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Randomised, single centre, single blind feasibility study to determine the safety and effectiveness of interferential stimulation when compared to standard of care for the maintenance of bone density in pre-menopausal women receiving a Gonadotropin-Releasing Hormone (GnRH) agonist

Submission date
11/07/2007

Recruitment status
Stopped

Registration date
02/11/2007

Overall study status
Stopped

Last Edited
11/11/2008

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
RSMED-K032652-BMD01

Study information

Scientific Title

Study objectives
One of the side effects of Gonadotropin-Releasing Hormone agonists (GnRHa), menopausal-type symptoms, means that women will experience any of the following symptoms: hot flashes, night sweats, insomnia, decreased libido, headaches, mood swings, vaginal dryness, changes in breast size, acne, muscle pains, dizziness, and depression. While these symptoms will disappear with the cessation of GnRH agonist treatment (e.g. Zoladex®), the other side effect, Bone Mineral Density (BMD) loss, may completely reverse its effects after treatment has been discontinued. Women may turn towards another drug therapy to minimise their menopausal-type symptoms and their amount of bone loss. When used in small doses, this add-back therapy does not impact on the effectiveness of the GnRHa.

Without an established combination therapy regimen, women should be provided with alternatives for restoring their BMD to their pre-treatment values. In addition, as it becomes increasingly apparent that health care companies are looking to reign in the costs provided to treat an aging populations plethora of diseases and conditions, it is necessary to continue combing the industry for safe, effective and economical alternatives - this study will investigate the safety and potential effectiveness of one of two forms of interferential stimulation to serve as such an alternative.

Of utmost importance when prescribing any therapeutic regimen is the physicians ability to safeguard patients safety and well-being, and to diminish the potential side effects of those therapies. GnRHa presents significant and sometimes irreversible side effects. For this reason, the use of interferential stimulation as a safe and non-invasive therapy to potentially minimise or eliminate the associated BMD loss in pre-menopausal, hypo-estrogenic women treated with GnRHa therapy should be considered and is the basis for this study.

Assuming that it is possible for interferential (external electric) stimulation to further minimise or eliminate BMD loss in hypo-estrogenic, pre-menopausal women receiving GnRHa, this study will support the need to continue researching the potential role of electrical stimulation in osteogenesis. Diseases such as osteoporosis, the most common bone disease worldwide, could definitely benefit from such research, with direct costs of osteoporotic fractures in the United States at approximately $17 billion in 2001. Osteoporosis poses a major risk for fracture, which leads to considerable morbidity, mortality, and expense worldwide. The cost of all osteoporotic fractures in Europe was estimated at 31.7 billion in 2000, and the total cost of osteoporosis in Australia has been estimated at $7.4 billion per year (International Osteoporosis Foundation). These costs demonstrate the need to introduce additional, safe, effective, and economical alternatives for the treatment of osteoporosis; electrical stimulation, namely interferential stimulation, may serve as an alternate form of treatment for this therapeutic area as well.

Added as of 11/11/2008: Please note that this trial was prematurely terminated on 04/11/2008 due to low patient recruitment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Unconditional approval received from the Oxfordshire Research Ethics Commiittee B (UK) on the 4th July 2007 (ref: 07/Q1605/56).

Study design
This is a prospective, randomised, single centre, single-blind, feasibility (proof of principle) study with 30 subjects equally randomised to three arms.

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of bone loss

Interventions
Concerning the three arms of the study, there are two treatment groups, one receiving constant (one hour per day) and the other varying (one hour per day) small electrical nerve stimulation (interferential stimulation) and the GnRH agonist Zoladex®, which will be compared to a control group receiving standard of care only (Zoladex®). The GnRH agonist Zoladex® will be administered in the clinic every 28 days: at baseline and study days 28, 56, 84, 112, and 140.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Gonadotropin-Releasing Hormone agonist (Zoladex®)

Primary outcome(s)
The principal research objective is to evaluate the safety of interferential stimulation when used by pre-menopausal women who are hypo-oestrogenic as a result of taking a GnRH agonist when compared to a control group (standard of care only). Safety will be assessed by the rate of adverse event reports.

Key secondary outcome(s))
The secondary research objective is to assess the effectiveness of interferential stimulation, after six months of treatment, in reducing BMD loss in the lumbar spine as measured by Dual-energy X-ray Absorptiometry (DXA). Two treatment groups, one receiving constant and the other varying small electrical nerve stimulation (interferential stimulation) and the GnRH agonist Zoladex®, will be compared to a control group receiving standard of care only (Zoladex®). The endpoint is the difference in BMD between the baseline and study month six DXA scans in the three study groups.

Completion date
30/03/2009

Reason abandoned (if study stopped)
The clincial study is prematurely terminated due to low patient recruitment. A total of 30 subjects were to be included, however, only 7 subjects entered the study after an 18 month period. The trial terminated officially on 04/11/2008.

Eligibility

Key inclusion criteria
1. Has provided informed and written consent to participate voluntarily in the study
2. Is a pre-menopausal woman between 18 and 46 years of age at the time of study entry
3. Has a normal T-score on Dual-energy X-ray Absorptiometry (DXA) evaluation of the hip and spine (T-score greater than or equal to -1 for the patients age group)
4. Is willing and eligible to take Zoladex® for six months
5. Is willing to follow non-hormonal contraceptive advice relating to GnRHa treatment if sexually active and of childbearing potential

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Is hypersensitive or uncomfortable with receiving electrical stimulation treatments
2. Has or has had any form of cancer (a contraindication to electrical stimulation)
3. Uses a cardiac demand pacemaker (a contraindication to electrical stimulation)
4. Is affected by or has a history of bone disease, such as osteoarthritis, Pagets disease, spondyloarthropathies or scoliosis
5. Has an unexplained abnormal uterine bleeding or endometrial carcinoma
6. Has pathological fractures or any fractures of the thoracolumbar spine
7. Has internal orthopaedic spinal fixation devices
8. Has a known history of collagen-vascular or auto-immune disease (e.g. systemic lupus erythematosis), bleeding abnormalities, immunodeficiency, chronic debilitating disease, or malignancy within the last five years
9. Is pregnant, or breastfeeding or intends to become pregnant in the next six months
10. Has a known hypersensitivity to Luteinising Hormone-Releasing Hormone (LHRH), LHRH agonist analogues or any of the components in Zoladex®
11. Has taken a GnRHa within the past two years

12. Has taken an androgen, calcitonin or bisphosphonate within the past six months
13. Has taken an oral oestrogen within the previous two months
14. Has taken systemic glucocorticoids for more than one month within the past year
15. Is currently taking anti-seizure drugs or pharmacological doses of cholecalciferol
16. Has endocrine disorders requiring therapy (except for type II diabetes or hypothyroidism)
17. Follows a medication regimen that has changed 14 days prior to enrolment (drugs interfering with bone metabolism are not permitted)
18. Has a history of analgesic or opioid abuse/addiction
19. Has participated in another clinical study involving an investigational device or drug within 30 days prior to enrolment
20. Is unable to attend all study visits or self-administer study treatments for a total of six months
21. Is unable to read or write in English

Date of first enrolment
01/09/2007

Date of final enrolment
30/03/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
John Radcliffe Hospital
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Sponsor information

Organisation
RS Medical (USA)

Funder(s)

Funder type
Industry

Funder Name
RS Medical (USA) - manufacturer of the Interferential Stimulator device

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration