be started. The initial rate of infusion should be enough to match the 90th percentile for the rate of decline in serum calcium. This can be obtained by multiplying the 90th percentile rate with ECF volume (15 L) and dividing by the conversion factor (0.2325 mmol/mL). If subsequent serum calcium continues to fall, then the infusion rate should be increased to match the 99th percentile for the rate of decline in serum calcium, and if necessary, the infusion rate can be further increased to match the 99.99th percentile if serum calcium continues to decline. When serum calcium is more than 2 mmol/L, the interval between blood tests should be short enough to prevent a fall below 1.6 mmol/L as symptoms of hypocalcaemia are common at this level. This interval can be calculated by dividing 2 to 1.6 mmol/L with the 90th percentile for the rate of decline in serum calcium in mmol/L/h.

While the infusion is in place when serum calcium is below 2 mmol/L, the interval between blood tests should be short enough to prevent a rise above 3 mmol/L. This interval is calculated multiplying the maximum rise (1 mmol/L) with total ECF volume, and divided by the infusion rate in mmol/h.

Intensive monitoring should be continued for a sufficient period to pick up 90% of cases where hypocalcaemia will develop. Once hypocalcaemia is present, monitoring should continue until serum calcium normalises.

All statistical computations were performed using SPSS for Windows version 13.0 (SPSS Inc, Chicago, Illinois, USA). Only 2-tailed tests were used, and all statistical tests were conducted at 5% level of significance unless stated otherwise.

Results

Case records of 63 patients with ICD-9 Code 588.81 (SHP) were screened, of which 36 satisfied the inclusion and exclusion criteria. Most of these patients were excluded as data collection was incomplete, or the calcium gluconate infusion regimen was not used.

Patient demographics were as follows: age (30 to 66 years); male (15), female (21); Chinese (18), Malay (13), Indian (4), Others (1). Ten (28%) patients were pre-treated with bisphosphonates. There was no significant difference between bisphosphonate and non-bisphosphonate groups in TSC ($P = 0.519$) or PER ($P = 0.438$). Twenty-seven (75%) patients were on haemodialysis, and none were on peritoneal dialysis. Most patients were on stable doses of calcitriol (0.5 to 2 /g/day) and calcium carbonate (1 to 2 g elemental calcium/day) prior to surgery, which was continued during the postoperative period. PTH levels after surgery were not checked in any of the patients. None of the patients were documented to have calciphylaxis. All patients had PTH levels above the target range based on their CKD stage (12.1 pmol/L in CKD stage 4, 33.0 pmol/L in CKD stage 5).[10] Seven patients did not have severe hyperparathyroidism as defined by persistent PTH levels above 88.0 pmol/L. Twenty-five patients had preoperative serum calcium levels within or below the normal range. Relevant preoperative factors are listed in Table 1.

Table 1. Relevant Preoperative Factors (n = 36)

No.	Dialysis	CKD stage	Bisphos.	ALP (U/L)	PTH (pmol/L)	Peak ca (mmol/L)	Gland vol (mL)
1	Y	5		522	263.2	2.31	4.2
2	Y	5	Y	483	161.8	2.32	1.0
3	Y	5		497	323.0	2.70	4.2
4	Y	5		582	276.0	2.80	7.9
5	Y	5		802	63.1	2.37	1.6
6		4	Y	1136	615.0	2.74	4.2
7		4		261	259.2	2.09	0.8
8	Y	5		397	87.3	2.27	4.2
9†	Y	5		2223	263.0	2.36	4.2
10		4		396	89.1	2.45	0.5
11	Y	5	Y	399	-	2.66	5.9
12	Y	5		165	174.2	2.49	0.5
13		4		218	291.4	2.52	0.3
14	Y	5		1145	148.9	2.18	0.6
15	Y	5		609	201.0	2.50	0.5
16	Y	5		733	172.3	2.32	0.6
17		4		289	370.2	2.32	0.2
18	Y	5	Y	622	87.9	2.33	1.6
19	Y	5	Y	1087	264.6	2.30	1.6
20	Y	5		317	63.2	1.92	0.5
21	Y	5		227	142.4	2.55	1.8
22	Y	5	Y	124	74.7	2.53	0.5
23	Y	5		137	382.0	2.74	7.9
24		4		168	140.3	2.43	0.2
25	Y	5		68	161.0	2.83	0.2
26	Y	5		121	128.8	2.61	0.1
27	Y	5	Y	94	98.2	2.62	5.3
28	Y	5	Y	387	114.1	2.38	4.2
29	Y	5	Y	464	503.3	2.42	1.8
30	Y	5	Y	327	532.0	2.24	14.1
31		4		872	72.6	2.27	1.8
32		4		1864	628.6	2.43	4.2
33	Y	5		330	300.0	2.90	7.9
34		4		696	128.2	2.74	0.5
35	Y	5		2096	34.2	2.36	4.2
36	Y	5		898	112.4	2.69	7.9

