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Are Psychotropics Responsible for Increased Fractures?

ARE PSYCHOTROPICS RESPONSIBLE FOR INCREASED FRACTURES

Many commonly used medications are being implicated in increased risk of osteoporotic fractures. Protein pump inhibitors were example. The psychotropics are getting scrutiny as well. You are listening to ReachMD, The Channel for Medical Professionals. Welcome to the Clinician's Roundtable. I am Dr. Leslie P. Lundt and with me today is Dr. Donald Robinson. Dr. Robinson is professor of pharmacology and medicine at the University of Vermont and the author of more than 175 scientific papers and neuroscience topics. In addition, he is a consultant on CNS Drug Development for Worldwide Drug Development.

### DR. LESLIE LUNDT:

Welcome to ReachMD, Dr. Robinson.

### DR. DONALD ROBINSON:

It's a pleasure to be with you.

### DR. LESLIE LUNDT:

Which psychotropics are implicated in the risk of osteoporotic fractures?

### DR. DONALD ROBINSON:

Well, there had been studies looking at all of the psychotropic agents and they have implicated most of them. However, the studies, the earlier studies had some limitations and so we now have the benefit of a couple of reliable large epidemiologic studies. It seemed to indicate that the serotonin-reuptake inhibitors and also the benzodiazepines are associated with a significant increased risk of osteoporotic fractures.

### DR. LESLIE LUNDT:

So, two of the most commonly prescribed medicines we use SSRIs and benzos.

**DR. DONALD ROBINSON:**

That's correct.

**DR. LESLIE LUNDT:**

Now, does it matter at what age one starts say that SSRIs, you know, more and more it seems like these medicines are being used in children and adolescents.

**DR. DONALD ROBINSON:**

Well, I think there are concerns that the 2 ends of the age spectrum in children and adolescents, there are still in the period of rapid bone growth and they therefore may be at some increased risk because of the changes that are going on in their skeletal structure. At the other end of the age spectrum and here, I would refer to subjects, who are at least 50 years of age or older, they are at risk because they are subject to osteoporosis and they did suggest that for adults 50 years of age or older, there is a 50% incidents of osteoporotic changes in women and in men about a 20% increased incidents of osteoporosis above the age of 50. So, therefore I would have some concerns about long-term use of the serotonin-reuptake inhibitors for one and perhaps also for the benzodiazepines in the older age group.

**DR. LESLIE LUNDT:**

Now, are the other antidepressants in the clear, say the SNRIs like Venlafaxine?

**DR. DONALD ROBINSON:**

Well, the studies to date does not implicate the SNRIs. I would say that it is probably because of insufficient data that we really do not have a conclusive answer to that. There is some of the earlier studies that were done, so I mentioned the earlier studies tended to be smaller in sample sizes and without all of the case controls that one would like, but they raise the possibility that the older tricyclic antidepressants were associated with some increased risk of osteoporotic fractures. So, I would think the best answer is that we do not have a clear answer about the risk of the tricyclics, which of course were dual-uptake inhibitors that is also true of some of the newer agents. We just do not have sufficient data.

**DR. LESLIE LUNDT:**

What is the role of this neurotransmitter system, be they serotonin or norepinephrine in bone metabolism that is something most of us do not know anything about?

**DR. DONALD ROBINSON:**

Yes, yes, it is very, very interesting actually because it is a fairly new finding and the evidence is emerging that the neurotransmitter drugs, that is the monoamine neurotransmitter drugs, serotonin and dopamine do have effects on bone metabolism. Now this is based on animal studies, but the studies clearly show that there are first of all anatomically, there are nerve terminals that innervate bone and the neuroterminals that had been studied in animal research shows that these receptors actually mediate several of the neuropeptides like calcitonin and also that they have effects on the monoamine neurotransmitter systems. So, that for example, the neurotransmitter dopamine has been implicated because the absence of dopamine receptors in animals, who had genetic deletions of the neurotransmitter dopamine transporter clearly have changes in their bones affecting the vertebrae and the long bones, so it is clearly evidenced that the dopamine transporter does affect the integrity of the skeleton and similarly for serotonin, they have now shown that serotonin receptors are present in the different types of bone cells including most importantly the osteoblast, which are one of the major cell types in bone production.

**DR. LESLIE LUNDT:**

**If you are just joining us, you are listening to the Clinician's Roundtable on ReachMD, The Channel for Medical Professionals. I am Dr. Leslie Lundt, your host and with me today is Dr. Ronald Robinson. We are discussing the increased risk of fractures with psychotropics.**

Do we understand what exactly serotonin does in the bone metabolism?

