A comprehensive approach to the management of male infertility following spinal cord injury

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Objectives: To review the outcomes of management of male infertility following spinal cord injury in a specialised fertility clinic.

Study Design: Retrospective review of medical records.

Setting: The Fertility Clinic of a 45-bed spinal cord injury service in New South Wales, Australia.

Methods: The medical and fertility clinic records of 113 males who attended the clinic between 1987 and 1997 were reviewed.

Results: The rates of semen retrieval using vibroejaculation and electroejaculation were 67% and 97% respectively. Thirty-one individuals (37%) and their partners sought assistance with the primary aim of achieving a pregnancy. Intravaginal insemination (IVI) undertaken at home following vibroejaculation resulted in a pregnancy rate per cycle of 22%. Electroejaculation and IVI proved less successful with a pregnancy rate per cycle of only 5%, although with intrauterine insemination (IUI) this rate improved to 30%. Micro-manipulation *in vitro* fertilisation (IVF) procedures, primarily intracytoplasmic sperm injection, were used in 18 couples resulting in a pregnancy rate per cycle of 19%. In the 31 couples there have been a total of 17 pregnancies in 97 cycle attempts for an overall pregnancy rate per cycle of 18% and a cumulative pregnancy rate per couple of 55%. Twelve of the pregnancies have resulted in 14 live births (including two sets of twins), there were three pregnancies ongoing at the date of review and there have been two spontaneous abortions.

Conclusion: The benefits of a specialised fertility clinic offering a comprehensive, client-focused approach with education, fertility assessment and a range of semen retrieval and assisted reproduction options, are highlighted.

Keywords: spinal cord injury; fertility; vibroejaculation; electroejaculation; insemination; intracytoplasmic sperm injection

Introduction

Male infertility is a well recognised complication following spinal cord injury (SCI) which, until recent years, had greatly reduced the reproductive potential of spinal cord injured males. The two major reasons for male infertility following SCI are anejaculation and poor semen quality. Previous studies have reported that only 5% to 18% of males following SCI are able to ejaculate,^{1–3} however, determination of the true frequency of ejaculation may have been confounded because of retrograde ejaculation in some patients.^{3,4}

Currently the two most common methods of semen retrieval are vibroejaculation and electroejaculation. Vibroejaculation was first used by Sobrero in 1965⁵ and popularised by Brindley who reported success in 59% of 81 patients whose injuries were of more than 6 months duration.⁶ Electroejaculation was first used by

Horne in 1948 and an ejaculate obtained in eight out of 15 spinal cord injured men.¹ Brindley, using his electroejaculation technique obtained an ejaculate (either antero- or retrograde) in 97 of 154 (63%) individuals.⁶ Using the Seager technique, Lucas and co-workers reported success in patients in whom the Brindley technique had failed.⁷ Various techniques for vibroejaculation^{8–10} and electroejaculation^{11,12} have been developed and refined since these early reports.

Despite improvements in semen retrieval procedures, the quality of the semen obtained is often poor following SCI. Both sperm motility^{11,13,14} and morphology¹⁵ have been found to be abnormal. These problems have been addressed by attempting to modify causal factors and also by using assisted reproductive technologies including *in vitro* fertilisation (IVF) techniques. Both conventional IVF^{16,17} and various micromanipulation techniques,^{18–20} have been used in partners of spinal cord injured males, although

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to date there have been relatively few reports regarding the latter.

At present, the incidence of SCI in Australia is 1.7 per 100 000 population. In New South Wales, the state of Australia in which this Spinal Injuries Unit is located, there are approximately 100–150 new cases of SCI each year.²¹ Most of these individuals are males aged between 15 and 40 years, in whom reproductive potential is frequently a very important issue. The Fertility Clinic of the Spinal Injuries Unit was established in 1987. Vibroejaculation and electroejaculation techniques have both been extensively employed, along with artificial insemination procedures and the micromanipulation IVF techniques of micro-injection sperm transfer (MIST) and intracytoplasmic sperm injection (ICSI), to achieve pregnancy. The purpose of this paper is to review the outcomes of the comprehensive approach used by this specialised Fertility Clinic in the management of male infertility following SCI for the 10 year period 1987–1997.