ALP: alkaline phosphatase; Bisphos. bisphosphonates; CKD: chronic kidney disease; PTH: parathyroid hormone

† Outlier removed from analysis

Objective 1: Calcium Flux

The mean PER from the extracellular calcium pool was 2.97 mmol/h (95% CI, 2.68 to 3.26), occurring 26.6 hours (95% CI, 18.4 to 34.7) postoperatively. A scatterplot of PER against timing of peak efflux suggests a linear relationship between the variables. One clear outlier (No. 9) was identified on a plot of Cook's Distance against Centred Leverage Value. With outliers excluded, the scatterplot was recharted with a regression line (Fig. 2). A standardised residual plot was charted for PER, confirming both Homoscedasticity and Normality of distribution. This was further supported by a non-significant Kolmogorov-Smirnov test ($Z = 0.994$, $P = 0.276$) against a normal distribution.

Pearson's correlation coefficient was determined to be 0.539, suggesting a large correlation between PER and timing of peak calcium efflux.[14] However, a scatterplot of PER against preoperative ALP did not show any clear relationship between the variables. The 90th percentile for the rate of decline in serum calcium was 0.07 mmol/L/h, the 99th percentile was 0.10 mmol/L/h, and the 99.99th percentile was 0.14 mmol/L/h.

Objective 2: Excursions

Of the 36 patients, 13 had excursions below 2 mmol/L, 22 had excursions above 3 mmol/L, and 29 had excursions outside of the target range of 2 to 3 mmol/L. Mean duration of low excursions was 19.5% (95% CI, 13.8 to 25.3), mean duration of high excursions was 14.6% (95% CI, 7.3 to 21.9), and mean duration of all excursions was 19.8% (95% CI, 14.2 to 25.4) of the treatment periods. Mean trough calcium for low excursions was 1.74 mmol/L (95% CI, 1.64 to 1.84), and mean peak calcium for high excursions was 3.28 mmol/L (95% CI, 3.14 to 3.41). Lowest trough calcium recorded was 1.35 mmol/L and highest peak calcium was 4.32 mmol/L.

Objective 3: Time Course of Hypocalcaemia

Mean time of onset for hypocalcaemia was 2.0 days (95% CI, 1.1 to 3.0) after surgery. Mean duration of treatment with calcium gluconate in patients without hypocalcaemia was 2.4 days (95% CI, 2.0 to 2.8), while mean duration of treatment in patients with hypocalcaemia was 3.8 days (95% CI, 2.7 to 5.0). An independent samples *t*-test with unequal variances shows a significant difference between the 2 groups (P <0.05).

At the end of the treatment period, 4 patients had persistent hypocalcaemia, of which 3 had significant calcium efflux (Table 2). In the 9 patients who recovered, mean time to recovery was 3.5 days (95% CI, 2.1 to 5.0) after surgery. The 90th percentile for the time of onset for hypocalcaemia was 4.3 days after surgery, and the 90th percentile for time to recovery from hypocalcaemia was 6.3 days after surgery.

Objective 4: Titration regimen

The 90th percentile rate of infusion = (0.07 x 15) ÷ 0.2325 = 4.4 mL/h, the 99th percentile rate of infusion = (0.10 x 15) ÷ 0.2325 = 6.4 mL/h, and the 99.99th percentile rate of infusion = (0.14 x 15) ÷ 0.2325 = 9.0 mL/h.

