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ABSTRACT

Menopause presents an opportunity for biomedicine (BM) and Traditional Chinese Medicine (TCM) to develop novel pharmaceuticals and integrative clinical protocols that can unify the array of symptoms experienced and minimise adverse effects of medications. This essay will focus upon BM and TCM approaches to menopausal associated **osteoporosis** with attention on bisphosphonates.

INTRODUCTION

"Osteoporosis is characterised by low bone mineral density (BMD) (a T-score of \leq -2.5 at the lumbar spine, femur neck, or total hip by bone mineral density testing) and micro-architectural deterioration of bone tissue, leading to decreased bone strength, increased bone fragility and a consequent increase in fracture risk. In Australia, approximately 72% of menopausal women will have osteoporosis or osteopenia" (Osteoporosis Australia, 2017). "Hypoestrogenism is a risk factor for Osteoporosis" (Pluchino et al., 2012) with oestrogen inhibiting bone resorption. "Osteoporosis occurs when osteoclasts degrade the bone matrix faster than osteoblasts rebuild it" (Luo et al., 2018).

Common symptoms of menopause include: brain/mental worries (e.g. sleep problems, anxiety and depression, fatigue, impaired concentration and memory); urogenital disorders (e.g. recurrent urinary tract infections, vaginal dryness); vasomotor symptoms (VMS) (e.g. hot flushes, night sweats); and, additionally, chronic diseases associated with ageing (such as **osteoporosis**, cardiovascular disease, cognitive impairment and dementia) (Bitar, 2023; Pluchino et al., 2012). Menopause involves multiple physical and mental conditions, environmental and social factors, which are all synergised in TCM paradigms, a holism that is advantageous (Xutian et al., 2019).

ADVERSE EFFECTS OF BISPHOSPHONATES

Women can be prescribed a cocktail of medications during the menopause including "Hormone Replacement Therapy (HRT), bisphosphonates, gabapentin and antidepressants" (Smart Engage, 2015). HRT is contraindicated for breast cancer patients, those with thromboembolic history, and for long term use by women under 60 (Eisenhardt & Fleckenstein, 2016; Lund et al., 2019; Radice, 2022; Venzke et al., 2010). Non-hormonal-based medication side effects include "insomnia, dizziness, nausea, diarrhoea, fatigue, dry mouth and constipation" (Lund et al., 2019).

"Bisphosphonate therapy is considered the primary BM preventative of fractures in women who are at least 10 years post menopause and recommended for reducing the risk of fractures in postmenopausal women over the age of 50 at high risk of fracture" (Osteoporosis Australia, 2017). Bisphosphonates work to inhibit bone resorption by shortening normal osteoclast function (Carter et al., 2005). Reported gastrointestinal side effects of bisphosphonates include "oesophageal erosions, dysphagia and gastric ulcers" (Carter et al., 2005; Lobo, 2007), more worrying is the "association between bisphosphonate therapy and osteonecrosis of the jaw" (Berardi et al., 2007; Carter et al., 2005; Sanna et al., 2005). There is no effective current treatment for jaw necrosis (Carter et al., 2005). Other anti-osteoporosis medications side effects include hot flushes, diarrhoea, facial flushing and links to oesophageal cancer, deep vein thrombosis, pulmonary embolism and renal failure (Lobo, 2007). Moreover, protection against osteoporotic fractures may require ten or more years of treatment "leading to patient compliance issues" (Eisenhardt & Fleckenstein, 2016).

EVIDENCE FOR TCM

The UK health service involves TCM in the treatment of menopausal symptoms (Eisenhardt & Fleckenstein, 2016). A 2020 review and 2018 systematic review and meta-analysis found that "compared to pharmaceutical treatment alone, **warm needle acupuncture** (with moxa on the needle) increased BMD of the femur and lumbar spine with acupuncture also increasing serum calcium and oestradiol levels, reducing serum alkaline phosphatase (ALP) and relieving pain" (Chandra Saunders & Berry, 2021; Luo et al., 2018). "**Electroacupuncture** had positive effects on serum calcium,

