ORIGINAL ARTICLE

Patients affected by premature ejaculation due to glans hypersensitivity refuse circumcision as a potential definite treatment for their problem

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Summary

The diagnosis of premature ejaculation (PE) was based on a score > 8 at the PEDT five-item questionnaire. Local anaesthetic treatment (LAT) was the first-line therapy. Subjects who obtained a normalisation of EPDT score (≤ 8) were considered responders to LAT and even affected by lifelong PE due glans hypersensitivity. We proposed to patients not completely satisfied with LAT to undergo circumcision as a potential definitive treatment for PE. All patients received exhaustive information about potential benefits, limitations and complications. In case of refusal, each man was asked for the reasons of his choice. A total of 152 patients were recruited. Hundred and twenty-four patients among 152 (81.6%) positively responded to LAT. Among the 124 LAT responders, 21 (17%) were completely satisfied. The remaining 103 men experienced adverse reactions. It was proposed to such patients if they would be interested to a definitive form of treatment to resolve their problem. All the patients responded positively to this question. Only four patients among them (3.9%) accepted. The remaining 99 (96.1%) refused providing the following reasons of their choice: absence of guarantees 82.8%; irreversibility of the procedure creating a permanent body alteration 75.7%; costs of the procedure 12.1%; fear of potential complications 7%.

Introduction

Premature ejaculation (PE) is likely the most common sexual dysfunction in men, with a worldwide prevalence of approximately 30% (Carson & Gunn, 2006). Some studies suggest that circumcision, determining a desensibilisation of the glans, would provide a certain benefit to male sexual health increasing the length of intercourse and improving the control over ejaculation (Senkul *et al.*, 2004).

The objective of this study was to evaluate a progressive therapeutic approach for PE based on the reduction in glans sensitivity.

Materials and methods

All patients coming to our centre seeking treatment for lifelong PE underwent a meticulous medical and sexual history and physical examination. The diagnosis of PE was based on the self-administered five-item questionnaire validated by Symonds *et al.* (2007), translated and adapted by the author in Italian. This clinical tool explores all the domains at the basis of diagnosis of PE: lack of ejaculatory control, decreased satisfaction with sexual intercourse, intrapersonal distress, negative impact on quality of life. From the answer to this questionnaire, the resulting score can range from 0 for normal subjects to 20 for very severe PE. Subjects were considered affected by PE it the total score was >8.

All patients signed an informed consensus form before being included in our protocol. Patients were not allowed to enter our study if any of the following exclusion criteria were present: (i) genital infection, (ii) depression and neurological disorder, (iii) erectile dysfunction (ED), defined as a score from the 5-item version of the International Index of Erectile Function (IIEF-5) minor of 21, (iv) concomitant presence of phimosis or a short frenulum, (v) current history of alcohol or drug abuse, (vi) use of tricyclic antidepressants, monoamine oxidase inhibitors or selective serotonin reuptake inhibitors (SSRIs), (vii) unstable relationship (Rosen *et al.*, 1999a).

Glans local application of a lidocaine/prilocaine anaesthetic cream prior to intercourse was the first-line treatment. As suggested by Busato & Galindo (2004), patients were instructed to apply a thin layer of cream to the glans penis, extending the coverage for up to 2 cm on the penile shaft and to cover the cream with a condom for 10–20 min before intercourse. Patients were asked to use this treatment each time they had intercourse. To be included in our protocol, patients were requested to use local anaesthetic treatment (LAT) for at least three times. The second consultation was scheduled after 1 month during which, by using again the EP diagnostic tool questionnaire, the grade of response to LAT, the grade of acceptance by the patients and the occurrence of possible adverse reactions were assessed. In particular, subjects who obtained a normalisation of EP diagnostic tool score (≤ 8) were considered responders to LAT. Furthermore, responders to LAT were even considered affected by lifelong PE due to glans hypersensitivity.

At this time, patients were asked whether they were completely satisfied with on-demand LAT. In case of a negative answer, they were further asked whether they would be interested in a potential definitive treatment to resolve their problem. We proposed to patients interested on a permanent resolution for PE to undergo circumcision as a potential definitive treatment based on permanent reduction in glans sensitivity.