**DR. DONALD ROBINSON:**

Well, it seems evident that serotonin does affect the bone production, as I said the serotonin receptor is involved in minimal production and so it has some clearly some effect, but exactly where other than knowing that it is an effect on the osteoblastic cell, which is one of the primary bone producing cell types, we do not know the exact metabolism. We do know for example that normal rodents who are treated that is mice treated clinically with the SSRI paroxetine and diminished bone structure and weakening of the bones, particularly the weightbearing sites of skeletal bone. It is also known that it has been shown in animal studies the monoamine transporters is important in bone production and that is true for both serotonin and for dopamine, so that the evidence is rather convincing that both serotonin and dopamine are in some ways involved in the physiology of bone production.

**DR. LESLIE LUNDT:**

Now, if dopamine is involved within that mean the antipsychotics are also likely to cause problems with fractures?

**DR. DONALD ROBINSON:**

Yeah. One would think so, but interestingly there are some fairly definitive epidemiologics where they have looked at all of the psychotropic agents in large populations with case match controls that suggests that the use of the antipsychotic drugs is not associated with increased risk of osteoporotic fractures.

**DR. LESLIE LUNDT:**

So what variables would increase the patient's risk to having fractures if they are on psychotropic medications?

**DR. DONALD ROBINSON:**

Well, the 2 agents that in larger studies definitively been shown to be associated with osteoporotic fractures are the SSRIs and also the benzodiazepines. To a lesser extent, some of the other antidepressants may also be involved with increased risk, but interestingly the use of lithium has been shown to decrease the risk of osteoporotic fractures, which is an interesting finding and it is probably related to fact that lithium has effects that would actually increase the generation of bone by these osteoblastic cells.

**DR. LESLIE LUNDT:**

What about diagnostically, are there certain diagnoses that might increase the patient's risk?

**DR. DONALD ROBINSON:**

Yes. There is a long list of related medical illnesses that are associated with increased risk of fracture. So, medical disorders like diabetes, hypertension, ischemic heart disease, rheumatoid arthritis of course and certain other medical disorders have been associated with increased osteoporotic fractures and then with regard to the mental health disorders, there is an association with the diagnoses of substance abuse or dependence, depression, dementia, and psychosis. So, there is quite a long list of medical and psychiatric diagnoses that are associated with increased risk of fracture. However, in this comprehensive epidemiologic studies, even when one factor in all of those increased risk factors, there is still an association as I mentioned with antidepressant drug use, particularly the SSRIs and also to a lesser extent with the use of benzodiazepines.

**DR. LESLIE LUNDT:**

What does this all mean Dr. Robinson to the practicing clinicians? Should we, for example, get bone density scans on our patients that are on benzos or SSRIs?

**DR. DONALD ROBINSON:**

Yes, take what it means, is the one may want to rethink the long-term use, long-term exposure to antidepressant drugs in the older age groups, and I do not know that it is clinically feasible or practical to do bone density studies, although in general that is probably a reasonable diagnostic procedure in any adult in the older age group, but I think in general the messages that there is an association with these agents and it is a dose related effect. The best clinical advice would be if one selection SSRI in an elderly patient to not continue the drug for prolonged periods of time and the same of course would be true with the benzodiazepines.

**DR. LESLIE LUNDT:**

And I assume just kind of come and send for us a recommendation such as weightbearing exercise when appropriate and calcium supplementation might be especially important in these patients.

**DR. DONALD ROBINSON:**

It is especially important that the patients at risks exercise regular, of course walking, other kinds of weight exercises are good as long as they are approved by their family doctor.

**DR. LESLIE LUNDT:**

Sounds good. Thank you so much for being on our show. This is an unrecognized problem.

**DR. DONALD ROBINSON:**

Yes. It is a pleasure to talk with you and it is clear that it is a new and emerging medical problem that suggested one should use some caution in the elderly using these particular psychotropic agents.

**DR. LESLIE LUNDT:**

I would like to thank our guest, Dr. Donald Robinson from Burlington, Vermont, recently voted the healthiest city in America by the way. We have been discussing the relationship between psychotropics and fractures.

I am Dr. Leslie Lundt, you are listening to ReachMD, The Channel for Medical Professionals. Please visit our website at [reachmd.com](http://reachmd.com), which features our entire library through on-demand podcasts. You may also call us toll free with your comments and suggestions at 888-639-6157. Thank you for listening.

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I am Dr. Lawrence Striker. Join me this week. I will be peaking with Dr. Susan Love. We will discuss Dr. Love's research foundation, which has recently launched in the army of women breast cancer research initiatives.

This is Dr. Lee Freedman. Please join me this week on the Clinician's Roundtable. We will be discussing enriching the residency experience with Dr. Ken Latimer and Dr. Ben Manios both were on a committee that recently published recommendations about how to change the residency experience.

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