Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

Survey on Effect of Methadone to Buprenorphine Shift in the Maintenance Treatment on Profile of Gonadal Hormones and Semen Analysis of Infertile Men

Protocol summary

Summary

Methadone and Buprenorphine have been used as opioid Substitution Treatment (OST) in the world since 40 & 18 years ago in order. Regardless of short period experience in the past, these treatments have 14 & 10 years history in Iran respectively. There is a lot of questions about unwanted side effects of these medications on structure & function of different organs of body which concerns clients & worries therapists. One of organs with most sensitivity about that, is Genital system and common questions of mostly young clients on maintenance treatments, especially those who tend to have child in the future, is about probable effects of methadone & buprenorphine on sperm & fertility. Accurate & scientific answer to this question and select of appropriate medication for each client, diminishes their concerns and increases therapeutic alliance. According to high prevalence & morbidity of opioid use disorder especially in young & middle-aged men, and widespread providing of OST with methadone & buprenorphine, we decided to substitute methadone by buprenorphine in men who receive OST and survey the effect of this shift on sexual hormones & sperm analysis. The study will be done on 40 participants from Rouyan institute who their infertility has been established and in the routine diagnostic procedures, there was not any finding except methadone consumption as an opioid substitution treatment. Primary routine laboratory tests (including TT, FT, LH, FSH, SHBG, PL, Semen Analysis) will done in the Rouyan Institute and after filling of inclusion criteria, clients will be refer to an experienced clinic in prescription of buprenorphine with appropriate access for continuing of study. Inclusion criteria: 1) men between 18 to 50 y/o; 2) at least 6 months on Opioid Substitution Treatment & 3 months from last illegal opioid use; 3) daily Methadone dose less than 60 mg/d; 4) certification of therapist physician on stability & readiness of client for shifting from methadone to buprenorphine; 5) diagnosis of methadone as the most important factor for undesirable hormonal & seminal analysis; 6) written & signed informed consent form. The participants will stay on 2 groups randomly. In the study group methadone will be substituted with buprenorphine and in the control group methadone will be continued. In both groups laboratory test including sex hormones (TT, FT, LH, FSH, SHBG, PL) and semen analysis will be done 3 times: before intervention,3 months & 6 months after beginning of intervention. Exclusion criteria: 1) evidence or signs of laps & relapse in buprenorphine treatment even with appropriate dose; 2) absence from treatment more than 2 consecutive or 3 undulant weeks; 3) absence from screening opioid urine test more than 2 consecutive or 3 undulant sessions; 4) absence from hormonal & seminal analysis more than 2 weeks after appointed time; 5) intolerance of methadone dose reduction for shifting to buprenorphine; 6) intolerance of buprenorphine side effects.

General information

Acronym

IRCT registration information

IRCT registration number: **IRCT2016011626040N1**
Registration date: **2016-04-26, 1395/02/07**
Registration timing: **registered_while_recruiting**

Last update:
Update count: **0**

Registration date

2016-04-26, 1395/02/07

Registrant information

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Name of organization / entity

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Recruitment status
Recruitment complete
Funding source
Tehran University of Medical Sciences

Expected recruitment start date
2016-04-03, 1395/01/15
Expected recruitment end date
2017-04-04, 1396/01/15
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Survey on Effect of Methadone to Buprenorphine Shift in the Maintenance Treatment on Profile of Gonadal Hormones and Semen Analysis of Infertile Men

Public title
Effect of Substitution of Methadone by Buprenorphine on Gonadal Hormones and Semen
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria: men between 18 to 50 y/o; at least 6 months on Opioid Substitution Treatment & 3 months from last illegal opioid use; daily Methadone dose less than 60 mg/d; certification of therapist physician on stability & readiness of client for shifting from methadone to buprenorphine; diagnosis of methadone as the most important factor for undesirable hormonal & seminal analysis; written & signed informed consent form. Exclusion criteria: evidence or signs of laps & relapse in buprenorphine treatment even with appropriate dose; absence from treatment more than 2 consecutive or 3 undulant weeks; absence from screening opioid urine test more than 2 consecutive or 3 undulant sessions; absence from hormonal & seminal analysis more than 2 weeks after appointed time; intolerance of methadone dose reduction for shifting to buprenorphine; intolerance of buprenorphine side effects.
Age
From **18 years** old to **50 years** old
Gender
Male