Materials and methods

Subjects

Since 1989, assessment of fertility has been offered to all recently injured individuals as part of a comprehensive primary rehabilitation programme. Other clients are referred to the Fertility Clinic from general spinal cord injuries clinics and community health professionals. Individuals or couples may also self-refer. During the 10 year period 1987–1997, a total of 112 individuals with SCI and one individual with Charcot-Marie-Tooth Disease have undergone electroejaculation, vibroejaculation or both procedures for semen retrieval. Table 1 illustrates the demographic details of this group.

Eighty-two of the 113 subjects (73%) underwent semen retrieval procedures for assessment of their fertility status and, in some cases, for cryopreservation of semen, including three individuals where collection of semen using electroejaculation was undertaken within 3 weeks of acute spinal cord injury. The other 31 subjects (27%) and their partners, attended the clinic with the primary aim of achieving pregnancy.

Table 1 Demographic details

Age (years)	Median	29.8
	Range	18–57
Time from injury to procedure	Median	7.2
	Range	6 days–21 years
Aetiology	Traumatic	109
	Non-traumatic	3
	Non-spinal	1
Level of injury	C ₁ –8	57
	T ₁ –9	35
	T ₁₀ –L ₂	20
	Non-spinal	1
	Total	113

Semen retrieval techniques

Vibroejaculation Until April 1991, vibroejaculation was the only semen retrieval procedure used in this clinic. It is generally accepted that for this technique to be successful, the injury must be rostral to the thoracolumbar emission centre (between T10 and L3). Reflex ejaculation was induced using either a Thrive 9000 (Daito Electric Machine Ind. Co. Ltd., Osaka, Japan) or Matoba ME 25 (Matoba, Japan) commercially available vibrator. The duration of the vibratory stimulus was typically 3½ min on with rests of 1 min and the cycle repeated up to three times if necessary. Those subjects at risk of autonomic dysreflexia received prophylaxis with nifedipine and blood pressure was closely monitored. Following a trial of vibroejaculation at the clinic, patients in whom the procedure could be performed safely were instructed in this technique so that it could be performed at home.

Electroejaculation In the period 1991–1997, electroejaculation became the most frequently used semen retrieval technique in our clinic. In those individuals susceptible to autonomic dysreflexia, electroejaculation was performed as the initial procedure. Frequently, when semen analysis alone was requested, no further procedures were required. Electroejaculation was performed using the 'Eljac' (Bosshard Biomed., Sydney, Australia) battery operated device. The patient was placed in the lateral decubitus position and the rectal cavity examined prior to the procedure to determine appropriate probe position and to exclude the presence of faecal material. Prophylaxis with Nifedipine was given if required. Retrograde flow of semen was most commonly managed using a technique of bladder neck tamponade, as described below. At each procedure there was a maximum of three cycles of stimulation with a maximum total duration of 45 s. Following the procedure, prostatic massage and milking of the urethra assisted with collection of the emission. The electrical stimulation parameters used and detail of both the vibroejaculation and electroejaculation procedures have been previously described.²²

Bladder neck tamponade A technique of bladder neck tamponade^{23,24} to prevent retrograde emission during electroejaculation procedures has been used in this clinic since October 1993. The technique used is simpler than some methods described.^{25,26} An all silicone 12 Fg, catheter with a 10 ml balloon is inserted into the bladder prior to the procedure and gentle traction applied during the procedure facilitating an antegrade emission which flows around, not within the catheter. The catheter is inserted using normal saline as a lubricant to avoid possible problems associated with the use of lubricant gels.^{24,27}

Prior to the introduction of this technique a buffer solution (HEPES/HTF Buffer, North Shore ART, Sydney) was instilled into the emptied bladder to minimise the adverse effects of urine on sperm motility²⁸ in any retrograde emission. The retrograde

specimen was then obtained by catheterisation after the procedure was completed. Bladder neck tamponade procedures have a theoretical advantage over use of instilled buffer solutions because they ensure that semen does not, at any time, come into contact with urine.

Fertilisation techniques

Artificial insemination techniques Intravaginal insemination (IVI) with semen collected using vibroejaculation was performed at home, in all instances. These couples received education in the clinic, prior to commencing the techniques at home. In the couples in whom IVI was performed with semen collected using electroejaculation, there was no sperm preparation or induction of ovulation and only limited monitoring of ovulation. The accuracy of ovulation detection was increased with the introduction of simple, inexpensive monitoring kits. Some couples had intrauterine insemination (IUI) performed at the associated assisted reproductive technology (ART) clinic and in these cases sperm washing and preparation and ultrasound monitoring of follicular maturation were used.

