



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Factors Affecting Bisphosphonate Therapy Compliance in Patients With Osteogenesis Imperfecta

Yoyos Dias Ismiarto^{1*}, Firdaus Ramli F¹, Doddy Putra Pratama Sudjana¹, Naufal Chairulfatah¹, Wendy Yolanda Rossa¹

¹Department of Orthopedic & Traumatology, Faculty of Medicine, Universitas Padjajaran/ RSUP Hasan Sadikin, Indonesia

ARTICLE INFO

Keywords:

Osteogenesis Imperfecta
Bisphosphonate
Compliance

*Corresponding author:

E-mail-address:

yoyosmiartounpad@gmail.com

(Yoyos Dias Ismiarto)

All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.32539/bsm.v4i4.170>

ABSTRACT

Introduction. Osteogenesis imperfecta (OI) is a genetic disease with clinical manifestations in patients' bones. This study aims to investigate the factors that influence the compliance of bisphosphonate in patients with OI.

Methods. A cross-sectional analysis method was conducted and data were obtained from questionnaires answered by OI patients that received bisphosphonate. The data obtained were statistically analyzed using chi-square.

Results. There were 121 OI patients, age range 0-5 years (62%). Almost all patients have insurance from national health (BPJS). In this study, the average treatment compliance was 81.7%, and patients were reported to have good medication compliance of $\geq 80\%$ of the treatment cycle, which was shown in 65 patients (53.7%). However, there is a relationship between parent education and treatment compliance ($P = 0.046$).

Conclusion. Good treatment compliance describes when the patient performs $\geq 80\%$ of its cycle. Factors affecting it are the condition of the patient and the location of health services. Therefore, there is a relationship between compliance with the number of treatment cycles.

1. Introduction

Osteogenesis imperfecta (OI) is a genetic disorder with a prevalence of 1 to 10,000 – 20,000 births. Clinical manifestations in patients' bone include decreased mass, brittleness, and connective tissue disorders. It is caused by an abnormality in type I collagen, and its incidence rate is observed on 1 per 20,000 – 50,000 live births. Furthermore, it does not correlate with specific gender or race, and it is classified into subtypes based on clinical manifestations and histological findings, as well as by dominant or autosomal genetic mutation inheritance pattern.¹⁻⁴

Management of this disease in patients aims to reduce fracture risk, prevent bone deformation,

and alleviate pain. However, due to the underlying etiology of the disease being a genetic disorder, and the managements are grouped into pharmacological, surgical intervention, and psychosocial therapy. In contrast, orthopedic management includes bracing, splinting, and orthotic. A common surgical intervention is rodding, which is placing metal material into a long bone to strengthen it and therefore, reduce the fracture risk. Pharmacological management includes growth hormone therapy, bisphosphonate administered orally or intravenously and gene therapy.²⁻⁴

Osteogenesis imperfecta is a chronic disease with long-term management that are given at certain

intervals. Its treatment success depends on the patient's management compliance. A study in Argentina on OI pediatric patients concluded that better compliance results in good quality of life. The management compliance depends on the number of treatment cycles assigned to patients, and it is declared as good when they have received at least 80% of the therapy cycle. There are several reasons for patients not to be absent and not compliant with treatment, these include duration, surgery, the occurrence of fracture, or sometimes with no reason. Other possible speculations are the length of stay in the hospital, which requires at least 3-days of infusion.⁷⁻⁹

Studies that are related to factors affecting therapy compliance in patients with osteogenesis imperfecta are rarely conducted. Their quality of life is highly dependent on compliance with therapy. Therefore, this study intends to study the factors affecting therapy compliance in patients with osteogenesis imperfecta in Hasan Sadikin Hospital, Bandung.

2. Methods

This is a retrospective analytical study, which is above all an investigative method that aims to broaden the research questions through a cross-sectional approach. Furthermore, it analyzed the relationship between each study variable. The subjects were parents of pediatric patients diagnosed with osteogenesis imperfecta that received bisphosphonate therapy and are willing to fill in a questionnaire regarding OI from January 1st – March 31st, 2020. Also, they met the inclusion criteria but not the exclusion criteria. The inclusion criteria were pediatric patients diagnosed with osteogenesis imperfecta that received bisphosphonate therapy, willing to fill in the questionnaire, and registered in Dr. Hasan Sadikin Hospital from January 1st – March 31st, 2020. In contrast, those that were not willing to fill in the questionnaire and did not receive bisphosphonate therapy were excluded. Data

obtained will be analyzed using SPSS and presented in the form of a table and graphic.

