Introduction

Hormone replacement therapy (HRT) is used to treat menopausal symptoms in women. Most women who take HRT for menopausal reasons are given an estrogen/progesterone combination, except those who have had a hysterectomy, as they do not need progesterone. HRT has shown to improve muscle function, lower mortality in younger postmenopausal women and protect against brain aneurysms. Data suggests that estrogen, in particular, can decrease the risk of heart disease when taken early in postmenopausal years. HRT (testosterone) is also prescribed to a growing number of men to reverse the gradual age-related decline of testosterone.

Use of hormone therapy changed when the 2002 Women’s Health Initiative, a 15 year investigation that was stopped three years early when a preliminary review of the data showed that women taking the combination of estrogen and progesterin had a higher rate of breast cancer, heart disease and stroke. Based on these findings and the concern about health risks attributed to hormone therapy, doctors became less likely to prescribe it.

However, a recent 2011 study found a slightly lower risk of breast cancer and no significant increase risk of heart disease, blood clots, stroke or early death among women taking estrogen only compared with women with hysterectomies who took placebo.

Doctors, in the meantime, started to prescribe bioidentical hormone therapy (BHRT). Bioidentical hormone therapy (BHRT) is a compound that is identical to the natural molecules that the body produces. The term does not indicate the source of the hormone, but refers to the chemical structure. In addition, BHRT is not made from animal waste; rather they are formulated from soy products or yams by pharmacists to match the body’s hormones identically. As a result, patients are likely to benefit from the use of human hormones without the side-effects associated with non-human hormones.

In addition to menopausal symptoms mentioned earlier, hormone loss is also associated with an increased likelihood of heart disease, bone loss, decreased cognitive function, loss of muscle mass, reduced sex drive, restless leg syndrome, mood swings, hair loss, osteoporosis, depression, weight gain, and thinning of the skin. BHRT has shown to have specific benefits such as improving cognitive function, improving mood and sleep, reducing neuronal secretion of Alzheimer’s β-amyloid peptides, and improving sexual function, muscle strength and body composition.

The newest technique is the implanting of a time-released pellet underneath the skin on the buttocks. By implanting the dosage beneath the skin, the implants consistently release small, physiologic doses of hormones providing optimal therapy. BioTE® Medical Hormone Pellet Therapy is the only method of hormone therapy that provides sustained hormone levels.
throughout the day for up to four to six months without any “roller coaster” effect as seen with oral and transdermal forms of hormonal therapy. Because the pellets are completely natural, Pellet Therapy is ideal for patients wanting the benefits of a natural hormone, without the drawbacks of a synthetic.

Pellets contain a natural plant source of estrogen and testosterone. A compounding pharmacist, using strict federal guidelines, compounds the estrogen and testosterone utilized in the pellets. These pellets, which are smaller than a grain of rice, are placed in the fatty tissue underneath the skin and most closely mimic the actions of healthy ovaries and testicles with regards to hormone release into the bloodstream. The implantation procedure is easily performed in the doctor’s office.

Abstract

There have been many articles published regarding the benefits of HRT and BHRT; particularly in breast cancer, prostate cancer, cardiovascular protection, and bone building/osteoarthritis. The purpose of this white paper is to summarize the results of these articles by each disease entity. Please note, however, that most of the articles did not specify HRT or BHRT, but the hormone therapy itself, such as estrogen, progestin and testosterone.

Prostate Cancer

The results presented are derived from literature published on prostate cancer between 2001 and 2011. Some cases of prostate cancer were newly diagnosed and most of the men were older in age (≥ 50 years). The size of the studies ranged from 71 to 2950 patients and the majority of the articles indicated that the patients’ prostate cancer was treated with testosterone or testosterone with estrogen. In one article androgen suppression therapy was given and in another article there was no treatment given. Administration of testosterone and estrogen varied and was comprised of implants, injections and transdermals. Endpoint measurements included prostate zonal volume, T serum and PSA levels, overall progression-free and cancer-specific survival.