All patients received exhaustive information about potential benefits, limitations and complications of this surgical procedure. In particular, it was explained that this intervention was found by some authors in the medical literature to be beneficial to male sexual health, improving the duration of intercourse and reducing the glans sensitivity. On the other hand, it was remarked that evidence provided by the literature was not strong enough to ensure the success of circumcision in improving the length of intercourse and that this intervention would mean an irreversible change of body image due to complete removal of the foreskin and the possible incidence of complications like scarring and other minor events (bleeding, haematoma, infections). In case of refusal, each man was asked for the reasons of his choice, giving the chance of multiple answers.

The main outcome measures were the analysis of response and compliance of LAT and the evaluation of the reasons of circumcision refusal. A chi-square test was employed for statistical analysis to calculate the differences in mean PE questionnaire score before and after LAT.

Results

We recruited 152 patients affected by lifelong PE eligible to be included in our protocol. Their mean age was 26.5 (± 9.5 SD), and the mean questionnaire score at baseline in our survey was 15.3 (± 2.3 SD). Among 152 patients 124 (81.6%) positively responded to LAT (Fig. 1). The mean questionnaire score after LAT reported by responders subjects was 5.8 (± 2.7 SD) ($P < 0.001$). Among the 124 LAT responders, 21 (17%) were completely satisfied with this kind of therapy did not report adverse reactions and did not demand any improvement (Fig. 2).

The remaining 103 subjects who had a normalisation of PE questionnaire with LAT complained about the following limitations of this therapeutic approach:

(1) Excessive loss of local sensation 27/103 (26.2%).
(2) Penile irritation 15/103 (14.5%).
(3) Loss of erection 18/103 (17.5%).
(4) Lack of spontaneity due to the on-demand treatment 56/103 (54.3%).
(5) Reduction in sexual arousal 45/103 (43.7%) (Fig. 3).

It was proposed to these patients whether they would be interested in a definitive form of treatment to resolve their problem. All the patients responded positively to this question.

After exhaustive counselling about benefits and limitations, we proposed to such men unsatisfied with LAT to undergo circumcision.

Only four patients among them (3.9%) accepted (Fig. 4).

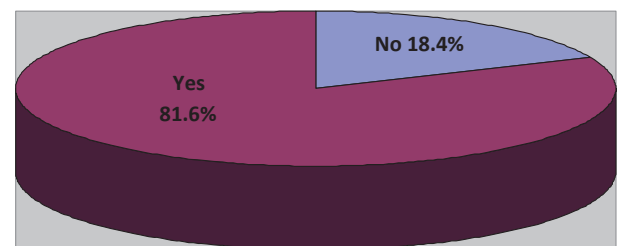The remaining 99 (96.1%) refused for the following reasons:

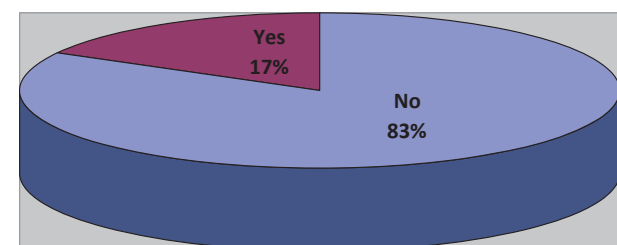**Fig. 1** Response to local anesthetic treatment.

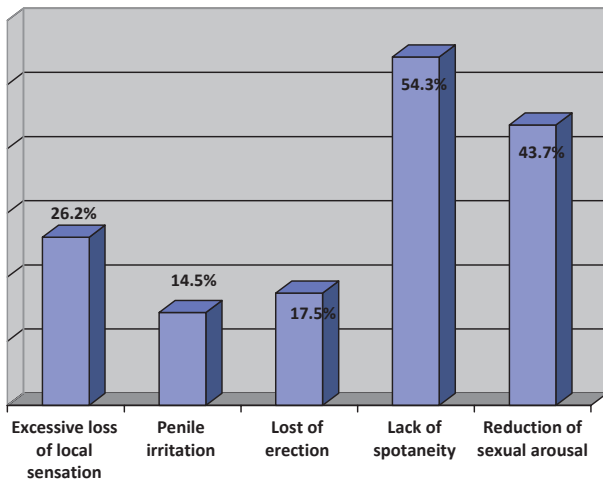**Fig. 2** Subjects completely satisfied with local anesthetic treatment.

