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Original Research Paper

Psychiatric

DEPRESSION, ANTIDEPRESSANTS AND RISK OF OSTEOPOROSIS

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ABSTRACT

Objective: Depressive disorders and use of spetial kind of most prescribed antidepressant- Selective Serotonine Reuptake Inhibitors are often connected with low bone mineral density (BMD). As incidence of depression is very high (10-16%), and first choice therapy for depression include SSRIs, aim of present study was to investigate if patients treated with this kind of antidepressants are at higher risk for osteoporisis compared with other antidepressives. If so spetial methods of prevention due to osteoporosis shoud be applied from the beginning of this therapy to prevent fractures and mortality of such patients.

Materijal and Method : 126 patients hospitalised at Psychisatric Clinic in Novi Sad, Serbia from 2014-2018. with diagnosis of depressive disorder, midlle intensity, (HAMA >20) , completed a comprehensive interwiev, had clinical measurements and BMD assessments at the spine,and total hip to find out if there sgns of disruption of mone metabolism. Patients were treated either with therapeutical dosis of SSRI)Selective Serotonin Reuptake Inhibitors)or SNRI (Selective Serononin and Noradrenalin Inhibitors)antidepressant .

Result: Osteoporosis was found in higere percent in both group of patients, but there were no evidence that patients treated with SSRI were at higher risk of osteoporosis.

Conclusion: In this investigation there were no difference of freqvence of osteopoenia and osteoporosis between patients treated with selective serotonine reuptake inhibiitors and patients treated with selectine noradrenaline reuptake inhibitors, but frekvence of osteopenia and osteopoorosis was higher in depressive patients compared to general population.

KEYWORDS :depression, antidepressants, osteoporosis

Introduction.

Depression represents the most common mental disorders with growing incidence in most part of the world,according to WHO reports [1,2,3]

The first choice of pharmacotherapy are antidepressants.Both depression and SSRI(Selective Serotonine Reuptake Inhibitors) ,the most prescribed antidepressants, are nowdays often associated with negative effect on bone mineral density (BMD), mainly in middle aged and older man and women. ([3,4,5]) Important evidence is that depression and osteoporosis have marked influence on qvality of life, morbidity and mortality of patients, and even more importance for health care isfreqvency of this two illness, and fact that comorbid they affect large population, worsening qvality of life , increased rate of fracture and mortality ([2,6]). Association between depression and osteoporosis which is characterized by systemic impairment of bone mass and microarchitecture is still unclear ([1,3,5]). The possible negative relation can be explained by lifestylechoice very often present in depressive patients , like excessive smoking, alcohol consumption,physical inactivity,problems with nutrition ([5,6]),and perhaps in common pathophysiologic mechanisms ([6,7]) Beside this hypothesis,last decade a numerous investigations indicate that SSRI may be responsible as independent factor, for loss of bone mineral density and disruption of bone metabolism. The way in which antidepressants disturb is still unclear ([5,6,7]) .Authors consider that it is very important for common healt to find out if patients who take SSRIs are in at higher risk for osteoporosis for early detection and prevenction this side effect([7,8,9])

The aim of this study was to find out if treating depression with SSRI increased risk of secondary osteoporosis in middle aged depressive patients compared to treatment with SNRI

There is a hypothesis, not still offitial confirmed,that SSRI induces skeletal changes and increased widely osteoporotic fracture risk in already at risk patients.([7,8,9])

Material and method :

126 inpatients, both men and women aged 55-72,hospitalised with diagnosis of Depressive disorder (midlle ,recurrent, HAMD more than 20) from 2014-2018 at Psychiatry Clinic, Clinical Centre of Vojvodina were included in study. Patients were devided in two subgropus regarded prescription of antidepressant therapy. First group(81) was treated with SSRI antidepressants(escitalopram, fluoksetine,sertraline), and the second group(45) was treated with SNRI.(venlafaxine). Sociobiographic and sociodemographic data were collected, including information about all medication.Other considered comorbidities were diabetes mellitus, hyperlipidaemia. hypertension, and hipothyreidismus, under medication control .Diagnosis of osteoporosis was based on the ICD 10 code. Clinical measurements and assessment of BMD at lumbal spine(L2-L4) and hip was made,using dual energy X ray absortiometry (DXA).Also, CrossLaps, osteocalcin and level of Ca and D vitamin were collected from blood sample.

