THE CORRELATION OF LOW DOSE AND LONG TERM CORTICOSTEROID THERAPY ON OSTEOPOROSIS IN PATIENT WITH CHRONIC DISEASE: A SYSTEMATIC REVIEW

Muhammad Brahma Dwianandra [a *], Pradana Zaky Romadhon [b,] Andre Triadi Desnantyo [c]

[a] Medical Program - Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia

[b]Department of Internal Medicine - Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

[c] [b]Department of Orthopedic - Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Abstract

Background: Corticosteroids are frequently used as immunosuppressants and strong anti-inflammatories; some patients must take the medicine for more than three months. In the general population, 2% of women under the age of 50 take corticosteroids, particularly in the case of patients with chronic diseases who do so as a form of treatment. A total of 19.6% to 38% of the population who took corticosteroids went on to develop glucocorticoid-induced osteoporosis.

Method: The method is looking for articles which consist of many study design which include the data upon patient with chronic disease who consume corticosteroid more than 3 months and most of the study population consume low dose. The patient bone mineral density assessment is using DXA scan, no diabetic patient included, patient consume supplementation or treatment for osteoporosis, and paediatric patient also excluded. For the article from databases we exclude review article, experimental study, and we only include English language article only.

Result: results of bone mineral density from DXA scan shows that femoral neck t score show -0,30 and other two Z score show -0,29 and -0,83. From the result of vertebrae BMD shows that T-score of -0,3 and Z score of -0,75 and 0,07. A single article show the BMD of forearm is -1,2 and lastly T-score show 0,41 on whole body BMD.

Conclusion: From 7 article obtained from searching and filtering of article. The article found to observe the effect of low dose and long-term corticosteroid to bone mineral density in patient with chronic disease is not significant, which also being influenced by multi factorial such as the onset of disease, part of the bone that assessed, and others

Keywords: Chronic 1; Corticosteroid 2; Osteoporosis 3; BMD 4

1. Introduction

The usage of corticosteroid as immunosuppressant and potent anti-inflammatory are widely use, some of the patient need to consume the medication for long term for more less 3 month. Especially patient with case of patient with chronic disease that will use corticosteroid as treatment, in general population 2% women younger than 50 years old are taking corticosteroid. From the whole population of people who received corticosteroid 19,6- 38% of the population get glucocorticoid induced osteoporosis.(Adami, Rahn and Saag., 2019). Some research from Europe and United states stated that the estimated prevalence of GC use is 0,7% to 17,1%. (Overman RA, Yeh JY, Deal CL., 2013) and (Laugesen K et al, 2017). It is also stated that the prescription rate of long-term GC has increased 34% over past 2- years (Fardet L, Petersen I, Nazareth I., 2011). Meanwhile in Korea, current prevalence of chronic oral GC use for more than 30 days increase from 0,16% in 2002 to 0,54% in 2015, which is significant and that is why we need to tackle all the major adverse effect of it (Oh TK, Song IA., 2020).

If the patient leave untreated, the adverse effect of GIOP will exist, and the bone resorption will hyperactive eventually will decrease the bone mineral and increase the calcium level in the blood. If the process continue for a long time, it will make the patient prone for fracture. Based on those consideration majority of the articles is proposing a BMD monitoring for the patient that consume long duration of treatment of corticosteroid, for example like patient with ITP. From the 10% of the patient who received glucocorticoid treatment are diagnose with fracture and 30-40% have radiographic evidence of vertebral fracture (Buckley et al., 2017). GCs have been reported to responsible for decrease in bone density and fracture risk approximately chronic GC treatment are diagnose with symptomatic fracture.

Based on the case of glucocorticoid-induced osteoporosis one of the solution is by doing monitoring of bone mineral density measurement to asses bone strength to know the risk of fracture. Based on the meta-analysis BMD alone cannot be relied on to detect all of the treatment related effect on other important contributor to bone strength and fracture risk reduction. Other than BMD as prophylaxis of osteoporosis, risendronate is also important for postmenopausal women and salmon calcitonin (Small, 2005). Other paper also mention the guideline of glucocorticoid induced osteoporosis treatment when a patient have a plan to start GCs and chronically treated patient with GCs more than 3 months (Buckley et al., 2017). The guideline separate into 2 groups, which are those less than 40 years of old and those age more than 40. It also concerned GC status “initiating or continuing GCs treatment” and fracture risk (low or medium or high). The guideline identified adults more than 40 years old had a prevalent of T score less than -2,5 at the hip or spine or FRAX

risk of fracture more than 20% as a prediction for 10 years from now. The guideline also include children and adults less than 40 years of old , high risk of fracture in young groups was defined as history of prior fracture. The moderate risk of fracture is considered if the patient treated by GCs for more than 6 month with more than 7,5 mg/day for the concentration. Also BMD Z score at hip or lumbar spine less than -3 or have rapid decline in bone mineral density of more than 10% over 12 month of GCs (Kanis JA et al., 2011).

