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การศึกษาเปรียบเทียบผลการติดของกระดูกขาทิเบียหักแบบปิด (AO classification 42A,42B,42C) ที่ได้รับวิตามินดี 2 และแคลเซียมภายหลังการผ่าตัด

Retrospective analysis of bone union rates in closed tibial shaft fractures (AO classification 42A,42B,42C) following vitamin D2 and calcium supplementation during post-operative treatment

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บทคัดย่อ

หลักการและเหตุผล : การให้วิตามินดีและแคลเซี่ยมภายหลังกระดูกหักช่วยให้กระดูกติดดีขึ้นในผู้ป่วย osteoporosis แต่ยังเป็นข้อถกเถียงในผู้ป่วยที่มีกระดูกขาทิเบียหักแบบปิด ว่าสามารถทำให้การติดของกระดูกดีขึ้นหรือไม่ เมื่อได้รับวิตามินดี 2 และแคลเซี่ยมภายหลังผ่าตัด

วัตถุประสงค์ : เพื่อหาว่าการให้วิตามินดี 2 และแคลเซี่ยมในผู้ป่วยกระดูกขาทิเบียหักแบบปิด สามารถเพิ่มอัตราการติดของกระดูกได้หรือไม่ เมื่อเทียบกับผู้ป่วยที่ไม่ได้รับ

วิธีการศึกษา : เป็นการวิจัยศึกษาแบบย้อนหลัง โดยการทบทวนเวชระเบียนผู้ป่วยกระดูกขาทิเบียหักที่ได้รับการรักษาที่โรงพยาบาลสุรินทร์ ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2555 - วันที่ 30 พฤศจิกายน พ.ศ. 2566 โดยเปรียบเทียบอัตราการติดของกระดูกระหว่างผู้ป่วยที่ไม่ได้รับวิตามินดี 2 (group 1) กับ ผู้ป่วยที่ได้รับวิตามินดี 2 และแคลเซี่ยม 1,000 มิลลิกรัม (group 2) ภายหลังการผ่าตัดดามกระดูก

ผลการศึกษา : ได้กลุ่มตัวอย่างทั้งหมด 202 คน โดยแบ่งเป็น 119 คน 83 คน ในกลุ่ม 1 และ กลุ่ม 2 ตามลำดับ พบอัตราการติดของกระดูกดังนี้ ร้อยละ 85.7 84.3 p=0.79 ซึ่งไม่มีนัยสำคัญทางสถิติ

สรุป : ผู้ป่วยกระดูกขาทิเบียหักแบบปิด ที่ได้รับการผ่าตัดดามกระดูกที่ได้รับวิตามินดี 2 และแคลเซี่ยม ภายหลังผ่าตัด พบว่าอัตราการติดของกระดูก ไม่มีความแตกต่างกันทางสถิติ

คำสำคัญ : วิตามินดี 2 กระดูกขาหักแบบปิด กระดูกทิเบียหักแบบปิด กระดูกทิเบียหัก อัตราติดของกระดูก แคลเซี่ยม

ABSTRACT

Background : While vitamin D and calcium have been shown to promote bone union in osteoporosis patients, there is controversy surrounding their effectiveness in accelerating union rates after operative treatment for closed tibial shaft fractures.

Objective : To compare the union rates between two groups of patients with closed tibial shaft fractures undergoing operative fixation: one group receiving vitamin D2 and calcium supplements (Group 2) and a control group without supplementation (Group 1).

Methods : A retrospective cohort study was conducted using electronic medical records from Surin Hospital for patients treated for closed tibial shaft fractures between January 1st., 2012, and November 30th., 2023. The primary outcome was the union rate, which was compared between two groups: those receiving vitamin D2 and calcium supplements and those who did not.

Results : A total of 202 patients met the inclusion criteria. One hundred nineteen patients did not receive vitamin D2 and calcium supplements (Group 1), while 83 patients received vitamin D2 and calcium at 1,000 mg (Group 2) post-operative fracture fixation. The union rate in Group 1 and Group 2 was 85.7% and 84.3%, respectively.

Conclusion : In patients with closed tibial shaft fractures undergoing operative fixation, there was no statistically significant difference in union rates between those who received vitamin D2 and calcium supplements and those who did not.

Keywords : vitamin D2, ergocalciferol, calciferol, close fracture shaft tibia, union rate, calcium.

