Fertility in men with spinal cord injury

Čehić, Ermin; Kasum, Miro; Šimunić, Velimir; Orešković, Slavko; Vujić, Goran; Grgić, Franjo

Source / Izvornik: **Gynecological Endocrinology, 2016, 32, 937 - 941**

Journal article, Accepted version
Rad u časopisu, Završna verzija rukopisa prihvaćena za objavljivanje (postprint)

https://doi.org/10.1080/09513590.2016.1202231

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:563798

Čehić E., Kasum M., Šimunić V., Vujić G., Grgić F. (2016) ***Fertility in men with spinal cord injury.*** **Gynecological Endocrinology, 32 (12). pp. 937-41. ISSN 0951-3590**

http://www.tandfonline.com/loi/igye20

http://dx.doi.org/10.1080/09513590.2016.1202231

Review article

Fertility in men with spinal cord injury

Running title: Male fertility with spinal cord injury

Ermin Čehić[1], Miro Kasum[2], Velimir Šimunić[3], Goran Vujić[2], Franjo Grgić[2]

[1]*Cantonal Hospital Zenica, Zenica,* Bosnia and Herzegovina

[2]*Department of Obstetrics and Gynaecology, University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Zagreb, Croatia*

[3]*Polyclinic IVF, Zagreb, Croatia*

Correspondence:

Prof. Miro Kasum, M.D., Ph.D., University Department of Obstetrics and Gynaecology, School of Medicine, University Hospital Centre Zagreb, Petrova 13, 10 000 Zagreb, Croatia

Tel: (+ 385) 1 4604646, Fax: (+385) 1 2376267 , E-mail: mkasum@gmail.com

Abstract

Keywords: spinal cord injury, fertility, erectile and ejaculatory dysfunction, asthenospermia

Young men comprise the overwhelming majority of men with spinal cord injury (SCI) which has been growing over the years. Owing to advances in physical medicine and rehabilitation remarkable improvements in survival rates have been reported, similar to those of the general population. However, many sexual and reproductive functions may be impaired due to erectile or ejaculatory dysfunction and semen abnormalities, characterized by normal sperm concentration and low sperm motility or viability in SCI males who have not fulfilled their parental project yet. Nevertheless, fatherhood is still possible owing to introduction of specialized medical management, by using various medical, technical and surgical methods for sperm retrieval in combination with assisted reproductive techniques. Erectile dysfunction can be managed by regimens which include the use of phosphodiesterase-5 inhibitors, intracavernosal injections, vacuum devices and penile prostheses. Semen can be obtained from the vast majority of anejaculatory men via the medically assisted ejaculation by use of vibratory or electrical current stimulations and via prostate massage or surgical procedures. Despite impaired sperm parameters, reasonable pregnancy rates similar to those in able-bodied subfertile cohorts have been reported. However, future research should focus on the optimization of semen quality in these men and on improving natural ejaculation.

Introduction

Spinal cord injury (SCI) is a specific medical state that has been increasing over the years in the whole world and especially in the United States of America. The yearly incidence of SCI in the United States is approximately 40 cases per million population without armed forces personnel and those at the scene of an accident. Each year there are approximately 12,500 new cases, with 240,000 to to 337,000 persons in the US currently living with SCI.. The majority (77-79%) of SCI occur to men between the ages of 16 and 45 with the average age at injury between 37 and 42, what is higher than in the rest of the world. More than half of all patients have never been married and have not fulfilled their parenteral project at the time of their injury [1,2].

Although there are still no interventions available that can reverse the neurological loss in men with SCI, advances in medicine particularly in the field of rehabilitation and physical therapy during the last 40 years has led to remarkable improvements such as higher survival rates, shorter hospitalizations and more effective treatments for spasticity and neuropathic pain [3]. In addition, application of modern therapeutic inroads has improved the mobility of persons with SCI and has facilitated their access to information, allowing better social inclusion and has removed the main concern from life support to focusing on patient's future quality of life, sexual dysfunction and fertility as well as the ability to father a child [4]. Many aspects of sexuality can be disrupted following SCI including individual's self-esteem and body image, problems with incontinence and decreased pleasure and sexual concerns which can involve erectile function, essential for intercourse and ejaculation function that is necessary for fertility and the ability to reach orgasm [5]. Reproductive functions may also be compromised and most of these patients are infertile and can not father children naturally due to sacral autonomic disruption, with consequent erectile dysfunction, ejaculatory dysfunction and semen abnormalities. Therefore, in spite of increased desire and willingness of men with

SCI to start a new family and become active members of communities in which they live, only 10% of individuals will father biologic children without medical contribution for semen retrieval [6].