Fig. 3 Adverse reactions due local anesthetic treatment.
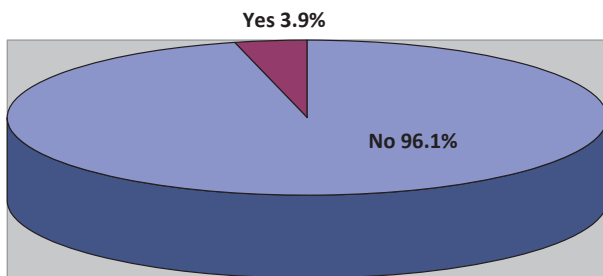

Fig. 5 Reasons for circumcision refusal.

Fig. 4 Subjects who accepted circumcision.

(1) Absence of guarantees about the effectiveness of such procedure: 82/99 (82.8%).

(2) Irreversibility of the procedure creating a permanent body alteration 75/99 (75.7%).

(3) Costs of the procedure 12/99 (12.1%).

(4) Fear of potential complications (bleeding, haematoma, infection, excessive scarring) 7/99 (7%) (Fig. 5).

Discussion

Aetiology of premature ejaculation

The pathophysiology of ejaculation has yet to be fully delineated and might include a combination of organic and psychogenic factors (Donatucci, 2006). A number of theories have been proposed regarding the causes of PE, but the two most likely are penile hypersensitivity and serotonin receptor sensitivity (Lue & Broderick, 2009). In particular, regarding the first theory, Xin *et al.* (1996, 1997) reported that men with PE have lower biothesiometric vibration perception thresholds and significantly shorter mean somatosensory evoked potential latency
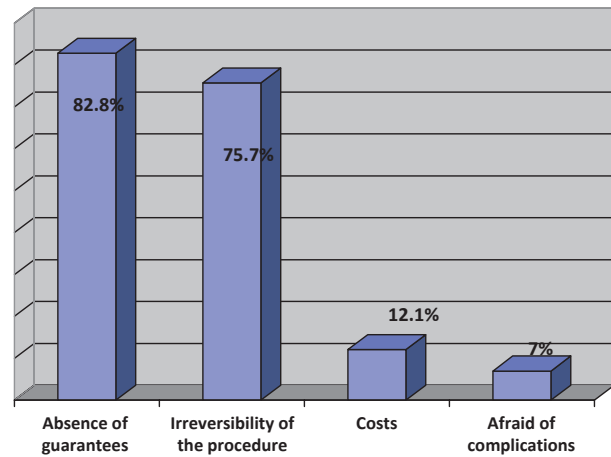
times of the glans and penile shaft than controls. These results suggest that men with PE have a greater cortical representation of sensory stimuli from the glans penis than do normal controls.

Limitations of current therapies for PE

Basing on the main theories about the pathophysiology of PE, penile hypersensitivity and serotonin receptor sensitivity, actually the most prescribed medications for this condition are topical anaesthetics and SSRIs (Giuliano & Hellstrom, 2008). Even if these kinds of drugs were both found to be effective for this purpose, they present many limitations. Firstly, they are off-label drugs: they have no specific indications for PE. Secondly, they both present adverse reactions. Topical anaesthetics can cause loss of penile sensation, retarded ejaculation, penile irritation, erectile dysfunction and decreased vaginal sensitivity in the female. Furthermore, topical anaesthetics require a period of time between application and maximum effect, and need either to be used with a condom or to be washed before intercourse, which might decrease arousal and reduce spontaneity (Morales *et al.*, 2007).

Selective serotonin reuptake inhibitors can determine psychiatric and neurological consequences, dermatological reactions, anticholinergic side effects, changes in body weight, cognitive impairment, drug–drug interactions, and sexual side effects other than delayed ejaculation (e.g. ED and loss of libido) (Rosen *et al.*, 1999b). Many authors consider adverse reactions caused by SSRIs questionable or not justified relating to the therapy of a not life-threatening condition as PE (Montague *et al.*, 2004). Furthermore, daily use of SSRIs is not indicated for individuals who usually have few intercourses per month.

Dapoxetine, the latest drug developed for PE treatment, has proved to have a better profile, however, its use is not free from adverse reactions such as nausea, diarrhoea, dizziness and headache (Buvat *et al.*, 2009). The on-demand use of dapoxetine can interfere with spontaneity of sexual intercourse. Furthermore, studies on dapoxetine presented some limitations that could be caused by financial support by pharmaceutical companies, which may jeopardise the neutrality and transparency of clinical research (Waldinger & Schweitzer, 2008).

