INPLASY PROTOCOL

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Conflicts of interest:
The authors declare no conflict of interest.

Efficacy of microsurgical varicocelectomy in the treatment of premature ejaculation: a protocol for systematic review and meta-analysis

Li, F[1]; Zhang, S[2]; Yao, H[3]; Fan, Y[4]; Shen, Y[6]; Li, G[7]; Chang, D[8].

Review question / Objective: **With this systematic review and if possible meta-analysis we urge to further evaluate the effectiveness and safety of microsurgical varicocelectomy in the treatment of PE. The results will offer clinical decisions for urologists and andrologists.**
Condition being studied: **Premature ejaculation (PE) is the most common type of sexual disorder among men which comprises a great of problems. varicocele (VC) is defined as the dilation of the pampiniform venous plexus draining the testicle. At present, selective serotonin reuptake inhibitors (SSRIs) antidepressants, topical anesthetics (TAs), tramadol, phosphodiesterase type 5 inhibitors (PDE5is) are the common alternative strategy to improve PE. However, these therapeutic measures with several shortcomings and side effects. Recently, the correlation between VC and PE has attracted the attention of some researchers. A few studies consider microsurgical varicocelectomy can be a new remedy for PE. But it is still absent enough a great deal of convincing evidence. The study will assess the effectiveness and safety of the microsurgical varicocelectomy treatment in PE patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 June 2020 and was last updated on 16 June 2020 (registration number INPLASY202060058).

INTRODUCTION

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METHODS

Search strategy: Electronic databases will include English databases (PubMed, MEDLINE, EMBASE, Web of Science, Cochrane Library) and Chinese databases (China National Knowledge Infrastructure, China Biology Medicine Database, Wanfang Database, VIP Database). All the above databases will be searched from their inception to December 2020 recognize related studies. The following search strategy will run in PubMed and tailored to the other database when necessary: ((("Varicocele/surgery"[Mesh]) AND (varicocele*[Title/Abstract] OR ligation[Title/Abstract] OR ligation of spermatic vein [Title/Abstract] OR Ligasure vessel sealing[Title/Abstract] OR artery ligation[Title/Abstract] OR vein ligation[Title/Abstract] OR veinembolization[Title/Abstract] OR surgery[Title/Abstract] OR Surgical[Title/Abstract] OR surgical ligation[Title/Abstract] OR *Surgical-Procedures,-Laparoscopic[Title/Abstract] OR varicocele-embolization[Title/Abstract] OR varicocele ligation[Title/Abstract] OR varicocele-outcome[Title/Abstract] OR varicocelectomy[Title/Abstract] OR varicocoelectomy[Title/Abstract] OR varicocolectomy[Title/Abstract] OR embolisation[Title/Abstract] OR mbolization[Title/Abstract] OR varicocelectomy[Title/Abstract])) AND (("Premature Ejaculation"[Mesh]) AND (ejaculation, premature[Title/Abstract] OR ejaculations, premature[Title/Abstract] OR pemature ejaculations[Title/Abstract] OR ejaculatio praecox[Title/Abstract] OR ejaculatio praecoxs[Title/Abstract] OR praecox, ejaculati [Title/Abstract] OR praecoxs, ejaculatio [Title/Abstract])). Besides, the reference lists of review articles will be searched for any possible titles matching the inclusion criteria. The researchers will also scan the database of Chengdu University of Traditional Chinese Medicine Library and our hospital's experts in endocrinology and urology will be consulted. Dissertations of degrees will be included. The WHO International Clinical Trials Registry Platform and Google Scholar will be searched for potential results. Besides, the ClinicalTrials.gov registry will be searched for any unpublished trials.

Participant or population: Inclusion criteria: ·Patients who have regular sexual life for more than half a year with a fixed sexual partner before the operation, clinically diagnosed as premature ejaculation (≥ 18 years old). ·Patients have been diagnosed with varicocele by physical examination and color Doppler ultrasonography of the male reproductive system. Exclusion criteria: ·Patients who have used antidepressants, topical anesthetics and other drugs to treat premature ejaculation within 3 months. ·Patients with a history of scrotal and spermatic cord injuries and congenital genitourinary abnormalities. ·Patients who have been operated on for varicocele. ·Patients with a history of tumors and diabetes in the past year. ·Patients with any other disease that may cause varicocele (such as external kidney tumor, hydronephrosis, etc.)

Intervention: The patients in the treatment group received microsurgical varicocelectomy (no restriction on the methods of operation and course of treatment).

Comparator: The control group could gain a placebo, no treatment, SSRIs antidepressants, TAs, PDE5is, exercise, or guideline-recommended conventional treatment.