Nevertheless, fatherhood is still possible owing to introduction of specialized medical management which can be complex, time-consuming and expensive. Erectile dysfunction can be managed by regimens available to the general population which include the use of phosphodiesterase-5 (PDE-5) inhibitors, intracavernosal injections, vacuum devices and penile prostheses. Semen may be obtained from the vast majority of anejaculatory men with SCI via the medically assisted ejaculation methods by using vibratory or electrical current stimulations, sperm retrieval is also possible via prostate massage or surgical procedures [7,8]. Although men with SCI were previously considered "hopelessly infertile", nevertheless with the application of these semen retrieval techniques the patients are currently "potentially fertile". By using various medical, technical and surgical methods for sperm retrieval with or without assisted reproductive techniques, numerous studies have reported reasonable fertility potential for men with SCI. The coincident application of assisted reproductive technology to these couples has yielded reproductive outcomes similar to those in able-bodied subfertile cohorts with reasonable pregnancy rates [9-13]. The purpose of the review is to analyse current management regimens responsible for impaired reproductive function as well as later fertility in men with SCI.

Erectile dysfunction

Reflexogenic and psychogenic erections are mostly impaired in men with SCI although their vascular and anatomic functions are usually intact [14]. Because the basic mechanisms for erection (normal vasculature and an intact S2-S4 reflex arc) are preserved in most men with SCI, these men respond well to oral administration of PDE-5 inhibitors, including sildenafil,

tadalafil and vardenafil, which inhibit the degradation of cyclic GMP in the penile corpora and maintain vascular smooth muscle relaxation [15].

Intracavernosal injections is a treatment that stimulates higher levels of cyclic AMP, another potent dilatator within the corpora cavernosa. Various agents, including papaverine, phentolamine, and alprostadil, have been administered intracavernosally for the purpose of treatment of erectile dysfunction. There is an 80% success rate with this therapy; however, possible adverse effects such as priapism and hematoma, must be discussed during patient's counseling [16].

Intraurethral application of suppository represents the medicated urethral system for erection (MUSE) which uses administration of alprostadil for treating erectile dysfunction. However, the absorption of alprostadil from the urethral lumen can be variable which can reduce the effectiveness of MUSE, especially in SCI patients who manage their bladders with intermittent catheterization. Nevertheless, some patients may prefer MUSE because it is less invasive than intracavernosal injection [17].

Vacuum erection devices work by inserting the penis into a rigid cylinder which creates a mechanism of negative pressure to draw blood into the penis and create an erection, in conjunction with a constriction band over the base of the penis to maintain erection. However, patients with SCI report lower satisfaction rates with vacuum erection devices compared to other treatments for erectile dysfunction, mostly due to loss of rigidity during intercourse or complications with the restriction bands [18].

Surgically implanted malleable penile prosthesis in patients with SCI represents an attractive option for erectile dysfunction because it is associated with low complication rates and the overall patient satisfaction rate of 79.2% [19]. Moreover, the three-piece inflatable penile prosthesis has the highest patient satisfaction rates and lowest mechanical revision rates of almost any medically implanted device [20]. However, alternative surgical treatments for

erectile dysfunction including Brindley sacral anterior root stimulator after sacral dorsal rhizotomy have also been reported recently with varying degrees of success [21].

.