Statistical analysis

Data analysis was conducted to compare the distribution of sociobiographic characteristics and comorbidities between two group of patients.by using x^2(Fisher Exact Test), t test and Kruskall Wollis test.

Results

In this investigation,65% were female. Mean age of patients were 57,3 (57,1 VS 57,5).85% female and 16% male were treated with SSRI s,similar to group treated with SNRI (80% vs 20%) and duration of treatment was similar between two group of patients,too.(97 day +23 vs 91 +19.day during actuall depressive episode. Mean dosage of antidepressant was in the group of SSRI in middle effective dosage sertraline 110 mg +10,5; escitalopram 15 mg + 5,2; fluoksetine 30 mg + 10,0 (tbl 1) as well as for SNRI. medium dosage

was 225 mg/die, ,with no significance difference between male and female. In 54,01% of female treated with SSRI osteopenia (42,6%) and osteoporosis (11,5%) were diagnosed by DXA, vs. male (52,7%), osteopenia was found in 42,3% and osteoporosis in 10,4%. In group of patients treated with SNRI osteopenia was detected in 43,1% of female and 41,6% in male. Osteoporosis was evidence in 9,5% of female and 9,0% of male, with no statistic significante differences.There were no signifficante difference in value of CrossLaps, oseocalcin and 15 (OH) D and in level of Ca. between two group of patients.

Smokers in both group of patients were present in high level (92% in patients treated with SSRI vs 93 % in patients treated with SNRI . In patients treated with SNRI BMI was slighlitely higher, but without signifficante difference 24,2 + 4,5 vs 26,45+5,0 in females and 24,5+1,7 vs 25,3 +3,3 for males (tbl.1)

Discussion .

There are numerous results that indicate about strong relation between depression, use of SSRIs and osteoporosis.Patients with depressive disorder are stronger related to higher risk of osteoporosis., probably throw lifestylechoices, lack of excersise,smoking, ,alcohol use, taking fast food Possibly neurobiological base for such hypothesis is hypercortisolemia in depression (lit)Depression causes activation of HPA axis (Hypothalamy-pituitary-adrenal) and this alteration ,which could be the crutial factor for increased risk of osteoporosis in depressed patients (lit)Actuall hypothesis consider that corticotroping realizing hormone (CRH)and persisting high level of cortisol in depressed patients lead to secondary hypogonadism, wich present one of the crutial risk factor for bone loss (14,15).Such negative influence could be responsible for higher incidence of osteoporosis in depressive patients, compared to general population (lit)On the other side, the mechanism throw which SSRI may cause bone loss is still unclear. One option is that SSRI demonstrate detrimental effects o BMD, throw disturb ing neuroendocrine metabolism in bone,due to interaction with lot of serotonin receptors located in osteoblasts, osteoclasts and osteocite.

Conclusion

The study results indicate that depressive disorder, middle intensity is connected with higher risk ofosteoporosis, but patients treated with SSRIs are not in higher risk of osteoporosis than patient treated with SNRIs.In future, larger cohort of patients have to be include in this kind of investigation.

Table 1

Parameters	Patients treated with SSRI (n=81)	Patients treated with SNRI(n=45)	P<0,01 SD
Age	57,1+6,1	57,5+4,3	ns
Sex Female Male	68 (84%) 13 (16%)	36 (80%) 9 (20%)	ns
Comorbidity hiperlipoproteinemia II a	70,5%	72,1%	ns
Comorbidity diabetes mell	9,1%	9,9%	ns
Comorbidity.hypertensio art	49,3%	51,3%	ns
Fracture in the past	24,2%	22,4%	ns
AD during current episode(daily dosage)	26% escitalopram 15mg +5,2 51% sertraline 110 mg+10,5 23% fluoksetine 30mg+10,0	Venlafaxin 225 mg = 37,5	
BMI Female male	24,2+2,5 24,5+1,7	24,7+3,3 25,3+3,7	ns
DXA Ostepenia(T score>1,5 SD) female male Osteoporosis(T score >2.5 SD) female male	42,6% 42,3 11,5% 10,4%	41,5% 43,6% 9,51% 9,00%	ns
CrossLaps	427,50 + 17,7	445,3+ 21,0	ns
Osteokalcine	38,01 + 8,17	37,5+6,15	ns
25 (OH)D	26,8 + 4,8	28,2+5,6	ns
Ca	1,0 + 0,1	1,1+0,1	ns

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