Based on those considerations there have several mechanism in dealing with glucocorticoid-induced osteoporosis. Firstly monitoring system, by doing DEXA scan for those people who planning to start the GCs, especially for the long term one in patient with chronic disease. Then asses the BMD Z score, by comparing the patient bone density to average bone density of people at the patient age and gender. From it, then we will calculate the T score which (less than -2 will be one of indication of monitoring) to know whether the patient has low bone density or not, and of the patient have we will also calculate with FRAX to determine the prognosis of this patient after 10 years ahead. We will also considering patient (age, weight, BMD, family history, and other clinical risk factor, such as RA, Secondary osteoporosis and GCs exposure) in it.

2. Materials and Methods

This research study method using systematic review. Systematic review is a method to collect all empirical prove that in line with the inclusion and exclusion criteria that has been made before the research is conducted to answer the source of problem. The criteria is made in order to minimized bias and to gain higher reliability. Research problem of this problem is determined with PICO. This guideline is the abbreviation to make research problem. PICO is consisted of 4 things: population, intervention, comparation, and outcome. The population is patient with chronic disease, intervention is low dose and long term corticosteroid, the comparation is healthy individual same age or healthy individual in age 30, and the outcome is in terms of BMD Z and T score.

The inclusion criteria for this research English written language, the bone mineral density diagnostic method by using dual-energy xray absorptiometry scan, the sample consume corticosteroid for more than 3 months. We will exclude the article if one of the exclusion criteria appear on the paper, which are diabetic patient, pediatric patient, review article, and experimental study article.

3. Results and Discussion

The assessment of literature is done by using quality assessment tool for studies from EPHPP (Effective Public Health Practice project) which the detail can be seen bellow. These quality assessment tools are consist of 7 main topic, which are selection Bias, Study design, Confounders, Binding, Data collection method, Withdrawal and dropouts, and Rating.

No	Author, Year, and Place	Selection Bias	Study Design	Confounders	Binding	Data Collection Method	Withdrawals and dropouts	Rating
1	Korczowska et al., 2003	Moderate	Strong	Strong	Strong	Strong	Strong	Strong
2	King J et al., 2006	Moderate	Strong	Strong	Strong	Strong	Strong	Strong
3	Paul D et al., 2004	Moderate	Strong	Strong	Strong	Strong	Strong	Strong
4	Sambrook P et al., 2000	Moderate	Strong	Strong	Strong	Strong	Strong	Strong
5	Engvall I et al., 2008	Moderate	Strong	Strong	Strong	Strong	Strong	Strong

From the search and filter of article produces 5 article. 2 of those article come from united states of America, and the rest are Poland, Australia, and Sweden. The study method of the papers are vary, which are randomized control study, cross-sectional study, (Randomized, double-blind, placebo-controlled trial), observational, and randomized multi-centre study. The article that I took are the article from year 2000 until year 2008.

This articles are consisted of vary of chronic disease, such as Rheumatoid Arthritis, systemic lupus erythematosus, bronchiolitis, emphysema, and congenital adrenal hyperplasia. The patient have different onset of disease, which started from the infancy until adult and recent acquired disease.

Due to the variety of disease the type of corticosteroid is also different, in this research the types are Prednisone, fludrocortisone, triamcinolone, and Prednisolone. Some of the paper do not mentioned the types of corticosteroid and the dosage. But some of them mentioned which vary from 0,05 mg/day of fludrocortisone until 7,5 mg of prednisolone. From the dose of different corticosteroid type we converted those dosage into prednisolone to equalize all of it.

Because the patient have variety of disease so the duration of treatment are vary, mainly we include

the paper which mentioned the duration of treatment more than 3 month. the least amount of time is 1 year and the most amount of time is 22 years. for the bone mineral density assessment tool we use DEXA scan or Dual-energy X-ray absorptiometry. The part of the bone that we assess are femur, forearm, lumbal spine, and whole body. Lastly, from the total population of this study reach 488 samples gained from 5 articles. The age from this study are vary, ranged from 13,8 until 80 years of age.