Phase
N/A
Groups that have been masked
No information
Sample size
Target sample size: **40**

Randomization (investigator's opinion)
Randomized
Randomization description
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Tehran University of Medical Sciences
Street address
Secretariat of Ethics Committee, Sixth Floor, Tehran University of Medical Sciences, Qhods St. Keshavarz Blvd.
City
Tehran
Postal code
Approval date
2015-11-16, 1394/08/25
Ethics committee reference number
IR.TUMS.REC.1394.1172

Health conditions studied

1

Description of health condition studied
Male infertility in opioid substitution treatment
ICD-10 code
N46
ICD-10 code description
Male infertility

Primary outcomes

1

Description
Follicle-stimulating hormone (FSH) blood level
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
mIU/ml (ELISA)

2

Description
Luteinizing hormone (LH) blood level

Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
IU/L (ELISA)

3

Description
Free Testosterone (FT) blood level
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
pg/ml (ELISA)

4

Description
Total Testosterone (TT) blood level
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
ng/ml (ELISA)

5

Description
Prolactin (PRL) blood level
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
ng/ml (ELISA)

6

Description
Sex Hormone Binding Globulin (SHBG) blood level
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
nmol/l (ELISA)

7

Description
Semen Volume
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
Ml

8

Description
Level of PH of semen
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
Ph Scale

9

Description
Number of spermatozoid in 1 Ml of semen
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
Million/ml

10

Description
Time for fluidity of semen
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
minute

11

Description
Shape of spermatozoides
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
Percentage of spermatozoides with normal shape

12

Description
Normal motility of spermatozoides
Timepoint
Before intervention, 3 months after beginning of intervention, 6 months after beginning of intervention
Method of measurement
Percentage of spermatozoides with normal forward motion

Secondary outcomes

1

Description
Daily methadone dose
Timepoint
Before substitution by buprenorphine
Method of measurement
mg/d

2

Description
Daily buprenorphine dose
Timepoint
After substitution of methadone
Method of measurement
mg/d

Intervention groups

1

Description
According to a randomized categorization, participants will be classified in 2 groups that will be informed. In the intervention group methadone will be substitute with buprenorphine, and maintenance treatment will continue for 6 months. Prescribed medication in the study group is buprenorphine hydrochloride (2 mg SL tablet) manufactured by Faranchimie, 8-16 mg/day, single dose for 6 months. Sampling for laboratory tests (5 cc blood for sex hormones and Seminal fluid volume in 1 ejaculation for semen analysis) will be taken 3 times: before intervention, 3 months, & 6 months after beginning of intervention. Opioid screening test will be done (by taking urine sample 10 cc) every month.

Category
Treatment - Drugs

2

Description
In the control group methadone will be continued as maintenance treatment for 6 months. prescribed medication in the control group is 5 mg methadone hydrochloride tablet, 40-60 mg/day, single dose, for 6 months. Sampling for laboratory tests (5 cc blood for sex hormones and Seminal fluid volume in 1 ejaculation for semen analysis) will be taken 3 times: before intervention, 3 months, & 6 months after beginning of intervention. Opioid screening test will be done (by taking urine sample 10 cc) every month.

Category
Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Iranian National Center for Addiction Studies

Full name of responsible person
Mohammad Reza Haddadi

Street address
No. 669, Qazvin Square, Sout Kargar Avenue

City
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Tehran University of Medical Sciences

Full name of responsible person
Nasim Vosoughi, Ph.D

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No. 88, School of Advanced Technologies in Medicine, Italia st. , Keshavarz Blvd.

City
Tehran

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Tehran University of Medical Sciences

Proportion provided by this source
100

Public or private sector
empty

Domestic or foreign origin
empty

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
empty

Person responsible for general inquiries

Contact

Name of organization / entity
Iranian National Center for Addiction Studies

Full name of responsible person
Mohammad Reza Haddadi

Position
Medical Degree/ Director of Buprenorphine Clinic

Other areas of specialty/work

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
empty
Study Protocol
empty
Statistical Analysis Plan
empty
Informed Consent Form
empty
Clinical Study Report
empty
Analytic Code
empty
Data Dictionary
empty