Results indicated that patients receiving testosterone had decreased prostate zonal volume irrespective of therapy up to middle age and increased thereafter. There was also improvement in quality of life and no evidence of increased risk of prostate cancer; however there was no difference in survival between regular therapy vs. intermittent hormone therapy. Results also indicated that administration of testosterone promoted growth of benign prostatic nodules and enhanced pre-existing prostatic malignancy. One article was inconclusive regarding T level and prostate cancer risk after testosterone treatment.

Patients receiving testosterone alone showed an increased risk of prostate cancer in men with low testosterone and patients receiving both testosterone and estrogen with high Gleason scores had lower testosterone and estradiol serum levels. Androgen suppression therapy, on the other hand, reduced disease progression and improved overall survival.
Osteoporosis/Bone Density

A review of published articles on osteoporosis and/or bone density published between 1976 and 2010 are summarized. Study size ranged from 12\textsuperscript{28} to 167\textsuperscript{29} patients and follow-up ranged from 6 months\textsuperscript{30, 31} to over 14 years.\textsuperscript{28} All of the articles except for one indicated that the patients’ osteoporosis/bone density loss was treated with estrogen/estradiol,\textsuperscript{28,30,32-42} testosterone \textsuperscript{29,31,43-52} or a combination of estradiol and testosterone.\textsuperscript{53-62} The remaining article indicated no treatment.\textsuperscript{63} Hormone replacement therapy was administered as subcutaneous or percutaneous implants,\textsuperscript{28,35,37,38,40,41,47,48,54-56,58,60-62} transdermal patches\textsuperscript{53,59} and oral tablets.\textsuperscript{36,39} Endpoint measurements included vertebral/femoral bone density,\textsuperscript{37,47,53,55,56,60-62} bone mineral density,\textsuperscript{28,29-36,38,40,4-44,48-52,54,57-59} bone volume,\textsuperscript{34,35} muscle mass,\textsuperscript{44} strength,\textsuperscript{45} and hormone and serum levels.\textsuperscript{37,44,46,48-50,58} Results indicated that patients receiving HRT had an increase in bone density, bone mineral content, bone formation, wall thickness and serum E2 levels.\textsuperscript{28-38,42-49,51,54,56,58,60,62} HRT also showed an improvement in muscle mass, strength, body composition, mood, libido, cardiovascular function and quality of life.\textsuperscript{30,39,42-46,49,50,54,59} Markers of bone formation improved as well as cancellous bone volume and there was a reduction in body fat and total cholesterol.\textsuperscript{30,35,43,50,58} There was also a reduction in bone fractures, myocardial infarctions and cancer.\textsuperscript{39,41} It was noted that subcutaneous estrogen was more effective than oral estrogen\textsuperscript{47} and that implants maintained or increased bone density whereas patches reduced bone density.\textsuperscript{53}

Cardiovascular Protection

A review of published articles on cardiovascular protection published between 1984 and 2012 are summarized. Study size ranged from 14 women\textsuperscript{64} to 2,416 men\textsuperscript{65} and follow-up ranged from 6 weeks\textsuperscript{66, 67} to 5 years.\textsuperscript{65} Treatment included testosterone,\textsuperscript{65,66,68-70} or a combination of estradiol alone followed by testosterone \textsuperscript{64,67,73,74} or estrogen and progesterone,\textsuperscript{71} or estradiol and nomegestrol acetate.\textsuperscript{72} Hormonal treatment was administered as subdermal or subcutaneous implants,\textsuperscript{64,66,72-74} injections,\textsuperscript{68} transdermals\textsuperscript{71} or oral tablets.\textsuperscript{68,71} Endpoint measurements focused on cholesterol levels, HDL, LDH,\textsuperscript{64,71-74} sex-hormone body globulin (SHBG),\textsuperscript{65} body fat,\textsuperscript{73} insulin levels,\textsuperscript{71} T-levels,\textsuperscript{65-67} BMI,\textsuperscript{71} systolic blood pressure,\textsuperscript{71} oxygen consumption\textsuperscript{70} and 6-minute walk tests.\textsuperscript{67} Results in patients treated with a combination of estradiol and testosterone showed a reduction in total cholesterol and LDL with an increase in HDL thus offering cardiovascular protection.\textsuperscript{64, 67,73,74} Body fat was reduced in patients taking estradiol alone\textsuperscript{73} and patients taking estrogen with progesterone or nomegestrol acetate had reduction in cardiovascular risk factors.\textsuperscript{71} Results in patients taking only testosterone showed improvement in functional capacity associated with heart failure, reduction in total cholesterol and SHBG, and a reduced risk of cardiovascular disease.\textsuperscript{65,66,68-70} Hormone implants showed similar changes in lipid profiles compared with oral forms of hormones.\textsuperscript{64}
Breast Cancer

