Clinical Evaluation of human embryonic stem cells (hESCs) induced with directed differentiation to gonadotrope cells to cure vasculogenic impotency and to improve coital frequency in males. An Open Study.

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Background:

Derivation of patient-specific syngenic hESCs from donor skin cells enhanced the prospect of autologous stem cells that are likely to prevent allorecognition. These cells can be selectively differentiated into predefined lineage by stepwise addition of proteins (like growth factor) or chemicals (like ligand) stimulants to steer directed motivation to recuperate hypothalamus that in turn transmits gonadotropin releasing factor setting off LH (Luteinizing hormone) and FSH (follicle-stimulating hormone) to sertoli cells and seminiferous tubule resulting Leydig cell to produce testosterone. FSH, in male by spermatogenesis enhances production of androgen-binding protein by the Sertoli cells of the testicles, while LH, stimulates interstitial cells of the leydig (Leydig cell). Their in vitro and in vivo transplantation has shown dramatic improvement in curing vasculogenic impotency and enhancing coital frequency in males.

Rationale: Hypothalamus transmits gonadotropin releasing factor to pituitary that sets off LH and FSH to Sertoli cell and Seminiferous tubule resulting Leydig cells to produce testosterone. This potential offers a rationale to evaluate the clinical efficacy and prospects of hESCs as a pharmacogenetic cell-based therapy to cure patients with vasculogenic impotency and to improve coital frequency in males.

Objective: To determine the clinical efficacy, tolerability and safety of hESC induced with directed differentiation to gonadotrope cells to treat and to

potentially cure vasculogenic impotency and to improve coital frequency in males.

Methods: Ten male subjects, age ranging between 18 and 70 years (mean 45.9 years) with clinically proven impotency and low testosterone level were recruited. To procure subject specific-syngenic-hESC, a skin biopsy was obtained from each subject. A pre-allocated disposable vial/syringe containing syngenic-hESC with the subject in a vehicle 0.5 ml was administered intravenously to the patient. Patients were examined on a weekly basis and those showing a progressive record of improvement and clinically tested increased testosterone level were considered as cured. To monitor treatment-related post-therapeutic events, subjects were given a log to record their daily experience.

Inclusion criteria:

Physically and Emotionally in good health at baseline
Do not have any STD including HIV
Do not have renal, hepatic, hematologic disorder including anemia, leucopenia or thrombocytopenia and infectious diseases
Have not used any antiviral or immunosuppressing therapy preceding 8 weeks baseline
No hypersensitivity to Hirudin, Refludin, Lepirudin, heparin or unfractionated Heparin (UFH) including serine protease inhibitors
Do not consume excessive alcohol or have smoking habit
Consent to comply with the study protocol including laboratory tests.

Criteria for clinical evaluation:

Clinically beneficial effects were assessed by:
Standard questionnaire about penile rigidity, improvement in arterial penile inflow (peak systolic velocity) by Duplex Sonography, both at the baseline and at scheduled clinic visits. Tolerability and treatment-related possible adverse effects at each follow-up visits were graded as the duration in days, and severity as (mild, moderate and severe) for headache, dizziness, gastrointestinal, urino-genital, nervous systems dysfunction or other unexpected symptoms.

Statistical evaluation:

Variables such as Height, Weight and Age were examined, mean values for clinical effectiveness of the treatment, penile rigidity and improvement in arterial penile flow as well as overall therapeutic success were noted.

Data were computed using an analysis of variance procedure, Duncan's test was followed to identify significant difference between mean values. $P<0.001$ were considered as significant.

RESULTS

After 6 weeks the Patients:

Treatment was well tolerated by all the patients with no dropouts. Patients reported marked Improvement as 5-6 times coital frequency per week. Subjects reported no treatment-related adverse events.

CONCLUSION

The study demonstrates that subject specific syngenic-hESC administered intravenously in a vehicle is safe, tolerable and significantly beneficial in contributing superior clinical efficacy to cure vasculogenic impotency and to improve coital frequency in males.