3. Results

There were 121 subjects of 45 (37%) males and 76 (63%) females. Their age was divided into two interval groups. There were 75 (62%) subjects aged 0-5 and 46 (38%) >5 years old. The age and gender characteristics of individuals are presented in Figure 1. In addition, the characteristics of therapy compliance were assessed based on the presence or absence of national health insurance, parental income, occupation, and education. Both in male and female subjects have a higher number of compliant patients, 25 (55.5%) out of 45 in male and 40 (52.6%) in females. There are also higher number of compliant patients in both age groups. Out of 75 subjects aged 0 – 5 years old, 54.6% of them were complaints. Similarly, out of 46 subjects aged >5 years old, 52.1% of them were complaints to the therapy given.

These groups are classified into national health and private insurance. In both groups, most patients were compliant with the therapy received. Regarding the national health insurance group, the percentage of compliant subjects was 51.0%. In the contrary, the percentage of complaint subjects was 65.2% for the private insurance group. The difference in treatment compliance based on parental income are presented in figure 4, and was classified into low (< Rp 500,000,00), middle (Rp 500,000,00 to Rp 2,500,000,00) and high income (> Rp 2,500,000,00) groups. The number of compliant subjects were higher in the low parental income group. However, in the middle and high parental income groups the number of compliant and non-compliant subjects was balanced. The difference in therapy compliance based on parental occupation is presented in figure 5, and it is classified into unemployed (housewives) and employed group. Both groups have a higher number of compliant subjects than non-compliant ones. 50.7% in the employed and 57.4% in the unemployed group were compliant. It is classified

into low (elementary, and junior high school), middle (senior, and vocational high school) and high education (diploma, bachelor, and profession). In the low education group, 100% of the subjects were not compliant. 57.6% and 54.3% were the subjects in the middle and high education groups that were respectively compliant to therapy. Factors affecting therapy compliance were analyzed to examine the correlation between variables, based on age and gender using Chi-square. A p-value was obtained to

determine the statistical relationship between variables (Table 1). It can concluded that there are no correlation between therapy compliance in patients with OI and, gender (P = 0.755), age (P = 0.790), insurance type (P = 0.219), parental income (P = 0.730), parental occupation (P = 0.534). On the contrary there is a correlation between parental education and therapy compliance in patients with OI (P = 0.046).

Table 1. Correlation Analysis of Factors Affecting Therapy Compliance

Variable	Therapy Compliance	
	Df	P-value
Gender	1	0.755
Age	1	0.790
Insurance	1	0.219
Parental Income	2	0,730
Parental Occupation	1	0,534
Parental Education	2	0,046

4. Discussions

This study analyzed 121 parents of pediatric patients diagnosed with osteogenesis imperfecta receiving bisphosphonate therapy at RSUP Dr. Hasan Sadikin from January 1st, - March 31st, 2020. This study examines the factors that influence patient compliance with medication. There was no significant relationship between age (P = 0.755) of the patients and gender (P = 0.790). Also, the number of compliant subjects was higher in males compared to females. This contradicts research conducted by Lertmarharit et al, Choi Kwon et al., which stated that female patients have better compliance than males.^{4,5} Meanwhile, research conducted by Vic et al, stated that there is no relationship between gender and compliance.⁶⁻⁹

Bisphosphonates are among the most commonly used treatment options, apart from, surgical intervention, psychosocial growth hormone, and gene therapies.² It has a long duration of treatment, depends on the response of each individual, and requires healthcare personnel guidance in drug's administration. Compliance of the

patient depends on the number of treatment cycles received. In addition, it is declared as good when the patient underwent at least 80% of the therapy cycle.⁷ There are several reasons for patients to be absent and not compliant with treatment. These include duration, surgery, the occurrence of fracture, or sometimes absent with no reason.³ However, research on the factors that influence treatment compliance of patients with osteogenesis imperfecta has never been conducted. Meanwhile, the quality of life is very dependent on patient compliance to the therapy.⁴⁻⁹

In addition to investigating the relationship between the gender and age, this research also examined the relationship between the type of insurance used, such as those using national health and private insurance; parental income, that is low (<Rp. 500,000), moderate (Rp. 500,000 - Rp. 2,500,000), and high income (> Rp. 2,500,000), and parents' occupation with compliance. These factors are related to the socio-economic condition of the patient and family members. In this study, no relationship was reported between the type of insurance used (P = 0.219), parental income (P = 0.694), and occupation (P = 0.465) with compliance.