serum ALP and pain" (Chandra Saunders & Berry, 2021). "Animal models suggest that acupuncture may offer protection against osteoporosis by regulating the osteoprotegerin/receptor activator of NF_KB/receptor activator of _KB ligand (OPG/RANK/RANKL) signalling pathways involved in the protection of bone tissue" (Chandra Saunders & Berry, 2021). Other animal studies suggest "TCM formulas reduce bone loss by decreasing bone resorption and increasing bone formation" (Zhang et al., 2016) through the mechanisms of Wnt/ β -catenin and MAPK pathways; and BMP/SMAD, OPG/RANKL/RANK and MAPK signalling pathways; kidney tonifying formulas have shown estrogen-like, antioxidant activity or regulate the function of hypothalamus-pituitary axis to enhance the estrogen level in serum; and Spleen tonifying formulas help active chemical constituents arrive at the skeleton site and regulate bone metabolism. "TCM formulas modulate bone metabolism networks modestly then alleviate symptoms of osteoporosis at low concentration through exerting synergistic effects of multi-components and multi-targets" (Zhang et al., 2016).

HOLISM IN TCM DIAGNOSIS

Zeng's TCM symptom analysis tool for **osteoporosis** lists 32 symptoms to support an **osteoporosis diagnosis** including tooth shaking, withered hair, shortness of breath and insomnia (Zeng et al., 2021). The Huangdi Neijing explains the Kidneys correspond to bone development, "at around 49 years of age, the women's Kidney Qi is gradually consumed, the Tian Gui, Ren and Chong vessels deplete, and the blood and Jing essence are insufficient leading to Yin-Yang disharmony and dysfunction of the Zang Fu organs" (Coyle et al., 2021; Eisenhardt & Fleckenstein, 2016; Flaws & Zhang, 1995; Maciocia, 2011; Marchment, 2020; Shen & Wang, 2012; Wang & Yu, 2021). "Menopause is shaped by a multitude of factors" (Eisenhardt & Fleckenstein, 2016; Kwee et al., 2007; Radice, 2022; Saunders et al., 2022) beyond biology with ethnicity a significant factor e.g. Asian women tend to report joint pain rather than VMS symptoms (Kwee et al., 2007; Saunders et al., 2022; Scheid, 2006, 2007).

LIMITATIONS OF CURRENT RESEARCH

Quantum theory may offer a perspective to explore the 'invisibility' of Qi, human consciousness and sub-consciousness (Xutian et al., 2019) inherent in TCM's Mind/Body paradigms. Randomised Control Trials (RCTs) are the gold standard in evidence-based medicine, like surgical interventions, acupuncture cannot be easily appropriated into RCT experimental study designs. Recent positive TCM trials lack the power of big data (Chandra Saunders & Berry, 2021; Eisenhardt & Fleckenstein, 2016). Biomedical evidence based interventions demonstrate little or no interest in the history or culture (central to TCM) overlooking insights resulting from 2000 years of continuous medical practice (Scheid, 2008).

CONCLUSION

In summary, menopause presents an opportunity for BM and TCM synergy. The biomedical approach to menopause ignores both mind/body interactions and the social construction of menopause. Each woman experiences menopause in her own way and with TCM, syndrome differentiation is delivered by personalised holistic diagnosis. Osteoporosis is one of many menopausal symptoms, TCM doesn't "separate the human body into segments treating one symptom at the expense of another" (Radice, 2022; Wolfe, 1998). An Australian study showed that half of the women surveyed had sought care from a Complementary and Alternative Medicine (CAM) Practitioner during menopause (Venzke et al., 2010) because they "perceive it to be safer than biomedicine and involve no associated long term harm" (Peng et al., 2014; Richard-Davis, 2014; van der Sluijs et al., 2007; Venzke et al., 2010). TCM is an alternative for women where HRT is contraindicated. Given the adverse effects of current medications such as bisphosphonates and promising potential of TCM studies so far (Azizi et al., 2011; Chandra Saunders & Berry, 2021; Eisenhardt & Fleckenstein, 2016; Mak, 2015), research support is warranted, notably in novel anti-osteoporotic drug development.

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