Ejaculatory dysfunction

Ejaculation is a reflex mediated by a spinal control center, referred to as a spinal ejaculation generator, which coordinates sympathetic, parasympathetic and motor outflow to induce the two phases of ejaculation, i.e., emission and expulsion. The ejaculatory reflex is coordinated by the spinal cord and depends on thoracolumbal sympathetic fibers from segments T10-L2 and somatic fibers from segments S2-S4. This reflex receives its somatic input primarily from the dorsal nerve of the penis, which is activated by the glans penis [22]. Additionally, the spinal ejaculation generator is under inhibitory and excitatory influence of supraspinal sites, including the nucleus paragigantocellularis, the paraventricular nucleus of the hypothalamus and the medial preoptic area [23]. Therefore, SCI can disrupt the nerve pathways responsible for ejaculation and lesions below T10 which vary in their adverse effect on ejaculatory function, depending on their extent and exact location. However, an injury at or rostral to the neurological T10 spares the reflex necessary for ejaculation [24]. Since the majority of patients with SCI men are not able to produce ejaculation by masturbation or sexual stimulation, semen retrieval can be successfully performed by the use of several medically assisted methods combined with assisted reproduction techniques, in order to further enhance their fertility potential [8].

Penile vibratory stimulation (PVS) is preferred by the patients with SCI and recommended as the first line of treatment for anejaculation because it is simple in use, non-invasive, safe, reliable, cost-effective and compared to other methods, yields the highest number of total motile sperm in antegrade fractions [8,25]. Mechanical stimulation, produced by the vibrator placed on the dorsum or frenulum of the glans penis, recruits the ejaculatory reflex to induce ejaculation [26]. A vibrator is applied for 2-3 minutes or until antegrade

ejaculation occurs. If no ejaculation occurs, stimulation is stopped for 1-2 minutes and then resumed. These steps are repeated for up to 10 minutes of stimulation and most patients who respond to PVS have little or no retrograde ejaculation. A wide variety of devices can be used to perform PVS, but the most effective devices are those delivering at least 2.5mm of amplitude. There are two single vibrators such as the FertilCare or Viberect capable of delivering these high amplitudes, but in cases which fail to induce ejaculation application devices with two vibrators or simultaneous use of electrical abdominal and vibratory stimulation may be recommended [7]. The ejaculatory success rate of the Viberect is somewhat lower (77%), than that reported (86%) of the FertilCare device in men with SCI whose injury was at or rostral to T10. However, the success rate of the FertilCare device is only 17% in patients whose level of injury is caudal to T10 [27,28]

Electroejaculation (EEJ) is a procedure for males with SCI that uses electrical current applied to the back of the prostrate gland through the rectum to stimulate the nerves around the prostate, as well as the seminal vesicles and smooth muscle fibres of the prostate to produce contraction of the pelvic muscles, resulting in antegrade ejaculation. In cases if no antegrade ejaculation occurs usually occurs retrograde ejaculation and therefore a catheter should be passed into the penis to collect any semen that may have gone into the bladder. However, if no ejaculate is found in the pellet of the centrifugated specimen the bladder may be lavaged with additional sperm washing buffer. Patients who cannot respond to PVS are often referred for EEJ, which must be administered by a physician trained in this procedure [7]. Comparing two methods of delivering EEJ, intermittent vs. continuous delivery of EEJ current it was confirmed that each method resulted in a similar mean total sperm count and total motile sperm in the total ejaculate, but a higher proportion of sperm was found in the antegrade fraction using the interrupted method. Therefore, the intermitent method in which electric current was turned on for 5 sec, then off for 5 sec, should be preferred as the technique of choice when EEJ is performed to obtain sperm for fertilisation. [29]. The majority of men

with SCI can undergo EEJ without anesthesia, but for patients with preserved pelvic sensation EEJ can cause significant discomfort, therefore it may need to be done in an outpatient surgical facility under conscious sedation or general anesthesia [30]. EEJ is a highly successful procedure with the ejaculatory success rate of 95%, however the 5% failure rate can often be attributed to cases in which men experienced pelvic pain on their first trial of EEJ and do not want to continue with further trials under sedation or general anesthesia [31].

Prostate massage (PM) is a simple method of semen retrieval in men with SCI which is performed by a physician who presses on the seminal vesicles and the prostate with a finger inserted into the patient's rectum. It may be recommended prior to surgical sperm retrieval in cases when PVS fails and EEJ is unavailable or requires anesthesia. However, sperm yields are typically low (up to 32%) with PM compared to PVS or EEJ, therefore it is not clear when to use it in algorithm of semen retrieval methods [7,32].