Likewise, economic factors are related to the expenses spent during treatment and parents' income. According to Swett et al., and Degoulet et al., those that do not have insurance and people with low incomes respectively possess the tendency to be non-compliant to treatment.^{8,9} Also, patients with health insurance may have problems related to the expenses that need to be paid. A study in Singapore by Wai et al. showed that there was no relationship between low monthly income and compliance in chronic hepatitis B patients.⁷⁻¹⁰

Another factor included in the analysis, that is assumed to be related to patient compliance is the level of education of the parents. It is categorized into the low, moderate, and high level of education of those that finished primary and junior high school, those that completed senior high school and vocational education, and those that equivalent to the associate, undergraduate, or professional training degree respectively. In this study, it was reported that there was a relationship between parents' level of education and patient compliance ($P = 0.046$), that is, the higher it is, the better patient compliance will be. This is in line with the study of Okuno et al., which states that the higher the level of education, the higher the patient compliance.¹¹ This increase is likely related to the better knowledge they have about the disease and the required therapy which will eventually increase compliance.⁸⁻¹² However, a study in the United Kingdom showed that groups of patients without high formal education were more compliant with treatment. This is because patients with a low levels of education trust their doctor more and with that, they strictly follow instructions.⁷⁻¹³ Therefore, the level of education is sometimes not the main predictor for determining patient compliance.¹⁰⁻¹²

The advantage of this study is that there is no previous one conducted to directly examine the factors influencing patient compliance. As a result, it can be used as consideration for more extensive studies. On the contrary, this can also be a

disadvantage since it will be difficult to compare with similar ones in other countries. This study analyzed and compared data related to patient compliance with osteogenesis imperfecta with others related to its principles in general.

5. Conclusion

The factor associated with compliance in patients with osteogenesis imperfecta receiving bisphosphonate therapy is the level of education. Meanwhile, age, gender, and economic factors did not have a significant relationship between the compliant and non-compliant groups of bisphosphonate treatment.

6. References

1. Beary JF, Chines AA. Osteogenesis imperfecta. UpToDate. 2020.
2. Alharbi S. A Systematic Overview of Osteogenesis Imperfecta. *Molecular biology*. 2015;05.
3. Pinheiro B, Zambrano M, Vanz A, Brizola E, Souza L, Félix T. Cyclic pamidronate treatment for osteogenesis imperfecta: Report from a Brazilian reference center. *Genetics and Molecular Biology*. 2019;42.
4. Lertmaharit S, Kamol-Ratankul P, Sawert H, Jittimanee S, Wangmanee S. Factors associated with compliance among tuberculosis patients in Thailand. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet*. 2005;88 Suppl 4:S149-56.
5. Choi-Kwon S, Kwon SU, Kim JS. Compliance with risk factor modification: early-onset versus late-onset stroke patients. *European neurology*. 2005;54(4):204-11.
6. Vik SA, Maxwell CJ, Hogan DB. Measurement, correlates, and health outcomes of medication adherence among

- seniors. *The Annals of pharmacotherapy*. 2004;38(2):303-12.
7. Herring JA, Tachdjian MO, Texas Scottish Rite Hospital for C. Tachdjian's pediatric orthopaedics. Philadelphia: Saunders/Elsevier; 2008.
 8. Swett C, Jr., Noonan J. Factors associated with premature termination from outpatient treatment. *Hospital & community psychiatry*. 1989;40(9):947-51.
 9. Degoulet P, Menard J, Vu HA, Golmard JL, Devries C, Chatellier G, et al. Factors predictive of attendance at clinic and blood pressure control in hypertensive patients. *British medical journal (Clinical research ed)*. 1983;287(6385):88-93.
 10. Wai CT, Wong ML, Ng S, Cheok A, Tan MH, Chua W, et al. Utility of the Health Belief Model in predicting compliance of screening in patients with chronic hepatitis B. *Alimentary pharmacology & therapeutics*. 2005;21(10):1255-62.
 11. Okuno J, Yanagi H, Tomura S. Is cognitive impairment a risk factor for poor compliance among Japanese elderly in the community? *European journal of clinical pharmacology*. 2001;57(8):589-94.
 12. Jin J, Sklar GE, Min Sen Oh V, Chuen Li S. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag*. 2008;4(1):269-86.
 13. Senior V, Marteau TM, Weinman J. Self-reported adherence to cholesterol-lowering medication in patients with familial hypercholesterolaemia: the role of illness perceptions. *Cardiovascular drugs and therapy*. 2004;18(6):475-81.