In vitro fertilisation (IVF) techniques Conventional IVF techniques, combined with gamete intrafallopian transfer (GIFT) or zygote intrafallopian transfer (ZIFT) have not been used with the partners of spinal cord injured males by this clinic, however, two types of micromanipulation techniques have been used. The microinjection sperm transfer technique which was used initially in this clinic is a variant of subzonal insemination in which more sperm (5–15) are injected past the zona pellucida and into the perivitelline space of each individual oocyte. More recently, the technique of intracytoplasmic sperm injection, has been used, in which a single sperm is injected past the zona pellucida and released directly into the cytoplasm of the oocyte using a micropipette. This technique is particularly useful in cases of severe male factor infertility as only one sperm is required for each oocyte and the possibility of multiple sperm penetration into the cytoplasm is eliminated. ICSI has now become the most commonly used IVF technique in the clinic.

Results

Semen retrieval

Vibroejaculation was used as the sole method to collect semen in 38 individuals (34%) and electroejaculation alone used in a further 46 (41%). Both techniques were tried in 29 individuals (25%).

Vibroejaculation Vibroejaculation was only attempted in those individuals with lesions above T10. Of the 67 individuals who used vibroejaculation, an ejaculate of

semen was obtained in 45 (67%). Sperm were seen in the ejaculate obtained in 42 of these 45 individuals (93%). In the other three cases no sperm were seen. In each of these three cases, for various reasons, further attempts at semen retrieval were not undertaken. Eight of the 45 individuals successfully using vibroejaculation had previously used electroejaculation as the first procedure to obtain semen. Twenty-two individuals (33%) were unable to successfully use vibroejaculation. Of these 22, in 21 cases an ejaculate could not be obtained using the vibrator and in one individual the use of the vibrator was unsafe due to severe autonomic dysreflexia not controllable by prophylactic measures.

Electroejaculation Electroejaculation procedures have been performed in 75 individuals, with an emission obtained in 73 (97%). Sperm were seen in the emission sample in 67 of these 73 individuals (92%). Thirty-three patients were given prophylactic Nifedipine to prevent autonomic dysreflexia. Bladder neck tamponade was employed in 28 individuals (37%). Of the 22 individuals in whom vibroejaculation was unsuccessful, 21 proceeded to electroejaculation with an emission obtained in all 21 cases. Four couples in this group have achieved a pregnancy using semen obtained with electroejaculation after vibrator use had failed.

Other semen retrieval techniques In three individuals more invasive semen retrieval techniques were required. Testicular biopsy was used in two cases and epididymal aspiration in a further instance. These techniques were used when micromanipulation IVF procedures had been planned and on the day of egg collection semen of adequate quality could not be obtained using either vibroejaculation or electroejaculation. Although fertilisation and embryo transfer was successful, ongoing pregnancies were not achieved in any of these cases.

Complications

Autonomic dysreflexia Autonomic dysreflexia was common during both vibroejaculation and electroejaculation procedures but in most cases was easily controlled with Nifedipine prophylaxis. However, one individual developed a severe headache during vibroejaculation and recordable blood pressure peaked at 200/160 mmHg. The headache persisted for 48 h before it resolved. Computerised tomography excluded an intra-cranial haemorrhage. Another patient also suffered significant dysreflexia while undergoing vibroejaculation. In this case there was a very severe headache, chest tightness and respiratory distress with an unrecordable systolic blood pressure and a diastolic blood pressure reaching 150 mmHg. The episode lasted approximately 5 min and further Nifedipine was required before the episode resolved. During electroejaculation one patient developed a bradyarrhythmia, blood pressure rise to 180/120 mmHg, severe headache and fluctuating pupillary dilatation after failure to

ejaculate. The episode persisted for 5 min and only settled after the procedure was repeated and an emission achieved.

Pain Mild rectal discomfort during electroejaculation occurred in some individuals with partially preserved rectal sensation. In five cases intravenous sedation was required and in a further two cases a general anaesthetic was required due to intolerable rectal pain.