Surgical sperm retrieval is a method of retrieving sperm from reproductive tissue, either by aspiration or through surgical exploration and may be performed as a last resort. According to algorithm for sperm retrieval based on the largest study of 3152 semen retrieval procedures in 500 men with SCI, it was recommended that patients who fail to respond to PVS should proceed to EEJ, but in cases if EEJ fails or is contraindicated, prostate massage or surgical sperm retrieval may be performed [28]. Various surgical techniques may be used including percutaneous epididymal sperm aspiration (PESA), microepididymal sperm aspiration (MESA), testicular sperm aspiration (TESA), testicular sperm extraction (TESE), microdissection testicular sperm extraction (Micro-TESE) and aspiration of sperms from the vas deferens [24]. Since sperm yields are very low with these surgical methods, the low motile sperm count obtained commits these patients with SCI to an in vitro fertilisation/intracytoplasmatic sperm injection (IVF/ICSI), as the most invasive and expensive techniques of assisted reproduction [7].

Semen abnormalities

Despite normal sperm concentration the semen quality in the majority of patients with SCI is poor due to low sperm motility, as the most notably abnormality and sperm viability [4,6,7,33]. It has been proposed that semen abnormalites may be a direct result of accessory gland dysfunction due to SCI-related dysinervation, various toxic seminal substances including elevated concentrations of pro-inflammatory cytokines and inflammasome components with leukocytospermia, since neutralization of these constituents resulted in improved sperm motility [7]. However, only a minority of these men with incomplete lesion of the spinal cord retain normal semen parameters and therefore it may be that completeness of SCI is an important risk factor influencing semen quality [34]. Since the majority of men with SCI have a distinct semen profile compared to the general population (commonly low sperm concentration concomitantly with low sperm motility), it was suggested that several indirect factors also contribute to abnormal semen characteristics. Semen abnormalites may be associated to the lifestyle factors of these patients, including bladder management, scrotal hyperthermia, infrequency or methods of ejaculation and years post-injury, which may be responsible for impairment of semen parameters. However, none of these factors alone may be the major cause of the decrease observed in semen quality [7]

Although no bladder management regime has been associated with normal semen quality in men with SCI it seems that patients who used intermittent catheterization had the highest sperm motility (27%), whereas those with an indwelling catheter had the lowest sperm motility (5%) [35]. It has been hypothesized that sitting in a wheelchair for prolonged periods of time leads to scrotal temperature in men with SCI compared with von-injured controls, however it appears that scrotal temperature does not contribute to poor semen quality [36]. Since majority of men with SCI cannot ejaculate without medical assistance it has been also been hypothesized that long periods between ejaculations may result in reproductive tract

stasis which can negatively affect sperm quality. However, no statistically significant improvement in sperm quality and normalization in sperm motility following repeated ejaculation by PVS or EEJ has been reported [37,38]. Via nvestigating the method of assisted ejaculation in patients with SCI much has been reported about their semen quality. In addition to earlier data about lower sperm motility from semen collected by EEJ compared to semen obtained by PVS [39], it was established that sperm motility may be significantly higher when obtained by masturbation (36,9%) than by PVS (25,9%) or EEJ (15%) [40]. Since the semen quality remains stable without clinically significant changes during the chronic phase of SCI after the injury, this information may be useful for family planning [41]. Therefore routine long-term cryobanking of semen harvested early after SCI cannot be recommended, because long-term cryopreservation of semen results in essentially immotile sperm with minimal viability [42]. Since semen cryopreservation may be detrimental on mitochondrial activity and DNA fragmentation in addition to conventional semen variables, therefore other studies to preserve fertility from patients with SCI and improve their seminal quality should be performed [43].

Assisted reproductive technology

Intravaginal insemination or so called “in-home insemination" is the least invasive technique for the majority of men with SCI who cannot ejaculate during intercourse and therefore the couple may collect the semen by PVS, which may then be deposited into the vagina to father a child. It is advisable that couples be evaluated in a clinic prior attempting insemination, the male partner for risk of autonomic dysreflexia and the optimal method of inducing ejaculation, whereas the female partner for the absence of any tubal or uterine pathology and for the presence of normal ovulatory cycles. [44,45].

