Serotonin: beyond menopause

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ABSTRACT

Serotonin is a brain neurotransmitter, a local gut-produced pro-kinetic agent and a platelets-released monoamine with haemostasis role. We focus on revealing the serotonin interferences with menopause mainly related to climacteric syndrome and bone health. This is a short commentary type of manuscript, centred on English language PubMed research. Serotonin is connected to the hypothalamic thresholds for temperature regulation in vasomotor symptoms that is why drugs that elevate the serotonin synaptic plaque exposure like SSRI (serotonin selective reuptake inhibitors) are indicated. Serotonin is also linked to bone field but its testing into the blood has not been unanimously found to be correlated with bone mineral density or menopausal bone remodelling markers. Conditions with age-related onset as carcinoid tumours bring a serotonin excess but not necessary a bone loss. From climacteric syndrome to bone regulation and to pathological domain of neuroendocrine neoplasia, serotonin plays a complex role on menopause's field.

Keywords: serotonin, bone, climacteric syndrome

INTRODUCTION

Serotonin, also named 5-hydroxytryptamine, is a molecule serving as central neurotransmitter, as local gut-produced pro-kinetic agent and a platelets-released monoamine with haemostasis role (1-3). A part from all these, serotonin is connected to the hypothalamic thresholds for temperature regulation in climacteric vasomotor symptoms that is why drugs that elevate the serotonin synaptic plaque exposure like SSRI (serotonin selective reuptake inhibitors) are indicated for menopausal complains (4). Serotonin is also linked to bone field by central positive actions that antagonises peripheral negative effects of intestine-derived 5-hydroxytryptamine (5).

OBJECTIVE

We focus on revealing the serotonin interferences with menopause mainly related to climacteric syndrome and bone health.

MATERIAL AND METHOD

This is a short commentary type of manuscript. The research is centred on English language written articles recently published in journals indexed in PubMed database.

RESULTS

Climacteric syndrome includes hot flashes and mood disturbances described in up to 70% of women and one third of females have these complains starting from peri-menopause (6-10). Traditionally, vasomotor symptoms are hot flashes and night sweats; a wave may last from one to five minutes (6-10). These aspects are presented up to 5 but even to 10 years depending on each person (mostly one to four years) (6-10). The flashes do not necessarily have a well revealed trigger as caffeine, physical and emotional stress (6-10). The underling mechanisms are represented by decreased levels of

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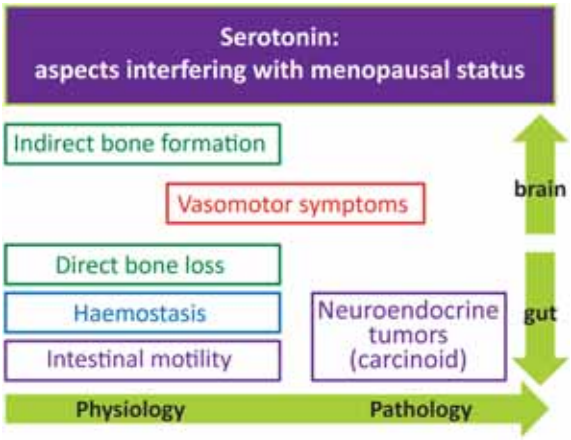

FIGURE 1. *Synthesis of main actions of serotonin that interfere with normal and pathological status, especially in menopause*

estrogens & progesterone that trigger neuroendocrine systems as serotonin and norepinephrine which cause a thermoregulatory dysfunction in hypothalamus reflected by higher core body temperatures as well as narrowing of thermoregulatory zone (6-10). The practical application of serotonin involvement is represented by the use of SSRIs for treatment of climacteric- related vasomotor disturbances especially in circumstances where estrogens are contra-indicated as incidental breast cancer or where concurrent depression symptoms may be reduced by antidepressants with dual function (6-10).

Regarding the bone, circulating serotonin has been found to be correlated with femoral areal bone mineral density in menopausal women but not in men (5). The OSTPRE study found that anti-depressive drugs which target serotoninergic pathways cause menopausal decrease of bone mineral density, a process that is accelerated by a higher drug dose (11). Is seems that an additional risk for osteoporotic fractures is brought by risk of falling caused by depression and associated therapy as well as co-morbidities with a higher risk on menopause as visual and blood pressure disturbances or neurological conditions (12). However, SSRI- related bone loss is also seen in premenopausal and younger women (13,14). In menopause, circulating serotonin, even involved in bone turnover, does not accurately predict future bone loss, potentially due to estrogen- independent mechanisms (15).

DISCUSSION

Regarding prior published manuscripts from Romanian experience, we mention the large use of blood serotonin assays as neuroendocrine marker for carcinoid tumours which became easily accessible during the last years since the therapy with somatostatin analogues is country wide available (16-18). This aspect includes menopausal population knowing that the onset of neuroendocrine neoplasia is age-related with a much higher chance to affect women in menopause rather than those in pre-menopause (16-18). Whether osteoporosis in these subjects is strictly menopausal due to estrogens lack or elevated serotonin as effect of tumour production represents a contributor to bone loss is still an open question (19). Another experience is related to circulating 5-hydroxytryptamine assessment targeting the possibility of becoming a bone remodelling marker (20). A study on 191 menopausal females having an average age of 57.1 years who were anti-osteoporotic drugs naïve showed a weak correlation between serotonin and bone formation marker osteocalcin in patients with osteoporosis and between the monoamine and bone formation marker alkaline phosphatase in subjects with osteopenia but not with DXA parameters (20). These results pointed that serotonin is still difficult to be framed in particular menopause-linked skeleton context.

CONCLUSION

From vasomotors symptoms included in climacteric syndrome to bone regulation and to pathological domain of carcinoid tumours, serotonin plays a complex role on menopause's field.

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