Rectal mucosal injury Although no significant rectal mucosal injury has been noted in any of the patients in this study, the long-term effects of repeated electroejaculation on rectal mucosa or other peri-rectal structures have not been described in the literature. There were no other complications.

Reproductive outcomes

The clinic has assisted 31 couples in their attempts to achieve a pregnancy and a total of 17 pregnancies have resulted. Twelve of the pregnancies resulted in 14 live births (including two sets of twins), there were two spontaneous abortions and three pregnancies were ongoing at the date of review. Table 2 shows the reproductive outcomes using different semen retrieval techniques, for the 31 couples actively seeking to achieve a pregnancy. The overall pregnancy rate per cycle for vibroejaculation and electroejaculation was 25% and 15% respectively.

In seven couples, who performed vibroejaculation and IVI at home, there were five pregnancies (four live births and one spontaneous abortion) achieved during 23 cycles. One couple used semen obtained by vibroejaculation in one cycle of ICSI resulting in another live birth.

Electroejaculation was used in conjunction with various levels of fertility enhancement. Electroejaculation and IVI was used in ten couples (22 cycles) resulting in one pregnancy and live birth; a pregnancy rate per cycle of 5%. Five couples underwent a total of ten cycles of IUI resulting in three pregnancies (two live births and one ongoing at 25 weeks gestation); a rate per cycle of 30%.

It should be noted that one couple used both vibroejaculation and electroejaculation with IVI, and one couple used electroejaculation with both IVI and IUI. Therefore, the total number of couples using IVI or IUI procedures is 20 (see Table 3).

Sperm obtained by electroejaculation was used in a total of six cycles of MIST in four couples, with one twin pregnancy resulting; a pregnancy rate per cycle of 17%. Thirty-five cycles of ICSI were performed in 16 couples using sperm obtained by electroejaculation, resulting in six pregnancies. Of these six pregnancies there was one set of live born twins, two singleton live births and two pregnancies ongoing at 18 and 28 weeks. There was one spontaneous abortion. This also gives a pregnancy rate per cycle for ICSI of 17%.

In summary, there have been a total of 17 pregnancies achieved during 97 cycle attempts resulting in a total pregnancy rate per cycle of 18% and per couple of 55%. One couple has achieved two pregnancies using two different techniques (vibroejaculation at home with AI and vibroejaculation with ICSI). Nine of the 17 pregnancies were achieved during 55 cycles using IVI or IUI techniques; a pregnancy rate per cycle of 16%. The pregnancy rate per cycle using micromanipulation techniques (MIST or ICSI) is slightly higher at 19% (eight pregnancies in 42 cycles).

Table 3 Summary of reproductive outcomes

	Pregnancy rate	Pregnancy rate/cycle
Vibroejaculation with IVI (Home)	(5/7) 71%	(5/23) 22%
Electroejaculation with IVI and IUI	(4/15) 27%	(4/32) 12.5%
IVI and IUI (vibro- or electroejaculation)	(9/20*) 45%	(9/55) 16%
MIST and ICSI (vibro- or electroejaculation)	(8/18) 44%	(8/42) 19%
Total	(17/31) 55%	(17/97) 18%

*One couple used both vibroejaculation and electroejaculation with IVI and one couple used electroejaculation with both IVI and IUI

Table 2 Reproductive outcomes for different semen retrieval techniques

	Procedures	Couples	Pregnancies	Live births	Spontaneous abortions	Cycles	Pregnancy rate/cycle %
Vibro-ejaculation	IVI (Home)	7	5	4	1	23	22
	ICSI	1	1	1	—	1	100
Total		8	6	5	1	24	25
Electro-ejaculation	IVI	10	1	1	—	22	5
	IUI	5*	3	2	—	10	30
	MIST	4†	1	2	—	6	17
	ICSI	16*†	6	4	1	35	17
Total			11	9	1	73	15

*Indicates one ongoing pregnancy; †indicates one twin pregnancy. N.B. The number of couples using electroejaculation in conjunction with the various procedures has not been totaled as several couples have used multiple techniques

Table 3 summarises the reproductive outcome results showing pregnancy rates per couple and per cycle.