Intrauterine insemination (IUI) involves collecting semen from the SCI male partner by using masturbation, PVS or EEJ and processing it in a laboratory to separate the sperms

from the semen and the motile from the nonmotile sperms during spontaneous or stimulated cycles in order to achieve pregnancy. According to recommended minimum of 2 million of motile spermatozoa for successful fertilisation through IUI [46], compared to the total motile sperm count of 5 million in the majority of ejaculation-positive PSV or EEJ in men with SCI, it appears that the ejaculate of men with SCI has a sufficient number of motile sperms for IUI and even intravaginal insemination [31].

Advanced reproductive technologies may be recommended in SCI patients with extremely low total sperm count when fertilisation is not possible or not indicated by intravaginal insemination or IUI. When the number of motile sperm is too low for conventional IVF, the method of ICSI is often used to achieve fertilization [13]. These procedures can be performed in patients whose ejaculated sperms were obtained by PVS versus EEJ [9,11,47-49], whereas after surgical sperm retrieval from the testicle, the epididymis and the vas deferens IVF or ICSI is mandatory [9,12,13]. The choice of assisted technology for patients with SCI is currently controversial, because it can be started directly by surgical sperm retrieval from reproductive tissue and followed by IVF/ICSI as a first line of treatment for anejaculation, bypassing examination of the ejaculate due to a lack of EEJ or PVS training and equipment [12, 13, 31]. Otherwise, since the majority of these patients have reasonable yields of total mobile sperms obtained by PVS or EEJ, it is advisable to begin with PVS as the first choice of treatment for semen retrieval, because the equipment is less expensive and administration is easier than EEJ and perform intravaginal or IUI if the total sperm count is sufficient [7,31].

Pregnancy outcome

Intravaginal insemination often results in good pregnancy rates in couples with SCI male factor infertility, with reproductive outcomes which are similar to outcomes for general male factor infertility, because various studies have reported reasonable pregnancy success rates (25-75% per couple) [7,9,10,13,45]. Evaluating the pregnancy rate of 43% in 60 of 140 couples, it was concluded that PVS combined with vaginal self-insemination may be performed as a viable, inexpensive option for assisted conception with couples when the SCI male partner has an adequate total motile sperm count and the female partner is healthy [45]. Finding the pregnancy rate of 37.8% in 17 of 45 couples it was reported that intravaginal insemination represents a reasonable option for men with SCI, which warrants consideration before proceeding to assisted reproductive technologies [10].

IUI represents a viable reproductive option with reasonable pregnancy rates (24-60% per couple) for such patients whose efficacy increases as the total motile sperm count increases and its use is also justified prior to including the methods of advanced reproductive technology [7,10,13]. When inseminated total motile sperm counts were greater than 40 million the pregnancy rate per cycle was 17.6%. However, in SCI men with counts of <4 million total motile sperm the pregnancy rate per cycle decreased sharply to 1.1% [30]. In a recent study 14 out of 57 couples achieved a total of 19 pregnancies with the pregnancy rate of 24,6% [30], whereas previous studies have reported higher pregnancy rates ranging between 26.7% and 78.6% [50,51].

Numerous studies have shown reasonable fertility potential for men with SCI. by using various medical, technical or surgical methods for sperm retrieval with IVF/ICSI procedures with variable success rates from 15 % to 75% [9,11.12, 47-49,52,53]. Despite lower pregnancy rates per cycle (15%) and pregnancy rates per couple (29%) in an earlier study of SCI patients treated with EEJ, it was concluded that ICSI or IVF may be a viable alternative for patients with anejaculation in whom intrauterine insemination failed [48].

