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P01

AN OPEN PRELIMINARY RANDOMIZED PROSPECTIVE CLINICAL TRIAL OF EFFICACY AND SAFETY OF THREE DIFFERENT VERAPAMIL DILUTIONS FOR INTRAPLAQUE THERAPY OF PEYRONIE'S DISEASE.

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Objective. We investigated the efficacy and safety of three different dilutions of Verapamil used in intraplaque injections in the attempt to reduce Peyronie's disease (PD) symptoms.

Materials and methods. 77 patients (age: 48 ± 9 years) with chronic PD were randomized into three groups, each receiving 12 intraplaque injections (one injection every two weeks) of 10 mg Verapamil in different dilutions. Group 1 (27 patients) used Verapamil 10 mg/4 ml, Group 2 (24 patients) used Verapamil 10 mg/10 ml, and Group 3 (26 patients) used Verapamil 10 mg/20 ml. The variables, assessed before therapy and eight months after therapy, were: erectile function (assessed by semi-structured interviews), plaque size, peak systolic velocity (PSV), end diastolic velocity (EDV), left and right cavernosal arteries (assayed with dynamic Duplex), pain (assessed with pain scale), penile curving (measured using photograph of pharmacologically-induced full erection), and side effects. Analysis of variance and the χ^2 test were used to analyze differences among the groups.

Results. There were no significant differences in baseline values between the groups. PSV of left and right cavernosal artery never modified significantly. Plaque area, penile curving, erectile function, EDV of left and right cavernosal arteries, and pain improved more significantly in Group 3 than in Groups 1 and 2. Side effects were ecchymosis, with no significant differences among the groups.

Conclusions. Dilution of Verapamil significantly improves its efficacy in improving Peyronie's disease symptoms.

P02

PROLIFERATION REGULATES THE PDE5 EXPRESSION IN RAT CORPORA CAVERNOSA CELLS.

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Although the primary role of vascular smooth muscle cells (SMCs) is contraction, they exhibit extensive phenotypic diversity and plasticity during normal development (Yoshida T. *Circ. Res.* 96:280-291 2005). The SMC can have two phenotype: proliferating and contractile (Owens G.K. *Physiol. Rev* 75:487 1995). We investigate expression of the type 5 phosphodiesterase (PDE5) during the corpora cavernosa SMC proliferation. Corpora cavernosa SMCs were obtained from 60 day old rat. We have previously showed in the same cells a drastic reduction of PDE5 when proliferation was stimulated with platelet-derived growth factor (PDGF) (manuscript in preparation). In order to better characterize the regulation of PDE5 during cells proliferation, we treated corpora cavernosa SMCs with insulin like growth factor I (IGF-I), which is involved in vascular SMC proliferation and migration, as well as in cells differentiation (Sowers J.R. *Hypertension*. 29; 691-699 1997). With semiquantitative RT-PCR, a significant decrease of PDE5 expression was detected in corpora cavernosa SMCs (6.7 ± 1.4 vs 4.0 ± 0.5 ; $p < 0.05$) after IGF-I treatment for 24 hours. These result were confirmed by quantitative real time PCR. To block cells proliferation we used tridimensional matrix culture. Indeed, during proliferation test, we observed that cells cultured on type I collagen do not proliferate, even after PDGF treatment. Then, we analyzed the expression of PDE5 in cell growth on collagen respect to cells cultured on polystyrene observing a significant decrease in its expression (1.3 ± 0.08 vs 0.5 ± 0.12 ; $p < 0.01$). Furthermore, we observed that the effect of PDGF on PDE5 is blocked in SMCs growth on collagen. To date many genes have been characterized as characteristic of differentiated phenotype of SMCs; all of them are down regulated during cells proliferation. In agreement with this and on the basis of our results, PDE5 can be now considered a marker of differentiated contractile phenotype of SMCs.