Background

Vitamin D and calcium play a crucial role in the bone healing process. Studies in animal models, elderly patients, and those with osteoporosis or osteopenia with fractures have shown that vitamin D supplementation enhances bone healing and increases the strength of the callus.[1-4] It has also been observed that patients with long bone fractures often present with low blood levels of vitamin D (hypovitaminosis D) upon admission, with 40-89% of patients falling below the standard levels.[5-8] Additionally, during the treatment of tibial and femur fractures, serum vitamin D levels were found to decrease significantly.[9] As a result, vitamin D supplementation is commonly administered to fracture patients to improve bone healing rates.

However, a study on patients with long bone fractures who received vitamin D3 supplementation found no significant difference in bone union rates.[5] This has led to ongoing debate about whether vitamin D and calcium supplementation effectively improve bone healing in fracture patients. Previous studies included long bone fractures at various sites (humerus, femur, tibia) without specific categorization of the fracture types, and when focusing solely on tibial fractures, the sample sizes were small (11-18 subjects)[5,10], limiting the conclusiveness of the results. Moreover, there has been no study on the effects of vitamin D2 (ergocalciferol, calciferol) supplementation at a dose of 20,000 units (500 mcg) per week, in conjunction with calcium 1,000 mg, specifically in closed diaphyseal tibial fractures, in terms of union rate and union time.

This retrospective study utilizes patient records from Surin Hospital and radiographic images to assess bone healing in patients who have completed the treatment period as per the available medical records. The study focuses on patients who underwent plate, nail, or locking plate surgery, as no significant difference in bone union rates was observed among these surgical methods. The outcomes measured are the bone union rate and the union time following the administration of vitamin D2 at 20,000 units (500 mcg) per week and calcium at 1 g for a minimum of one month.

Objective

To determine whether vitamin D2 (ergocalciferol, calciferol) supplementation at a dose of 20,000 units (500 mcg) per week, along with calcium 1,000 mg for more than one month, improves bone healing in patients with closed tibial shaft fractures (Close fracture shaft tibial AO classification 42A, 42B, 42C) at the diaphysis, who have undergone open reduction and internal fixation (ORIF) with metal implants.

Secondary Objective: To evaluate if there is a difference in the union time of the fractures.

Methods

Study Designs

This is a retrospective cohort study using a quantitative research approach, conducted by reviewing OPD and IPD databases and electronic radiographs from Surin Hospital between January 1st., 2012, and November 30th., 2023, using the HosXP program. This study was approved by the Human Research Ethics Committee of Surin Hospital, with the approval number 64/2567, dated June 29th., 2024.

Participants

The baseline union rate of tibial fractures from previous studies was around 90%.[11-13] Sample size calculation was based on the hypothesis that vitamin D2 and calcium supplementation would increase the bone union rate by 10% from the baseline rate. Since no previous studies have directly investigated this specific approach, the researchers proposed that a 10% improvement in the union rate would be a cost-effective outcome for treatment. The study was conducted with a 95% confidence level and 80% power. The calculated sample size required at least 74 participants in each group, using the n4study program for sample

size calculation.[14-16] Inclusion criteria included patients aged 18 to 60 years, closed fracture shaft of tibia (AO classification 42A, 42B, 42C), post-operative X-ray with evidence of bone union at least 24 weeks after surgery; if X-ray not seen bridging bone at least one cortex in AP view and at least one cortex on the lateral view at 4 weeks, follow-up X-rays must be available for at least 16 weeks in definition of delay-union and 24 weeks in definition of non-union, underwent ORIF with narrow plate and screw, narrow locking plate, or interlocking nail. Exclusion criteria were patients with multiple bone injuries, intracranial hemorrhage, hemiplegia or paraplegia, have undergone bowel resection or nephrectomy, patients with conditions affecting calcium absorption and excretion, chronic kidney disease (ESRD), hyperparathyroidism, fixation gap greater than 3 mm, osteopenia or osteoporosis.

Statistical Analysis:

Descriptive statistics were used to describe general characteristics of the population, including frequency distribution, percentages, and standard deviation. Chi-square tests were used to compare union rates, nonunion rates, delayed union rates, underlying diseases, and fractures according to AO classification. The student's t-test was used to compare union times. Statistical analysis was performed using Microsoft Excel 365 version 2403 (Build 17425.20176).