Investigating fertility potential of men with psychogenic anejaculation and SCI patients treated with EEJ, it was found that combination of EEJ and ICSI gives reasonable results with fertilisation rates of 47% and 57%, respectively [52]. Comparing IVF/ICSI outcomes with sperm obtained by PVS or EEJ in male factor infertility patients with and without SCI, the fertilisation rate was significantly lower in the SCI group compared with the non-SCI group (56% versus 71,4%), without statistically significant difference in the pregnancy rate per couple (58,1% versus 57,9%) [47]. However, surgical retrieval of fresh sperm by using TESE in combination with ICSI in patients with SCI, may possess more advantage due to high pregnancy rate per couple (74%), than ejaculated sperm for ICSI and therefore may offer optimum outcome as a most promising choice for SCI couples desirous of pregnancy. Additionally, pregnancy rate per fresh testicular sperm-ICSI was significantly higher than that per frozen-thawed sperm-ICSI (64% versus 25%) [53]. These results have been confirmed recently following TESE and ICSI in SCI patients after repeated trials of EEJ or PVS with the clinical pregnancy rate of 30.2% per cycle and 59.3% per couple and live birth rate of 62.5% [12]. Although some studies [42,43,53] don't recommend freezing sperm in SCI patients, the results of ICSI outcomes using frozen/thawed sperm obtained after PVS or surgical sperm retrieval may be encouraging (pregnancy rates per couple 50% versus 75%) and cryopreservation could be performed in such patients as a preventive measure [11]. (Table I)

Conclusions

Despite abnormal semen parameters in men with SCI favourable pregnancy rates have been achieved in many couples owing to currently used assisted methods for semen retrieval in combination with the assisted reproductive techniques. Since semen quality seems to be primarily affected by changes in seminal plasma further research of the optimization of semen quality in these men and on improving natural ejaculation may be required.

Declaration of Interest: The authors report no declarations of interest.

Table I Pregnancy outcome in patients with men with spinal cord injury following assisted reproductive technologies

Asissted reproductive technology	Studies	Pregnancy rate (%) per couple
Intravaginal insemination	Leduc BE [9] Kathiresan AS et al. [10] Sønksen J et al. [45]	25-70%
Intrauterine insemination	Kathiresan AS et al. [10] Ohl DA et al. [30] Rutkowski SB et al. [50] Pryor JL et al. [51]	24-60%
In vitro fertilisation/Intracyto-plasmatic sperm injection	Leduc BE [9] Bechoua S et al. [11] Raviv G et al. [12] Kathiresan AS et al.[47] Schatte EC et al. [48] Mc Guire C et al. [49] Gat I et al. [52] Kanto S et al. [53]	29-75%

References

1. NSCISC. Spinal Cord Injury - Facts and Figures at a Glance, 2014. Available from: https: //www.nscisc.uab.edu/ Public Documents/facts_figures_docs/Facts%202014.pdf
2. Devivo MJ. Epidemiology of traumatic spinal cord injury: trends and future implications. Spinal Cord 2012;50:365-72
3. Ragnarsson KT. Medical rehabilitation of people with spinal cord injury during 40 years of academic physiatric practice. Am J Phys Med Rehabil 2012;91:231-42.
4. Restelli AE, Bertolla RP, Spaine DM et al. Quality and functional aspects of sperm retrieved through assisted ejaculation in men with spinal cord injury. Fertil Steril 2009;91:819-25.
5. Courtois F, Charvier K. Sexual dysfunction in patients with spinal cord lesions. Handb Clin Neurol 2015;130:225-45.
6. Utida C, Truzzi JC, Bruschini H et al. Male infertility in spinal cord trauma. Int Braz J Urol 2005;31:375-83.
7. Ibrahim E, Lynne CM, Brackett NL. Male fertility following spinal cord injury: an update. Andrology 2015; [Epub ahead of print]
8. Sonksen J, Ohl DA. Penile vibratory stimulation and electroejaculation in the treatment of ejaculatory dysfunction. Int J Androl 2002;25:324–32.
9. Leduc BE. Treatment of infertility in 31 men with spinal cord injury. Can J Urol 2012;19:6432-6.
10. Kathiresan AS, Ibrahim E, Aballa TC et al. Pregnancy outcomes by intravaginal and intrauterine insemination in 82 couples with male factor infertility due to spinal cord injuries. Fertil Steril 2011;96:328-31.