A review of the published literature between the years 1941 and 2013 is summarized and focuses on women with breast cancer or history of breast cancer and pre and post-menopausal women and the effects of HRT. Three articles studied female monkeys, mice and transsexuals respectively. Study size ranged from six patients to over one million and follow-up ranged from 3 months to 32 years. Treatment consisted of a variety of hormones that included progestins, estradiol/estrogen, testosterone and combinations of arimidex and testosterone, estrogen and testosterone, estrogen and progestagen, testosterone and anastrozol and BHRT. The hormones were administered as subcutaneous pellets/implants, patches, injections or orally. Endpoint measurements included progression and recurrence of breast cancer, relative risk of invasive breast cancer, plasma T levels, Rosner/Colditz breast cancer score, quality of life, overall survival, ease of menopausal symptoms, and relative risk of hormone therapy. Endpoint measurements in female monkeys focused on mammary epithelial proliferation, in transsexuals tumor or cancer development and in mice tumor progression rate and survival.

Patients taking estrogen showed improvement in menopausal symptoms, no increase in the risk of recurrence of breast cancer or of death, a reduced risk of colorectal cancer and osteoporosis, a reduction in fractures and myocardial infarctions and an increase in bone density. Prevention or reduction in estrogenic cancer risk was found in patients taking a combination of estrogen and testosterone, mortality rate did not increase due to breast cancer, and testosterone counteracted proliferation of breast cells and exerted a protective role. A combination of estrogen and progestins had mixed results. Some studies found a low risk of breast cancer and no trend in increasing breast cancer with increasing duration of HRT; whereas, other studies noted that use of HRT increased the risk of breast cancer compared to women never on HRT. Patients treated with testosterone/androgens showed an ease in menopausal symptoms, cardiovascular benefits, and no risk or recurrence of breast cancer. However, an excess of testosterone was found to be the principal growth stimulator of breast cancer. It was also found to be beneficial to implant testosterone at the operation site in women and a study with BHRT found it to be safer than synthetic HRT. A study using a combination of testosterone and anastrozole showed an improvement in menopausal symptoms without increasing estradiol levels.

Results in a study on transsexuals found that a combination of testosterone and estrogen increased the probability of tumors with the duration of exposure to cross-sex hormones. Mammary epithelial proliferation was noted to increase in female monkeys after receiving a combination of testosterone and estradiol, and l-norcholesterol (radiotherapy) prevented local regional recurrence and metastatic spread after tumor resection in mice.

Conclusion

In summary, treatment with HRT and/or BHRT was found to improve quality of life and increased bone density, bone mineral density and muscle mass. Mood, libido and cardiovascular function improved and body fat was reduced, as well as cholesterol and LDH. Risk of prostate and breast cancer was reduced in the majority of the cases reviewed and there was an
improvement in menopausal symptoms. Subcutaneous/percutaneous implants were the most common form of HRT/BHRT administration followed by transdermals and oral hormones. As with any medication, consultation with a physician is recommended to discuss personal risks and whether any version of HRT/BHRT is appropriate to be prescribed.
Appendix A – References

6. LaCroix AZ, Rowan T, Chlebowski RT, Manson JE. Health outcomes after stopping conjugated equine estrogens among postmenopausal women with prior hysterectomy. JAMA 2011; 305:1305-1314.