Definitions in the Study:

1. **X-ray Union:** Assessed by an orthopedic specialist using radiographs, defined by the presence of bridging bone in at least one cortex on AP view and at least one cortex on the lateral view.[17,18]

2. **Delayed Union:** Defined as the absence of X-ray union at 16 weeks.

3. **Nonunion:** Defined as the absence of X-ray union at 24 weeks.

4. **Union Rate:** The proportion of fractures that achieve X-ray union within 24 weeks relative to the total number of operated patients, expressed as a percentage.

5. **Union Time:** The duration required for X-ray union within 24 weeks.

6. **Delayed Union Rate:** The proportion of patients experiencing delayed union relative to the total number of operated patients, expressed as a percentage.

7. **Nonunion Rate:** The proportion of patients experiencing nonunion relative to the total number of operated patients, expressed as a percentage.

8. **Infection:** Defined as documented wound infection, redness, or receipt of antibiotics beyond two weeks post-surgery without other recorded causes, during the fracture healing period of at least two weeks.

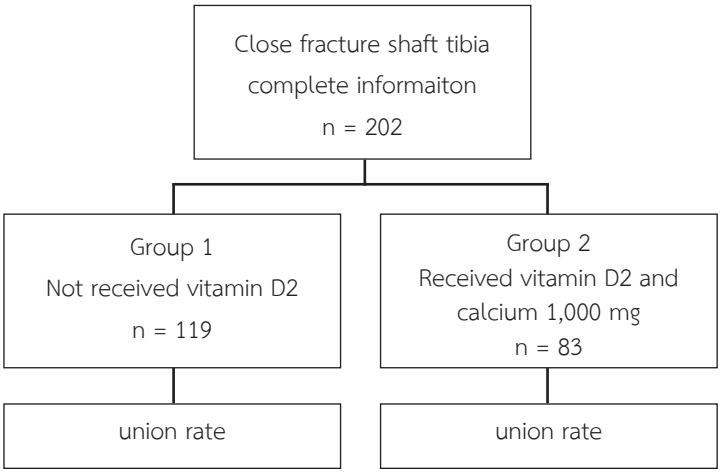

Figure 2: Study Methodology.

Results

A total of 202 patients with closed tibial fractures met the study criteria, consisting of 152 males and 50 females. The participants were divided into two groups: 119 patients in Group 1 (no vitamin D2 supplementation) and 83 patients in Group 2 (received vitamin D2 and 1,000 mg of calcium). There were no statistically significant differences between the two groups in terms of sex, smoking status, co-morbidities, use of nonsteroidal anti-inflammatory drugs (NSAIDs), fracture type according to AO classification, the proportion of surgical fixation methods used, post-operative infection rates, incidence of instrument failure, or the time to surgery after fracture. However, the mean age was significantly different between the groups (Table 1).

Table 1: Baseline Characteristics of the Patients

Characteristics	Group 1 control (n = 119)	Group 2 Vitamin D2 and calcium (n = 83)	p-value
Age (yrs.), mean(±SD)	34.9±13.2	39.4±17.6	0.048*
Sex (Male: Female)	86:33	66:17	0.24
Smoking	33	25	0.71
NSAID received	19 (16.0%)	11 (13.3%)	0.59
Infection rate	10 (8.4%)	12 (14.5%)	0.17
Instrument failure rate	5 (4.2%)	3 (3.6%)	0.83
Underlying disease	10	9	0.56
HT	5	4	
DM	1	0	
HT/DM	1	4	
HIV infection	3	1	

Table 1: Baseline Characteristics of the Patients (ต่อ)

Characteristics	Group 1 control (n = 119)	Group 2 Vitamin D2 and calcium (n = 83)	p-value
Fracture AO classification			0.75
42A*	82 (68.9%)	53 (63.9%)	
42B*	31 (26.1%)	25 (30.1%)	
42C*	6 (5.0%)	5 (6.0%)	
Operation			0.15
ORIF narrow plate	70 (58.8%)	39 (47.0%)	
ORIF LCP	47 (39.5%)	40 (48.2%)	
ORIF nail	2 (1.7%)	4 (4.8%)	
time to operation			0.48
0-1 day	68 (57.1%)	51 (61.4%)	
2-7 day	38 (31.9%)	27 (32.5%)	
8-21 day	13 (10.9%)	5 (6.0%)	

*p-value < 0.05

Table 2: Bone Union Rate and Union Time

	Group 1 control (n = 119)	Group 2 Vitamin D2 with calcium (n = 83)	p-value
Union rate (%)	85.7%	84.3%	0.79
Nonunion rate (%)	14.3%	15.7%	0.79
Delay union rate in 16-24 wks. (%)	25.2%	19.3%	0.43
Union rate in 16 wks. (%)	60.5%	65.1%	0.51
Union time (wks.) ±SD	10.6±3.6	11.2±3.5	0.33

*p-value < 0.05

There was no statistically significant difference between the groups in bone union rate, union time, delay union rate, and nonunion rate (Table 2).