11. Bechoua S, Berki-Morin Y, Michel F et al. Outcomes with intracytoplasmic sperm injection of cryopreserved sperm from men with spinal cord injury. Basic Clin Androl 2013;23:14.
12. Raviv G, Madgar I, Elizur S et al. Testicular sperm retrieval and intra cytoplasmic sperm injection provide favorable outcome in spinal cord injury patients, failing conservative reproductive treatment. Spinal Cord 2013;51:642-4.
13. Brackett NL, Lynne CM, Ibrahim E et al. Treatment of infertility in men with spinal cord injury. Nat Rev Urol 2010;7:162-72.
14. Everaert K, de Waard WI, Van Hoof T et al. Neuroanatomy and neurophysiology related to sexual dysfunction in male neurogenic patients with lesions to the spinal cord or peripheral nerves. Spinal Cord. 2010;48:182-91.
15. Rizio N, Tran C, Sorenson M. Efficacy and satisfaction rates of oral PDE5is in the treatment of erectile dysfunction secondary to spinal cord injury: a review of literature. J Spinal Cord Med 2012;35:219-28.
16. Lebib BA, Laffont I, Boyer F et al. [Intracavernous injection in the treatment of erectile dysfunction in the spinal cord injured patients: about an experience with 36 patients.] Ann Readapt Med Phys 2001;44:35-40.
17. Bodner DR, Haas CA, Krueger B, Sefte AD. Intraurethral alprostadil for treatment of erectile dysfunction in patients with spinal cord injury. Urology 1999; 53:199–202.
18. Denil J, Ohl DA, Smythe C. Vacuum erection device in spinal cord injured men: patient and partner satisfaction. Arch Phys Med Rehabil 1996;77:750-3.
19. Kim YD, Yang SO, Lee JK et al. Usefulness of a malleable penile prosthesis in patients with a spinal cord injury. Int J Urol 2008;15:919-23.
20. Henry GD, Wilson SK. Updates in inflatable penile prostheses. Urol Clin North Am 2007;34:535-47.

21. Lombardi G, Musco S, Wyndaele JJ, Popolo GD. Treatments for erectile dysfunction in spinal cord patients: alternatives to phosphodiesterase type 5 inhibitors? A review study. Spinal Cord 2015 [Epub ahead of print]
22. Giuliano F, Clement P. Neuroanatomy and physiology of ejaculation. Annu Rev Sex Res 2005;16:190-216.
23. Coolen LM, Allard J, Truitt WA. McKenna KE. Central regulation of ejaculation. Physiol Behav 2004;83:203-15.
24. Sultan R, Vaucher L, Bolyakov A, Paduch DA. Anejaculation. In:Goldstein MS, Schlegel PN, editors. Surgical and Medical Management of Male Infertility. 1st ed. Cambridge: University Press, 2013. pp 105-119.
25. Ohl DA, Quallich SA, Sønksen J et al. Anejaculation and retrograde ejaculation. Urol Clin North Am 2008;35:211-20.
26. Brackett NL. Semen retrieval by penile vibratory stimulation in men with spinal cord injury. Hum Reprod Update 1999;5:216-22.
27. Castle SM, Jenkins LC, Ibrahim E et al. Safety and efficacy of a new device for inducing ejaculation in men with spinal cord injuries. Spinal Cord 2014;52 Suppl 2:S27-9.
28. Brackett NL, Ibrahim E, Iremashvili V et al. Treatment for ejaculatory dysfunction in men with spinal cord injury: an 18-year single center experience.J Urol 2010;183:2304-8.
29. Brackett NL, Ead DN, Aballa TC et al. Semen retrieval in men with spinal cord injury is improved by interrupting current delivery during electroejaculation. J Urol 2002;167:201-3.
30. Ohl DA, Wolf LJ, Menge AC et al. Electroejaculation and assisted reproductive technologies in the treatment of anejaculatory infertility. Fertil Steril 2001;76:1249–55.
31. Kafetsoulis A, Brackett NL, Ibrahim E et al. Current trends in the treatment of infertility in men with spinal cord injury. Fertil Steril 2006;86:781-9.