When serum calcium is more than 2 mmol/L, the maximum interval between blood tests to prevent a fall below 1.6 mmol/L = (2 - 1.6) ÷ 0.07 = 5.9 hours. To prevent serum calcium from exceeding 3 mmol/L, the maximum time interval between tests for an infusion rate of 4.4 mL/h = (1.0 x 15) ÷ (4.4 x 0.2325) = 14.7 hours. The corresponding interval for an infusion rate of 6.4 mL/h = (1.0 x 15) ÷ (6.4 x 0.2325) = 10.1 hours, while the interval for an infusion rate of 9.0 mL/h = (1.0 x 15) ÷ (9.0 x 0.2325) = 7.2 hours.

From the study data, a reasonable titration regimen would be to check serum calcium and albumin immediately after surgery, and every 6 hours thereafter. An intravenous infusion of 10% calcium gluconate can be started at 4.5 mL/h when serum calcium falls below 2.0 mmol/L. If on the subsequent blood test serum calcium continues to fall, then the rate is increased to 6.5 mL/h and blood testing done on a 4-hourly basis. If serum calcium still falls in spite of this, then a rate of 9.0 mL/h can be used and this should be adequate for 99.99% of cases. The infusion can then be discontinued once serum calcium recovers above 2.0 mmol/L (Table 3).

Monitoring of serum calcium should be carried out for at least 4 days, which should pick up almost 90% of cases where hypocalcaemia will develop. Once hypocalcaemia is detected, monitoring should continue until serum calcium normalises and the calcium gluconate infusion is stopped. If hypocalcaemia is still present 6 days after surgery, which is the 90% upper limit for recovery, it is likely to be persistent. Provided there is no clinical evidence of neuromuscular irritability and the electrocardiogram is normal, the intravenous infusion should be stopped. The patient is then maintained solely on the preoperative dosage of oral calcitriol and calcium supplementation.[10]

In these patients, blood testing should still be on a 6-hourly basis for the next 24 hours, and if serum calcium falls more than 10%, the infusion should be restarted and the dosage of oral supplementation increased. For patients who maintain a stable calcium level on oral treatment, they can then be followed-up on an outpatient basis with further titration to keep serum calcium at the lower end of the normal range.

Discussion

Calcium shifts in the immediate postoperative period after parathyroidectomy for SHP are especially difficult to

Table 2. Patients with Persistent Hypocalcaemia

No	Final ca (mmol/L)	Final efflux (mmol/h)	10% threshold (mmol/h)	PER (mmol/L)
4	1.85	0.000	0.116	2.295
5	1.98	1.161	0.147	3.829
11	1.98	0.386	0.148	3.578
36	1.81	0.144	0.128	4.050

PER: peak efflux rate

Table 3. Infusion Regimen

Threshold ca (mmol/L)	Infusion rate (mL/h)	Test interval (h)
>2.0	Nil	6
<2.0	4.5	6
Ca. falls after infusion @ 4.5	6.5	4
Ca. falls after infusion @ 6.5	9.0	4

Preoperative oral calcium and calcitriol dose to be maintained. Monitor serum calcium for at least 4 days. If hypocalcaemia persists 6 days after surgery, discontinue infusion and continue monitoring for a further 24 hours.

characterise due to metabolic derangements caused by renal impairment, altered metabolism of vitamin D and PTH, renal bone disease, and intermittent dialysis. To overcome this, a simplified model was used in which the known calcium influx into the extracellular compartment from the infusion together with the change in serum calcium was used to calculate the net calcium efflux due to metabolic causes (Fig. 1). The advantage of using this simplified model is that quantitative estimates for overall calcium flux can be obtained without needing to determine each individual component. This also takes into consideration the effect of oral calcium and calcitriol supplementation.

The only variable that could not be accounted for was calcium movement as a result of dialysis, as retrospective data for calcium changes in the dialysate fluid were unavailable. It was, however, observed that each dialysis episode consistently caused a sudden net calcium influx of 0.5 to 5.5 mmol/h only for the next reading, and this returned to baseline subsequently. So for purposes of this study, the first reading immediately after a dialysis session was ignored to account for this effect.