Discussion

The Fertility Clinic provides a comprehensive service for SCI individuals and their partners, including education and baseline fertility assessment as well as the latest advances in fertility enhancement. It is client focused, offering a range of semen retrieval techniques and assisted reproductive options, allowing couples to choose the methods most suitable for their circumstances. Overall, the results of this study, revealing a pregnancy rate per cycle of 18% and a cumulative pregnancy rate of 53% support this comprehensive approach.

Vibroejaculation and electroejaculation have both proven to be favourable methods of semen retrieval in this study. The success rates of 67% for vibroejaculation and 97% for electroejaculation are comparable with those previously reported.

For vibroejaculation the reported rates have varied from 19–96%.^{8–10,29,30} Lochner-Ernst *et al*,³¹ recently reported a rate of 65%, while Sonksen and others have suggested that the rates can be increased by optimising vibration parameters, particularly the peak-to-peak amplitude.^{10,32} Rates of semen retrieval of up to 89% have been reported using electroejaculation, with better equipment and techniques having led to improved safety and wider use.^{13,33–35}

Prior to 1991 vibroejaculation was the only semen retrieval technique used in our clinic. The success rate using the variable vibrators was initially low and several individuals suffered significant episodes of autonomic dysreflexia with vibroejaculation, despite prophylactic Nifedipine. For these reasons electroejaculation became the more frequently used technique in the initial years following its introduction. This was particularly the case when patients were attending for assessment of fertility potential and/or cryopreservation of semen (rather than to achieve a pregnancy) and when patients were known to have had previous episodes of autonomic dysreflexia from other causes.

There has been little documented in the literature regarding the relative severity of autonomic dysreflexia induced using either technique, although it has been suggested that it may be easier to control with electroejaculation as there is prompt resolution of symptoms when the stimulus is removed.³⁶ This has been the experience of this clinic. Brindley noted that when using electroejaculation the blood pressure rapidly returned to a safe level after stimulation was ceased, and often the procedure could be resumed within 1 min.³³ He has also described several cases where vibroejaculation caused more severe and prolonged symptoms compared to electroejaculation.³⁷ Further investigation of autonomic dysreflexia induced by these techniques is warranted.

Since completion of this present study the clinic has recommenced vibroejaculation as the initial procedure

for most individuals, using the Ferti[®] Care personal vibrator (Multicept, Rungsted, Denmark). This vibrator allows vibration parameters to be optimised.¹⁰ Preliminary results of an ongoing study in the clinic confirm that it is successful in some individuals in whom vibroejaculation has previously failed.

Electroejaculation will remain the only option for acute phase collection of semen when vibroejaculation will not be successful due to the presence of spinal shock. Despite earlier reports to the contrary,^{38,39} acute phase collection of semen by electroejaculation as recommended by Mallidis *et al*,⁴⁰ has been successfully used in this clinic and has provided specimens suitable for cryopreservation. Electroejaculation will also remain appropriate for low lesions and when semen retrieval by vibroejaculation is inconsistent and a micromanipulation IVF procedure has been planned.

To date, it has rarely been necessary to use more invasive methods of semen retrieval in this clinic. However, microsurgical techniques for aspiration of sperm from the vas deferens, epididymis and testes, in combination with IVF procedures, have become more commonly used in the management of anejaculation.^{41,42} These techniques have also been successfully applied to the spinal cord injured population^{26,43,44} and it is likely that they will be used more frequently in the future, when sperm of adequate quality cannot be obtained by either vibroejaculation or electroejaculation. Donor insemination will also remain an option for those few individuals in whom no sperm can be obtained.

Many possible factors contributing to poor semen quality in SCI males have been identified, and include seminal fluid stasis,⁴⁵ urinary tract infection,⁴⁶ increased scrotal temperature,^{47,48} antisperm antibodies,^{35,49–51} urine contamination due to retrograde ejaculation,²⁸ catheter composition,²⁴ the use of lubricants,^{24,27} endocrine disturbances⁵² and increased reactive oxygen species in semen.⁵³ The method of bladder management used has also been shown to affect semen quality.⁵⁴ In a previous study by this clinic, both method of bladder management and neurological level proved to be significant factors affecting the presence of motile sperm. Low pressure bladder emptying by catheter drainage (either permanent indwelling catheter or intermittent self catheterisation) resulted in a higher percentage of motile sperm compared to individuals using reflex voiding or straining.²² For this reason, education emphasising appropriate bladder management, prevention and early treatment of urinary tract infection and reduction in scrotal temperature, is an important component of the clinics' approach.