P03

EFFECTS OF CIGARETTE SMOKE EXTRACT ON SPERM MOTILITY AND CHROMATIN/DNA INTEGRITY

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Cigarette smoking seems to have a detrimental effect on male reproductive function. Further evidence of the damage caused by cigarette smoking on spermatozoa can be inferred by the low success rate in assisted reproductive technique programs when the male partner smokes. However, other authors failed to find any effect of cigarette smoking on sperm parameters. This discrepancy may relate to limiting factors intrinsic to *in-vivo* studies, such as the presence of concomitant andrological diseases and the variability of cigarette compound blood concentrations among smokers (e.g., puffing habits, puffing intensity, lung surface). To overcome these limitations, we investigated the effect of cigarette smoke extract (CSE) on motility, mitochondrial membrane potential (MMP), chromatin integrity and apoptosis in spermatozoa obtained from healthy non-smoking men with normal sperm parameters. Motile spermatozoa, separated by swim-up, were exposed to graded concentrations (0, 1%, 3% and 5%) of CSE obtained from 2 research cigarettes (Kentucky 2R4F) for 3 and 24 hours. The following endpoints were evaluated: sperm motility and, by flow cytometry, sperm MMP, chromatin integrity, phosphatidylserine (PS) externalization and DNA fragmentation. CSE suppressed in a concentration- and time-dependent manner sperm motility and increased the number of spermatozoa with lower MMP, the main source of energy for sperm motility. To our knowledge, this is the first report of CSE effect on sperm mitochondrial function. CSE increased also, in a concentration- and time-dependent manner, the number of spermatozoa with PS externalization and DNA fragmentation, early and late apoptotic signs, respectively. These effects of CSE were observed at concentrations which approximate those in the blood of a mild smoker. In addition, they were of even greater magnitude than those obtained with TNF- α , a cytokine known for its negative impact on sperm function, used as positive control. Since transmission of smoking-induced sperm DNA alterations has been demonstrated in pre-implantation embryos and may predispose offspring to a greater risk of malformations, cancer and genetic diseases, these findings suggest that men seeking fertility should quit smoking.

P04

A SEXUAL MEDICINE (DIAGNOSTIC-THERAPEUTIC) APPROACH TO MALE-FEMALE SEXUAL DYSFUNCTIONS AS SUPPLIED IN AN SSN IN A REGIONAL REFERRALS CENTRE

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Objectives: Sexual medicine is an interdisciplinary field, grounded on a large variety of expertises, both medical and psychological. Sometimes, the diagnoses and therapy of sexual dysfunction (SD) are based on single pathological symptoms. This has tended to devalue/exclude not only the constituent psychological aspects of the individual's and the couple's sexuality but also co-morbidity and specific social/cultural context. Instead of this, we should be able to offer to the patient a possibility of recovering his own "completeness" by interdisciplinary approaches which permit him to receive a precise "road to recovery" specifically tailored to his/her needs and to those of his/her partner. **Design and Methods:** Such an interdisciplinary approach to SD is supplied by an SSN in Mestre-Venice in the new "dell'Angelo" Public Hospital. To access this service, the patient does not require a referral from his/her GP. The patient can simply "turn up at the door". After an etiopathologic and differential diagnosis of the SD made by a multi-disciplinary team followed by investigation of the presence of any biological and/or psychological contributory factors, we design an integrated and personalized therapeutic programme (pharmacotherapy coupled with psychosexual counselling, surgical intervention, psychotherapy either on alone or combined with other treatments) and follow up. **Results:** Since we opened our doors, our "Centre for Sexual Medicine" has been approached by some 941 people (803 males and 138 females) who came to us suffering from some forms of SD. The prevalent male SDs were erectile dysfunction and premature ejaculation; those among female patients were subjective and/or genital arousal disorders, orgasm-phase disorders, dispareunia or vaginism.

Conclusions: This approach treats DS not as an expression of a single pathological factor but as the result of a complex series of factors working in concert on the whole organism and the connections which inevitably surround it. The choice of therapeutic treatment is thus not solely predetermined by or limited to the specialization of the individual therapist involved but renders possible a clear identification of what is needed for the patient to make the correct choice of therapy for him/herself taking into consideration many other factors.