Finally, topical anaesthetics and SSRIs are both symptomatic agents: they are not a definitive treatment and their discontinuation leads to the status quo ante. Therefore, regarding behavioural therapies, they are rarely successful in the long term, as most benefits are lost within 3 years of treatment without regular follow-up therapies (De Amicus *et al.*, 1985; Metz & McCarthy, 2003). In addition, the high cost and limited availability of well-trained sex therapists means that this approach is not always a practical first-line treatment and unsuitable for men with no stable and supportive sexual partner.

Does a potential definitive treatment for PE exist?

Mulhall (2006) affirmed that 'the ideal drug for PE should be an on-demand-dosed treatment with a high rate of efficacy and a short onset of action, should not interfere with sexual spontaneity, and should not have sexual side effects'. Similarly, Hellstrom (2006) proposed that 'considering that the frequency of sexual intercourse is highly variable, and spontaneity in sexual intercourse is usually an important factor, the ideal treatment for PE would be a discrete and 'on-demand' therapy with rapid action, effective from the first dose and with high efficacy on IELT and patient-reported outcomes, a low incidence of side effects, and have no unwanted effects on the partner'.

After many years in which it was long discussed about the best treatment for PE, we can wonder 'Does a potential definitive treatment exist that is stable to free patients from the slavery of on-demand use?'.

Three kinds of surgical treatment providing glans desensibilisation were proposed with this objective: frenulectomy, circumcision and penile dorsal neurotomy. In a previous study by our study published in this journal, frenulectomy was found to be an effective procedure in improving the intravaginal latency time and in reducing the PE questionnaire score in subjects affected by a short frenulum. Dorsal neurotomy is a very drastic approach to provide desensitisation. This invasive and irreversible measure is reported to be effective but has failed to gain wide support in the medical community (Romero & Rebello, 1994; Fischer Santos *et al.*, 2001).

The role of circumcision in treatment of PE

The prepuce (foreskin) is an anatomical structure of the male external genitalia of all human and nonhuman primate (Cold & Taylor, 1999; Aslan *et al.*, 2004). The length of a normal prepuce is 6.4 cm (range 4.8–9.2 cm), meanly occupying 93% of the penile shaft (Aslan *et al.*, 2004)**.** It is a simple fold of skin composed by outer keratinised skin and an inner mucosal layer, which are very rich in nerves (Tuncali *et al.*, 2005; Hsieh *et al.*, 2006). The abundance of myelinated and nonmyelinated nerve fibres explains the high sensitivity of the human foreskin and its function as erogenous tissue (Cold & Taylor, 1999).

Circumcision is a surgical procedure consisting in the removal of the prepuce. It was performed since the times of ancient Egypt for several reasons: medical, religious, cultural and social. The practice of circumcision in all newborn is a religious requirement for the Islamic and Jewish communities and for many African populations. In the Western countries, the most common indication for this kind of intervention is the therapy of phimosis, although some men may require it for aesthetic and functional purposes. Furthermore, circumcision was found to have a protective role against HPV infection and penile cancer (Tobian & Gray, 2011; Albero *et al.*, 2012).

The surgical ablation of the prepuce removes many of the corpuscular receptors from the penis. As a consequence, the residual exposed glans mucosa becomes more keratinised with an increase in the number of cell layers in glandular mucosal epithelium (Fink *et al.*, 2002). These modifications were supposed to determine a decreased glans sensitivity (Senkul *et al.*, 2004).

The effects of circumcision on male sexuality are very controversial. There are few and heterogenous studies investigating this topic, which often present limitations.

Senol *et al.* (2008) concluded that circumcision may contribute to sexual satisfaction by prolonging pudendal evoked potentials latency (Senol *et al.*, 2008). Zhang *et al.* (2006), studying the effects of redundant prepuce on PE, found circumcision an effective method to treat PE. Using the Brief Male Sexual Function Inventory (BMSFI) questionnaire to assess sexual performance, Senkul *et al.* (2004) affirmed that adult circumcision does not adversely affect sexual function and that the increase in the ejaculatory latency time can be considered an advantage rather than a complication. In a study led by Namavar & Robati (2011), the surgical removal of foreskin remnants in adults previously circumcised determined a significant improvement of the IELT. The patients evaluated in this study reported an improvement of the frequency of intercourse per week, a better appearance of their penis after surgery and an increased partner

satisfaction. However, another Iranian study by Hosseini *et al.* (2008) found that post-circumcision mucosal cuff length is not a risk factor for PE, leading to completely opposite conclusions than those by Namavar & Robati (2011). In a group of 22 heterosexual male adults, sexually active with a stable partner, Cortés-González *et al.* (2009) found a reduction in PE frequency from 31.8% to 13.6% after circumcision.

