Bone metabolism in children with severe fractures was examined, risk factors for fractures were characterized, and effects of LED (light-emitting diode) irradiation on the risk factors for fractures were investigated. Since insufficiency fracture in children with severe cerebral palsy can be caused without obvious external force in daily care, it is sometimes handled as a medical accident and can lead to a lawsuit. It is very important to explain the possibility of an insufficiency fracture to guardians before a fracture is caused. However, risk factors for fractures in bone metabolism has not been well investigated and preventive treatment of fractures have also not been established. Risk factors in bone metabolism were investigated in 14 cases of insufficiency fracture in children with severe cerebral palsy accompanied by akathisia in this study. Fractures were likely caused around 8 years old when children grew rapidly, and either IGF-1 or BAP showed low values in all cases. A group with LED irradiation consisting of 25 cases indicated a normal value of IGF-1 related to bone growth, BAP related to bone density and NTX/Cr. A case irradiated to LED for more than one month clearly showed normal bone metabolism compared with the change within a non irradiated group after one year. LED irradiation increased bone density and femur cortical bone thickness, and improved bone age. Adequate effects were not seen in two children at 14 years of age. The commercially available LED light bulbs that we used have a peak at 446-477 nm in the blue wave length, but also have second peaks at 574 nm in green, at 590 nm in yellow, and even 612 nm in orange and 660 nm in red are included. Although it is thought that such a variety of wave lengths might have a good influence on bone metabolism; exposure time and distance, number of regions, and time period irradiated to LED are important factors, since the LED power density is low (0.9 mW/m² with a 30 cm distance). Our results suggest that LED irradiation can be a phototherapy to activate human homeostasis.
ture, and examined effects of LED (light-emitting diode) irradiation on bone density, bone age, and bone metabolism in children with severe cerebral palsy.

Patients and Methods

Bone density, bone alkaline phosphate (BAP; osteogenic marker), type I collagen cross-linked N-telopeptide (NTX; urinary bone resorption marker), and insulin-like growth factor-1 (IGF-1) were examined using 14 cases of insufficiency fracture in children with severe cerebral palsy accompanied by akathisia. Bone density was investigated using the digital image processing (DIP) method. Two cases were investigated from before the fracture, and the other cases were examined more than one year after fracture.

LED irradiation was performed on 25 children with spastic quadriplegia accompanied by akathisia (12 boys and 13 girls), and their age was between 5 to 18 years old, with the average at 8 years of age.

For LED irradiation, the LDA9DH EVERLEDS (100 V/9.2 W) LED lamp made by Panasonic Corp. was used. Limbs were irradiated on a bed for 60 minutes per day using four LED bulbs (825 lm, wave length: 400-700 nm) for all 25 cases. The shortest irradiation period was for one month and the longest one was for two years. Bone density, bone age, bone metabolism BAP, NTX, and IGF-1 were continuously investigated before and after irradiation, and they were compared with a rate of change of BAP, NTX, IGF-1 and bone density after one year in 57 cases of akathisia without LED irradiation (average age: 8 years). The thickness change of femur cortical bone in the supracondylar femur, which tends to have a vulnerability to fracture, was also examined by CT before and after irradiation.

These studies were conducted based on the approval of the ethics board at Shinano Handicapped Children’s Hospital and with the guardians’ consent in all cases.

Results

The average age when fractures were caused was 8 years of age in 14 cases of insufficiency fracture, and either IGF-1 or BAP showed low values in all cases; low BAP and IGF-1 values were observed in 11 and 9 cases, respectively. Bone density was low in 8 cases. NTX/Cr increased in 4 cases, decreased in 5 cases and changed from increase to decrease in 3 cases. As many as 12 cases showed low values with multiple markers, IGF-1, BAP, and bone density.

After LED irradiation, the IGF-1 value improved to normal levels in 5 out of 8 cases with low IGF-1 values. The average rate of change in the group without irradiation after one year was 0.12, and clear increases were seen in the group with LED irradiation (p<0.001) (Fig. 1). The BAP value also improved to normal levels in 7 out of 13 cases with a low BAP value after irradiation. The average rate of change in the group with-
out irradiation after one year was -0.02, and clear increases were seen in the group with irradiation (p<0.001) (Fig. 2). The NTX/Cr value improved to a normal level in 5 out of 8 cases with low NTX/Cr values. The average rate of change in the group without irradiation after one year was -0.1, and clear increases were seen in the group with irradiation (p<0.05) (Fig. 3). The NTX/Cr value also improved to normal levels in 4 out of 6 cases with a high NTX/Cr value. In cases that were irradiated intermittently, NTX/Cr returned to a high value after reaching normal levels with irradiation, and decreased again when irradiation resumed.

Light-Emitting Diode(LED) irradiation in insufficiency fractures

Fig. 2: The BAP value also improved to normal levels in 7 out of 13 cases with a low BAP value after irradiation. The average rate of change in the group without irradiation after one year was -0.02, and clear increases were seen in the group with irradiation (p<0.001).