32. Arafa MM, Zohdy WA, Shamloul R. Prostatic massage: a simple method of semen retrieval in men with spinal cord injury. Int J Androl 2007;30:170-3.
33. Patki P Woodhouse J, Hamid R et al. Effects of spinal cord injury on semen parameters. J Spinal Cord Med 2008;31:27-32.
34. Iremashvili VV, Brackett NL, Ibrahim E et al. A minority of men with spinal cord injury have normal semen quality--can we learn from them? A case-control study. Urology 2010:76:347-51.
35. Ohl DA, Denil J, Fitzgerald-Shelton K et al. Fertility of spinal cord injured males: effect of genitourinary infection and bladder management on results of electroejaculation. J Am Paraplegia Soc 1992;15:53-9.
36. Brackett NL, Lynne CM, Weizman M et al. Scrotal and oral temperatures are not related to semen quality of serum gonadotropin levels in spinal cord-injured men.J Androl 1994;15:614-9.
37. Hamid R, Patki P, Bywater H et al. Effects of repeated ejaculations on semen characteristics following spinal cord injury. Spinal Cord 2006;44:369-73.
38. Das S, Dodd S, Soni BM et al. Does repeated electro-ejaculation improve sperm quality in spinal cord injured men? Spinal Cord 2006;44:753-6.
39. Brackett NL, Lynne CM. The method of assisted ejaculation affects the outcome of semen quality studies in men with spinal cord injury: A review. NeuroRehabilitation 2000;15:89-100.
40. Kathiresan AS, Ibrahim E, Modh R et al. Semen quality in ejaculates produced by masturbation in men with spinal cord injury. Spinal Cord 2012;50:891-4.
41. Iremashvili V, Brackett NL, Ibrahim E et al. Semen quality remains stable during the chronic phase of spinal cord injury: a longitudinal study. J Urol 2010;184:2073-7.

42. Krebs J, Göcking K, Kissling-Niggli M, Pannek J. Cross-sectional study of the sperm quality in semen samples from spinal cord injured men after long-term cryopreservation. Andrology 2015;3:213-9.
43. da Silva BF, Borrelli M Jr, Fariello RMet al. Is sperm cryopreservation an option for fertility preservation in patients with spinal cord injury-induced anejaculation? Fertil Steril 2010;94:564-73.
44. Kathiresan AS, Ibrahim E, Aballa TC. Pregnancy outcomes by intravaginal and intrauterine insemination in 82 couples with male factor infertility due to spinal cord injuries. Fertil Steril 2011;96:328-31.
45. Sønksen J, Fode M, Löchner-Ernst D, Ohl DA. Vibratory ejaculation in 140 spinal cord injured men and home insemination of their partners. Spinal Cord 2012;50:63–66.
46. Cao S, Zhao C, Zhang J et al. A minimum number of motile spermatozoa are required for successful fertilisation through artificial intrauterine insemination with husband's spermatozoa. Andrologia 2014;46:529-34.
47. Kathiresan AS, Ibrahim E, Aballa TC et al. Comparison of in vitro fertilization/intracytoplasmic sperm injection outcomes in male factor infertility patients with and without spinal cord injuries. Fertil Steril 2011;96:562-6.
48. Schatte EC, Orejuela FJ, Lipshultz LI et al. Treatment of infertility due to anejaculation in the male with electroejaculation and intracytoplasmic sperm injection. J Urol 2000;163:1717-20.
49. Mc Guire C, Rustom P, Grainger R, Flynn R. Electrocautery stimulation for male infertility secondary to spinal cord injury: the Irish experience in National rehabilitation hospital. Urology 2011;77:83-7.
50. Rutkowski SB, Geraghty TJ, Hagen DL et al. A comprehensive approach to the management of male infertility following spinal cord injury. Spinal Cord 1999;37:508–14.

51. Pryor JL, Kuneck PH, Blatz SM et al. Delayed timing of intrauterine insemination results in a significantly improved pregnancy rate in female partners of quadriplegic men. Fertil Steril 2001;76:1130–5.
52. Gat I, Maman E, Yerushalmi G et al. Electroejaculation combined with intracytoplasmic sperm injection in patients with psychogenic anejaculation yields comparable results to patients with spinal cord injuries. Fertil Steril 2012 ;97:1056-60.
53. Kanto S, Uto H, Toya M et al. Fresh testicular sperm retrieved from men with spinal cord injury retains equal fecundity to that from men with obstructive azoospermia via intracytoplasmic sperm injection. Fertil Steril 2009;92:1333-6.