On the other hand, the majority of authors remain sceptical and very critical about circumcision outside its proper indication for phimosis. Collins *et al.* (2002) demonstrated no statistically significant changes in any of BMFSI parameters of male sexual function after circumcision. Paradoxically, Zwang (1997) proposed that circumcision, denuding the penis and fully exposing the very sensitive area of the corona to direct stimulation, can cause a greater incidence of PE. O'Hara & O'Hara (1999) carried out a survey of women's preferences for the circumcised or intact penis in their male partners. The women reported that their circumcised male partners were more likely to have PE than were intact partners. Using the BMFSI questionnaire to study the effects on circumcision on male sexual functions, Kim & Pang (2007) found no statistically significant differences in sexual drive, erection and ejaculation between circumcised and uncircumcised men. There was a slightly longer IELT in uncircumcised men than in circumcised men, even if this difference was not significant. Furthermore, circumcised men reported decreased masturbatory pleasure and sexual enjoyment. The authors concluded that adult circumcision adversely affects sexual function in a significant number of men, possibly because of loss of nerve endings. In addition, 9% of the circumcised men reported severe scarring of their penises (Kim & Pang, 2007). Performing a cross sectional study in a primary care setting, Tang & Khoo (2011) found erectile dysfunction, circumcision, Indian ethnicity and frequency of sexual intercourse of ≤ 5 times per month predicting factors for PE. In an Internet survey, Son *et al.* (2010) reported that educational level, marital status and duration, average income, sexual orientation, smoking, alcohol consumption and circumcision status showed no difference in the PE and non-PE groups. Investigating the IELT distribution in the general male population, Waldinger *et al.* (2009) found that circumcision and condom use had no significant impact on the median IELT.

In conclusion, the usage of circumcision for lifelong PE is based on two main issues: firstly, some studies provide a certain grade of evidence that this intervention, determining a desensitisation of the glans, improves the time of intercourse (Senkul *et al.*, 2004). Secondly, many patients affected by lifelong EP complain about the palliative effect provided by on-demand therapies and ask their physician if a definitive cure for their problem exists.

Considering the conflicting data reported in the literature about the role of circumcision for the therapy of PE, it was decided to select properly men to be included in this protocol. Even if complex diagnostic procedures investigating the glans sensitivity like biothesiometric vibration perception thresholds and somatosensory evoked potential latency are available, it was decided to consider the positive response to LAT at the same time therapeutic and diagnostic of PE caused by glans hypersensitivity. Due to the conflicting evidence reported in the literature about the effects of circumcision on male sexual health, it is crucial to inform correctly patients interested to undergo this surgical procedure to cure PE: in this study, all patients considered candidates to circumcision were meticulously informed about benefits, limitations and complications. The absence of guarantees about its effectiveness and the irreversibility of this procedure resulting in a permanent modification of genital appearance were the main reasons why patients affected by lifelong PE due to glans hypersensitivity did not accept circumcision as a potential definitive treatment for their problem. This study showed that, in presence of an appropriate and correct counselling about the existing evidences provided by the official medical literature about the role of circumcision in delaying ejaculation, almost all patients refuse this intervention.

Conclusions

This study outlined fundamental aspects to better understand lifelong PE:

(1) The majority of patients affected by this condition respond positively to LAT.

(2) The efficacy of LAT suggests that glans hypersensitivity is a key factor in the aetiopathogenesis of PE.

(3) Even if effective, only few patients are completely satisfied with LAT; the majority of men experience side effects.

(4) In this study, all patients who reported side effects due to LAT were interested in a potential definitive therapy for PE.

(5) On a theoretical basis, circumcision could be a potential treatment for PE: it is a simple surgical procedure performed worldwide, which provides a permanent reduction in glans sensitivity.

(6) Due to conflicting evidence reported in the literature about the effects of circumcision on male sexual health, it is crucial and ethically correct to adequately inform patients interested to undergo this surgical procedure to cure PE.

(7) The absence of guarantees about its effectiveness and the irreversibility of this procedure resulting in a

permanent modification of genital appearance were the main reasons why patients affected by lifelong PE due to glans hypersensitivity did not accept circumcision as a potential definitive treatment for their problem.

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