Artificial insemination techniques have been used regularly in the clinic since it was established. Vibroejaculation with insemination is popular with many couples as it can usually be performed safely and in privacy at home. Dahlberg *et al*²⁶ reported a pregnancy rate per couple of 42% using this

technique. In this clinic the rate per couple was 71% and the rate per cycle was 22%. These rates were substantially higher than for the group using electroejaculation and IVI (10% per couple and 5% per cycle). Possible factors contributing to greater success at home include differences in sperm motility between different retrieval techniques^{29,55} and neurological levels,²² improved sperm motility with increased vibrator use at home^{9,56} and increased number of inseminations per cycle.

The first reported pregnancy with electroejaculation and artificial insemination occurred in Australia in 1975.⁵⁷ Our study found that the pregnancy rate for electroejaculation with IUI (60% per couple and 30% per cycle) was higher than for electroejaculation with IVI (10% per couple and 5% per cycle). This difference may be explained by the fact that IVI was performed without any sperm preparation, induction of ovulation or accurate monitoring of ovulation. The combined rates for electroejaculation with IVI or IUI were 27% per couple and 12.5% per cycle. This is similar to previously reported rates,^{13,18,35} including Brackett *et al*,¹⁷ and Chung *et al*,¹⁹ who both found a rate of 10% per cycle. In an attempt to improve upon these pregnancy rates IVF techniques and more recently micromanipulation procedures such as ICSI have become more commonly used.

Although conventional IVF techniques have not been used with partners of our spinal cord injured males, previous studies have revealed pregnancy rates per cycle for assisted ejaculation and conventional IVF or IVF/GIFT of between 20% and 50%.^{16,18,49} Using MIST or ICSI in 18 couples, this clinic found a pregnancy rate per cycle of 19% and a per couple rate of 44%. There have been relatively few reports on the use of micromanipulation procedures in the partners of SCI males.^{18,44,58} Hultling *et al*,²⁰ comparing conventional IVF to an IVG/ICSI protocol, found a higher fertilisation rate after the introduction of ICSI but no difference in the clinical pregnancy rate. They found a pregnancy rate per cycle for the IVF/ICSI protocol of 31% and a cumulative pregnancy rate per couple of 56%. The pregnancy rates per cycle and per couple in a similar study by Denil *et al*,⁵⁹ also reporting on IVF/ICSI, were 14% and 46% respectively.

There remains substantial debate in the literature regarding the optimal approach to achieving pregnancy once sperm are retrieved. Several authors advocate IUI as initial therapy,^{17,26,31} while others suggest that IVF/ICSI should be the next step if home insemination is unsuccessful.²⁰ This present study found that the pregnancy rates for IVI/IUI procedures were similar to those achieved using MIST/ICSI. Continuing experience with ICSI in the spinal cord injured population may lead to better pregnancy rates than are currently being achieved. Conventional insemination techniques, however, will remain an important option, particularly in health care systems similar to the Australian system where IVF procedures

such as ICSI are not covered under the universal health insurance scheme and are beyond the financial reach of many couples.

Conclusions

Participation in a fertility programme may be time consuming, expensive and psychologically demanding, leaving couples feeling as though they have little control over their own situation. Under these circumstances, it is important to offer a range of fertility options allowing couples some choices in the decision-making process. These options may include the use of a vibrator with home insemination initially, the opportunity to proceed later to electroejaculation with IVI or IUI, and ultimately to progress to IVF or ICSI if required. Additionally, acute phase electroejaculation with cryopreservation of semen may be offered as another alternative.

In the 10 years since the establishment of this fertility clinic, there have been major advances in the field of enhancement of male fertility following SCI. There is better understanding of the multifactorial aetiology of reduced semen quality following SCI and better management has resulted. Semen retrieval techniques have also improved and success is now expected in most individuals, using either vibro- or electroejaculation. The increased use of the microsurgical procedures in the future should ensure that sperm can be obtained from almost all SCI males. Insemination and IVF procedures have been refined and with the introduction of micromanipulation techniques, even spinal cord injured men with extremely poor semen quality now have increased reproductive potential.

While the advances in all of these areas are significant independently, a comprehensive and holistic approach that provides spinal cord injured males and their partners with several options has proven to be both desirable and successful.

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