It was hypothesised that the severity of renal bone disease is related to the magnitude of POH after parathyroidectomy for SHP, as was demonstrated previously in PHP.[12] However, no clear relationship was found on the scatterplot of PER against preoperative ALP. A possible reason for this is the increased prevalence of blood-borne hepatitis in haemodialysis patients, and could have been overcome if bone-specific ALP was available.[15,16] Gamma-glutamyl transferase and the liver transaminases are not useful in excluding a hepatic cause for raised ALP due to decreased enzyme levels in CKD.[17,18]

The relationship between severity of POH and its time course was also examined. A large positive correlation was found between PER and the timing of peak calcium efflux after surgery, suggesting that severe cases will experience their calcium trough later.

The single outlier excluded from analysis (No. 9) was an unusual case with the highest preoperative ALP reading in this study, and whose trough calcium was delayed until the 6th postoperative day. This was similar to the authors' previous study in PHP in which the single outlier also had extremely high ALP levels and concomitant vitamin D deficiency.[12]

Of the 36 cases analysed, 13 (36%) developed hypocalcaemia with onset mostly on the second to third postoperative day. Of these, 9 (25%) patients recovered early within a further 24 to 48 hours, while the remaining 4 (11%) patients had persistent hypocalcaemia at the end of the treatment period. The time course of hypocalcaemia seems to be delayed in SHP compared with previous studies on PHP, and is likely related to the increased severity of POH.[3,4] Of the 4 patients with persistent hypocalcaemia, 1 had normalised calcium levels 2 weeks after surgery. Unfortunately, follow-up records for the other 3 patients could not be traced as they had been transferred to hospitals in other states.

The current infusion regimen has a number of shortcomings. In spite of frequent blood testing, 29 (81%) out of 36 cases had excursions out of the target serum calcium range, with a tendency to over-replacement and hypercalcaemia. The main reason for this is the high initial infusion rate of 10 mL/h, which exceeds the replacement requirements in over 99.99% of cases. In addition, a standard titration regime was not used leading to significant variation between physicians in infusion rate adjustments.

Six-hourly blood testing appears to be adequate, although this should be cut down to 4-hourly if a higher infusion rate is needed to maintain serum calcium levels. Monitoring of serum calcium for 4 days should detect most cases of postoperative hypocalcaemia, and treatment is usually of limited duration. If hypocalcaemia persists 6 days after surgery, the infusion should be stopped. By this time, the patient is unlikely to have significant neuromuscular irritability, and maintenance on oral treatment should be safe. While this new regimen should prevent high calcium excursions, low excursions will still occur in about a third of patients, but this should not pose a significant risk provided the calcium gluconate infusion is started promptly on detection of hypocalcaemia.

By providing a timeframe for discontinuation of intravenous treatment, this will shorten the period of intensive calcium monitoring in patients with persistent hypocalcaemia, which in this current study was carried out for an average of 9 days after surgery. In 3 out of the 4 patients with persistent hypocalcaemia, the average efflux for the final 24 hours of treatment was significant, and close monitoring during the first 24 hours after discontinuation of intravenous therapy is advisable. Moreover, lowering the frequency of blood testing to 6-hourly when serum calcium is above 2.0 mmol/L should reduce the testing burden in the majority of patients who do not experience significant hypocalcaemia.

Bisphosphonate pre-treatment did not seem to make a significant difference to TSC or PER, a finding similar to the authors' previous study in PHP.[12] However, neither study was specifically powered to look for this effect.

While calculations of PER are useful in that they offer an insight into the dynamics of calcium movements after parathyroidectomy for SHP, it is uncertain how closely they reflect true calcium flux in patients given that the data was obtained retrospectively. In view of this, all computations related to the titration regimen were based on direct serum calcium measurements rather than derived indices

such as PER, so as to ensure that the resulting scale is as reliable as possible. In addition, the results from this study need validation in a prospective trial using the suggested infusion regimen in Table 3, and it is likely that further refinements will be needed before the regimen can be used with confidence.

There are a few areas in this study which could have been improved. Only 11 out of 36 patients met the K/DOQI criteria for parathyroidectomy in that they had severe hyperparathyroidism associated with hypercalcaemia refractory to medical therapy.[10] This could have resulted in more severe POH, with 4 of the patients developing persistent hypocalcaemia.

The use of ionised calcium instead of albumin-corrected serum calcium would have been preferable as there is some evidence to suggest that ionised calcium is superior in a dialysis setting.[19] However, this is not readily available in our centre and blood samples need to be collected under stringent conditions to ensure their reliability.

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