Discussion

The baseline characteristics showed that the group receiving vitamin D2 and calcium was, on average, 5 years older than the group that did not receive these supplements, with this difference being statistically significant. This factor may contribute to a lower bone union rate in the group not receiving vitamin D2. The overall union rate for both groups ranged from 84.3% to 85.7%, which is lower than previously reported rates of 90.6% to 97.5% in studies by Phieffer, et al., Zura R, et al., and Tian R, et al.[11-13] Several factors might explain this discrepancy, such as the definition of nonunion this study defined nonunion as absence of union

by 24 weeks, whereas Morshed S. used a timeframe of more than 36 weeks.[17] Additionally, the evaluation of bone healing in this study was based on radiographic evidence of callus bridging of cortices, with an intraclass correlation coefficient (ICC) of 0.75, which is lower than the ICC of 0.86 associated with the RUST score.,[18,19] potentially leading to discrepancies in union assessments. Differences in follow-up schedules, variations in surgical fixation methods, the use of NSAIDs postoperatively (13.3-16.0% in each group), and a higher infection rate (8.4-14.5%) compared to 1.6% reported by Doshi P et al.[20] might also have influenced the results.

The union rate was 85.7% in the group not receiving vitamin D, compared to 84.3% in the group receiving vitamin D2 and calcium, with no statistically significant difference between the groups. Therefore, in the group receiving vitamin D2 supplementation at a dose of 20,000 units (500 mg) per week, along with calcium 1,000 mg for more than one month, there was no observed improvement in bone healing in patients with closed tibial shaft fractures (AO classification 42A, 42B, 42C) who had undergone open reduction and internal fixation (ORIF). This could be due to the small sample size or selection bias, where patients who appeared to be at higher risk for delayed healing were more likely to receive vitamin D2 and calcium supplementation. As a result, the supplementation group may have appeared to have worse outcomes despite these interventions.

The delay union rate was 25.2% in the group not receiving vitamin D2, compared to 19.3% in the group receiving vitamin D2 and calcium, suggesting a trend toward a lower delay union rate in the supplemented group, though this difference was not statistically significant. The mean union time was 10.6±3.6 weeks in the group not receiving vitamin D2, compared to 11.2±3.5 weeks in the group receiving vitamin D2 and calcium, with no significant difference between the groups.

Limitations

This study utilized vitamin D2, which differs from previous studies that often-used vitamin D3 (calcitriol). Furthermore, blood levels of vitamin D were not measured prior to treatment, which might explain the lack of difference in union rates between groups. This retrospective study required at least one month of vitamin D2 and calcium supplementation post-surgery; however, the dosage and duration of vitamin D2 supplementation varied, with some patients receiving 20,000 units of vitamin D2 on different schedules (Monday, Wednesday, Friday; weekly; or starting 1 to 3 months postoperatively), potentially affecting the union rates. Additionally, variability in postoperative care, such as early weight-bearing leading to hardware failure or subsequent surgeries, might have influenced outcomes. A retrospective power analysis indicated that a larger sample size would be required to detect differences, as this study was limited to data from Surin Hospital over a 10-year period with fewer than 100 cases per group, although this is more than previous studies like Haines N, et al.[5], which had 17-18 cases per group.

Recommendations

Based on this study, a union rate of 85.7% was observed. To detect a 10% difference in effect size, a sample size of 131 patients per group would be needed. Therefore, a multicenter study with a randomized prospective controlled trial design is recommended to increase sample size and reduce selection bias. Consistent dosing and type of vitamin D supplementation would also be beneficial.

Conclusion

Among patients with closed tibial shaft fractures who underwent surgical fixation, supplementation with vitamin D2 (ergocalciferol) at 20,000 units per week or more, along with 1,000 mg of calcium postoperatively, did not significantly affect the union rate or union time compared to those who did not receive these supplements.

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