No	Title	Corticosteroid Type	Corticosteroid Dose	BMD Part	Duration of Treatment	Equal Dose (Prednisolone)	total population	Mean Age
1	The Effect of Long-term Glucocorticoids on Bone Metabolism in Systemic Lupus Erythematosus Patients: The Prevalence of Its Anti-inflammatory Action upon Bone Resorption	prednisone	25,3+- 28,1 g accumulation dose	Forearm	108+- 82 months	9 mg	38	46.4 ± 12.8
2	Long-Term Corticosteroid Replacement and Bone Mineral Density in Adult Women with Classical Congenital Adrenal Hyperplasia	Fludrocortisone	0,05-0,15 mg/d	Lumbal and whole body	22 years		15	51
3	Loss of Bone Density with Inhaled Triamcinolone in Lung Health Study II	Triamcinolone	1,200 micro gram	femoral neck and lumbal spine	3 years	1,5 mg	201	55
4	Osteoporosis with Low Dose Corticosteroids: Contribution of Underlying Disease Effects and Discriminatory Ability of Ultrasound versus Bone Densitometry - rheumatoid arthritis			femoral neck and lumbal spine	13,6+-1,8 Months	6.8 ± 0.4 mg	76	18-80
5	Impact of low-dose prednisolone on bone synthesis and resorption in early rheumatoid arthritis: experiences from a two-year randomized study	Prednisolone	7,5 mg	femoral neck and lumbal spine	24 months	7,5 mg	70	51
						Total Population	400	

Femoral Neck Bone Mineral Density

From the result of the data obtained there are no significant decreasing amount of bone mineral density, the score is categorized as normal bone mineral density either from Z score from 2 articles shows that (-0.29 ± 1.17 and –0.83 ± 0.16) and other paper show T score of -0.30. which based on those comsideration there is no significant changes in BMD of femoral neck.

Lumbar Spine Bone Mineral Density

Lumbar spine result of DXA scan shows that low bone mineral density is not detected in this case a study show T score of -0,3 and two other studies presenting Z score of (0,07 +- 1,45 and –0.75 ± 0.20). from the score it is interpretated as normal bone density.

Forearm Bone Mineral Density

From the forearm single article state that BMD T score show -1,2 which interpretate as osteopenia. The first reason is due to the patient sample is suffer from systemic lupus erythematosus. The patient here have different dosage based on the severity of the disease, ranged from 0 to 60 mg daily.

Whole Body Bone Mineral Density

The data gained from an article showed 0,41 as the BMD T-score which considered as normal bone density. Regardless the patient start the mediaction since infancy or very long term of corticosteroid, but the bone mineral density of this patient is still normal

No	Author, Year, and Place	Study design	femoral neck T	L2-L4 T	Forearm T	T score T	Data Form
1	Korczowska, 2003, poland	Randomized Controlled			-1.2 ± 1.4		T score
2	King J, 2006, USA	Cros-sectional				0.41 (1.42)	T score
3	Paul D, 2004, USA	Randomized, double-blind, placebo-controlled trial	-0.29 ± 1.17	0,07 +- 1,45			Z score
4	Sambrook P, 2000, Australia	Observational	–0.83 ± 0.16	–0.75 ± 0.20			Z score
5	Engvall I, 2008, Sweden	randomized multi-centre study	-0.30 (-0.51 to 0.06)	-0.03 (-0.39 to 0.18)			T score

4. Conclusion

Indeed that there are several lackness in the process of making this systematic review, some of those lackness are the patient age is mpre than 50 years of age which impacting towards menopausal factors for female patient, the gender are not separated in BMD measurement, the patient disease impact the bone mineral density testing and the dose is not adjusted to either low or high dose. So based on those consideration it is better for the next research to choose the sample that do not have disease that able to influence BMD result, younger patient, onset of treatment is controlled, and determining the dosage of corticosteroid.

Eventhough the disease are vary and the onset or dosage are vary either, there is no significant influence of corticosteroid to osteoporosis in patient with chronic disease, which already showed by the normal level or bone mineral density on each patient bone density test. But sometimes preventive measure need to be done since the cause of corticosteroid to osteoporosis is multifactorial, such as dose or duration dependent. - The next research better to use the disease that do not influence the Bone Mineral Density such as hematologic autoimmune.

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