Fig. 3: The NTX/Cr value improved to a normal level in 5 out of 8 cases with low NTX/Cr values. The average rate of change in the group without irradiation after one year was -0.1, and clear increases were seen in the group with irradiation (p<0.05).
The bone density increased after LED irradiation. The average rate of change in the group with irradiation after one year was 16.86±17.6, while in the group without irradiation was 3.34±6.87 (p<0.05) and healthy children (from 5 to 18-year-old) were 6.66±4.05 (p<0.05), and clear increases were seen in the group with irradiation (Fig. 5). Regarding the course of bone density and bone age, in an 8-year-old boy with severe cerebral palsy, bone density increased after irradiation and the bone age of the carpal bone also improved;
the bone age was 3 years 6 months old at age 8 and it turned to 9 years old at age 10 (Fig. 6). Also in a case of a 5-year-old child with severe cerebral palsy, bone age improved from 2 years 6 months old to his age at one year after irradiation (Fig. 7). In a case of an 8-year-old child with severe cerebral palsy, intermittent irradiation was performed 15 days per month on average at home and continued in total for one year. Before irradiation, the BAP was low at 35.8 but it increased to 66.2 after irradiation; NTX/Cr was high at

**Bone density and bone age**

![Graph showing bone density and bone age](image)

**Fig. 6:** Severe cerebral palsy, 8-year-old boy: Bone density increased after irradiation and the bone age of the carpal bone also improved; the bone age was 3 years 6 months old at age 8 and it turned to 9 years old at age 10.

**Bone age**

![Images of bone density at different ages](image)

**Bone age:**

- **Bone age: 3 year 6 months**
  - Age: 8 year old
  - 9 year old

**Fig. 7:** Severe cerebral palsy, 5-year-old girl: Bone age improved from 2 years 6 months old to his age at one year after irradiation.
Discussion

Risk factors regarding bone metabolism for insufficiency fracture in children with severe cerebral palsy are not clear. It is known that fractures tend to be caused around 13 years of age when children grow rapidly through bone development, even in healthy children. This investigation on 14 cases of insufficiency fracture in children with severe cerebral palsy showed that fractures were caused at an average of 8 years of age, and also indicated that a fracture tends to be caused during the bone development period. Regarding bone metabolism, either IGF-1 or BAP showed low values in all cases and NTX/Cr did not have a clear trend, including cases with high and low values and cases that changed value from high to low. Based on this result, it is necessary to improve low IGF-1 and BAP values and to normalize NTX/Cr to prevent insufficiency fractures. But currently, because there is no treatment to improve IGF-1 and regarding BAP and NTX/Cr no osteogenesis promoting agents are applicable for children and no therapy is available to accelerate bone resorption; therefore, preventive treatment of insufficiency fractures in children with severe cerebral palsy have not been established.

In this study, LED irradiation normalized the low values of IGF-1 related to bone development, low values of BAP related to bone density, and high and low NTX/Cr values. A group with irradiation for more than one month showed a clear improvement when compared with the rate of change of a control group, the average 8 years old children with severe cerebral palsy without irradiation, after one year. Regarding BAP and NTX/Cr, the group with irradiation also showed a clear improvement compared with a least significant change, which is an indicator for improvement in adult pharmacotherapy. Cases irradiated intermittently revealed the effectiveness of LED irradiation; irradiation interruption deteriorated the condition and irradiation resumption improved the condition again. Although bone density did not change for a short time, when irradiation was continued over time, bone density and bone age of the carpal bone also improved after an improvement of bone metabolism. LED irradiation improved IGF-1 (for which no treatment is available until now) and also improved bone metabolism more than pharmacotherapy without concern for side effects; therefore it becomes clear that LED irradiation can be a dream treatment for children with severe cerebral palsy.

We previously reported the possibility of changing in markers of bone metabolism after LLLT 3). Regarding the markers of bone metabolism, the group with LED irradiation showed a clear improvement compared with the group with LLLT irradiation. But the exact comparison was not completed, because of the discrepancies between the irradiation conditions.

The characteristics of LED include easily obtaining a light that does not contain unnecessary ultraviolet or infra-red rays, as opposed to many light sources such as sunlight, fluorescent light, and incandescent light; LED are safer and more efficient than sun bathing. Although it is known that VD increases after sun bathing, but no consensus has been reached about the effectiveness of bone metabolism.

Regarding two cases where adequate effects were not seen, the declined homeostasis because of a relatively older age at 14 years old with severe impairment was thought to be a reason for the insufficient effect. Cases with insufficient improvement were seen with commercially available LED machines with only a blue wave length. The commercially available LED light bulbs that we used in this investigation have a peak at 446-477 nm in a blue color wave length, but also have second peaks at 574 nm in green and at 590 nm in yellow and even include 612 nm in orange and 660 nm in red. We think that such a variety of wave lengths has a good influence on bone metabolism 5). Since LED light bulbs are commercially available and their power density is low, 0.9 mW/m2 with a 30 cm distance, irradiation time and distance, number of regions, and time period irradiated to LED are important factors 2).
Bone density by the digital image processing

a)

The thickness change of femur cortical bone

b) Irrad. period for 1year

Before irrad. 1year 6months 2year 4months

Figs 8: 8-a) Severe cerebral palsy, 8-year-old girl: Intermittent irradiation was performed 15 days per month on average at home and continued in total for one year. Before irradiation, the BAP was low at 35.8 but it increased to 66.2 after irradiation; NTX/Cr was high at 830.7 before irradiation but it turned to 639.1, a close to normal level; and bone density also increased.

8-b) Thickness of the cortical bone in the supracondylar femur became thick and the increase of cortical bone thickness was also observed by CT measurement over time.
dren with severe cerebral palsy.
2) LED irradiation normalized values of IGF-1 related to bone growth, and BAP and NTX/Cr related to bone density.
3) LED irradiation increased bone density and improved femur cortical bone thickness and bone age.
4) LED irradiation can be a safe and inexpensive therapy that is performable at home to prevent insufficiency fracture in children with severe cerebral palsy by activating human homeostasis.

References