Study designs to be included: All the RCTs of microsurgical varicocelectomy for the management of PE patients will be included without publication status restriction or writing lan.

Eligibility criteria: All the RCTs of microsurgical varicocelectomy for the management of PE patients will be included without publication status restriction or writing language. letters to editors, review articles, case reports, conference abstracts, cross-sectional studies, and all observational studies will be excluded. Primary outcome: 1) Improvement in sexual intercourse time, as measured by the intra-vaginal ejaculation latency time (IELT), which could assess the time from when the penis is inserted into the vagina until the beginning of ejaculation. Secondary outcomes: 1) Chinese Index of Sexual Function for Premature Ejaculation-5 (CIPE-5) scores. 2) Visual Analogue Score (VAS), which is used to evaluate the pain of participants. 3) Premature ejaculation diagnostic tool (PEDT), whose item ranges from 0 (no problem) to 4 (very serious problem). The higher the score, the more severe the symptoms. 4) The success treatment rate (after treatment the participants comparing to the control group) and the complications rate. 5) Serum testosterone levels.

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Main outcome(s): 1) Improvement in sexual intercourse time, as measured by the intra-vaginal ejaculation latency time (IELT), which could assess the time from when the penis is inserted into the vagina until the beginning of ejaculation.

Additional outcome(s): 1) Chinese Index of Sexual Function for Premature Ejaculation-5 (CIPE-5) scores. 2) Visual Analogue Score (VAS), which is used to evaluate the pain of participants. 3) Premature ejaculation diagnostic tool (PEDT), whose item ranges from 0 (no problem) to 4 (very serious problem). The higher the score, the more severe the symptoms. 4) The success treatment rate (after treatment the participants comparing to the control group) and the complications rate. 5) Serum testosterone levels.

Quality assessment / Risk of bias analysis: The risk of bias will be independently assessed by two reviewers and any differences will be resolved through consultation or the participation of a third reviewer. The RCTs will be evaluated using the Cochrane "risk of bias assessment" tool. The tool assesses the risk of bias mainly in the following 7 aspects: random sequence generation, allocation concealment, the blinding method for patients, researchers and outcomes assessors, incomplete result data, and selective reports. As recommended by the Cochrane manual, the risk of bias in each of these areas will be assessed as low or high depending on whether the criteria were met or not met, and the lack of information will be recorded as unclear. In most cases, disagreements will be settled by discussion between the 2 reviewers. If disagreement remained after discussion, a third reviewer will be consulted before taking the final decision on the disagreements.

Strategy of data synthesis: We will use RevMan5.3 software for meta-analysis. For dichotomous data (e.g., effective and ineffective), we will calculate risk ratio (RR)

and 95% confidence intervals (CIs). For continuous data, when the measurement method and unit are consistent, we will calculate the weighted mean difference (WMD) and 95% CIs. When the measurement methods and units are inconsistent or the mean values of different experiments differ greatly, we will use the standardized mean difference (SMD) and 95% CIs as the composite statistics.

Subgroup analysis: If there is significant heterogeneity in the included trials, we will identify the source of heterogeneity through subgroup analysis and manage the heterogeneity: 1) The duration and severity of VC. 2) Intervention features: unilateral varicose vein surgery or bilateral varicose vein surgery. 3) The duration and severity of PE. 4) whether with other sexual dysfunctions. 5) demographic characteristics of the patients: age, marital and family status, region, race, and ethnicity. 6) follow-up time.

Sensibility analysis: A sensitivity analysis will be performed to test the robustness of the review result and to detect the source of heterogeneity. This can be done by excluding trials with a high risk of bias or eliminating each study individually. And, the impact of methodological quality, sample size, and missing data will be assessed. Then the analysis will be repeated after the exclusion of low methodological quality studies and the results compared with the previous meta-analysis.

Country(ies) involved: China.

Keywords: microsurgical varicocelectomy; premature ejaculation; treatment; protocol.

Contributions of each author:
Author 1 - Fuhao Li - Fuhao li provided the conceptualization and drafted the manuscript.
Author 2 - Song zhang - Song Zhang contributed to the project administration.
Author 3 - Hangyu Yao - Hangyu Yao contributed to the data curation and the formal analysis.
Author 4 - Yueyue Fan - Yueyue Fan contributed to the data curation and using the software.
Author 5 - Yifeng Shen - Yifeng Shen contributed to the formal analysis and using the software.
Author 6 - Guangsen Li - Guangsen Li supervised the review and edited the final manuscript.
Author 7 - Degui Chang - Degui Chang also supervised the review and edited the final manuscript.