ASN-PH-020919
ISSN: 2315-537X

International Journal of Herbs and Pharmacological Research
IJHPR, 2013, 2(1): 1 – 5.
www.antrescentpub.com

RESEARCH PAPER

TOBACCO INDUCED PRIAPISM IN WISTER RAT: A CASE REPORT

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Received: 10th November, 2012 Accepted: 10th January, 2013 Published: 31st January, 2013

ABSTRACT

In an eight-week study on the effect of potash-tobacco dust ingestion on rats, a persistent penile erection for days was observed amongst some of the rats under study. This study involved a total of 42 Wister rats of weights ranging between 150-300g and grouped into four groups (A, B, C and D). Group A served as control, while groups B – D served as test groups and received 2g, 4g, and 6g of tobacco-dust, as well as 0.4g, 0.8g, and 1.2g of potash respectively, with water given ad libitum. By the 4th week, a persistent penile erection was observed in one of the rats in group C, and by the 6th week, a similar incident occurred in group C and D respectively, prompting serial observation. By the 8 week, gangrenous changes were observed, followed by necrosis and death of the rats on the 10th day from onset. The control rats (group A), which received normal feed and water, remained normal.

Keywords: ***Priapism, Rat, Tobacco, Potash, Penile erection***

INTRODUCTION

Persistent penile erection, often unrelated to sexual stimulation, is a pathologic condition called *Priapism* (Burgu et al., 2007). Two distinct forms of *Priapism* have been described as '*veno-occlusive'* and '*arterial'*. In contrast to the arterial form, erection is always painful in veno-occlusive cases. The veno-occlusive form is associated with hypoxia and therefore, can cause fibrosis of the cavernous bodies which often leads to erectile dysfunction. The arterial form however, is not considered an emergency since the functional outcome is better (Burgu et al., 2007). Generally, *Priapism* is a rare entity with a different etiology in humans than in animals, and may be idiopathic, drug induced, or related to some medical problems like sickle cell disease or leukemia. This case report presents an incidence of *Priapism* in rats subjected to potash-tobacco dust combination diet for eight weeks.

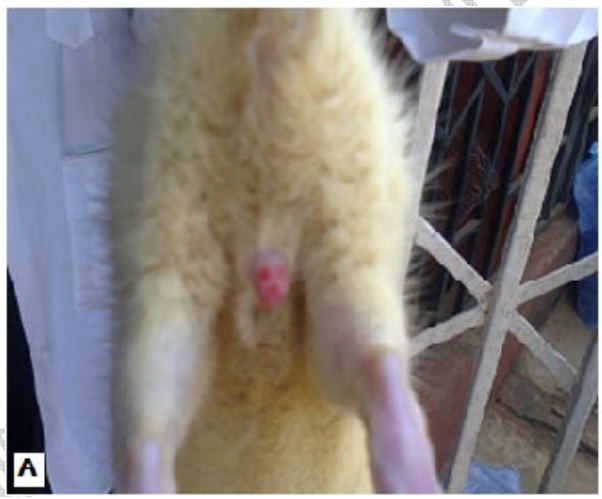
CASE PRESENTATION

A research work on the effects of oral tobacco dust mixed with potash on liver protein enzymes and cellular architecture of Wister rats was conducted at Anthonio Research Centre, Ekpoma, Edo State, Nigeria. A total of 42 Wister rats of weights ranging between 150-300g were involved. The research work was designed to last for eight weeks but was sub-divided into early acute (2 weeks), late acute (4 weeks), early chronic, (6 weeks), and late chronic (8 weeks). The animals were grouped into A, B, C and D. Group A (n=6) served as the control, while groups B-D (n=12 respectively) served as test groups. Test groups B, C, and D, received 2g, 4g, and 6g of tobacco-dust (as recommended by Bagchi et al., 1994), as well as 0.4g, 0.8g, and 1.2g of potash respectively.

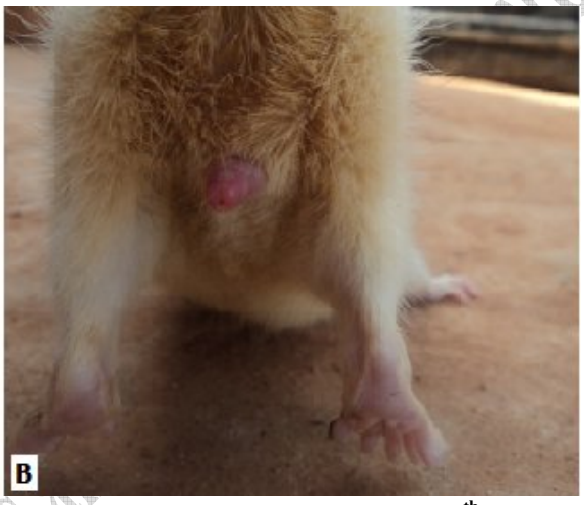
At the 4th week of the experiment, a persistent penile erection was observed in one of the rats in group C as shown in figure 1A below. The rat was however, sacrificed the next day following experimental design. At 6 weeks also, a

similar incident occurred in group C and in group D and were observed on the same day as shown in figures 1B and 1C. While the affected rat in group C was sacrificed following experimental design, that of group D was subjected to serial observation.

On day eight (8) from onset of persistent penile erection, gangrenous changes appeared as shown in figure 1D below. This was followed by tissue necrosis and eventual death of the rat by day ten (10). The rats in group A (control) remained normal till the end of the experiment.



Rat in Group C present *Priapism* at 4th week



Rat in Group C present *Priapism* at 6th week

Rat in Group D present *Priapism* at 6th week

Rat in Group C present *Priapism* at 6th week as at the 8 days of the onset of persistent penile erection

Figure 1: A, B, and C showing persistent penile erection (*Priapism*), Group D as at the 8 days of the onset of persistent penile erection (*Priapism*) with gangrenous changes.

DISCUSSION

Priapism has been noted as an adverse effect of both first- and second-generation anti psychotic medications, which accounted for 15-26% of cases of priapism induced by medications (Sood et al., 2008; Thompson et al., 1990) with majority of the reported cases in boys with sickle-cell disease and in new born. Thirteen newborn cases of *Priapism* have been reported since the 1st case in 1876 and peripheral alpha-1 adrenergic blockage has been considered as another main cause of *Priapism* (Segraves, 1989), while trazodone with its alpha-1 antagonistic properties, has been reported to induce *Priapism* (Du Toit et al., 2004).

Literatures reveal that many cases of *Priapism* are induced and according to Seyed et al (2012), drug (quetiapine) induced *Priapism* has been observed in a 30 year old single unemployed man addicted to tobacco cigarette smoking. Ruan et al (2007) also reported a case of *Priapism in a* 49-year-old male with intractable chronic low back pain due to diffuse lumbar degenerative disc disease, lumbar spondylosis under epidural morphine, and bupivacaine infusion chemotherapy. Sildenafil has also been implicated in inducing *Pripapism* in 25 year old married healthy male (Aggarwal et al., 2010). Interestingly, the incidence of priapism was arrested in all the cases, within days of discontinuing the intake of the drugs.

Available evidence shows that smokeless tobacco contains nicotine, nitrosonornicotine (NNN), and 4-(methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK), which mediates the substantial release of nitric oxide in the body (Lam et al., 2003). Meanwhile, nitric oxide (NO) is believed to play an important regulatory role in penile erection. Several studies have found the enzymatic activity generating NO (NO synthase; NOS) in the penile erectile bodies, located in both nerve fibres and endothelial cells (Burnett et al. 1992 and Dail et al. 1995). The relaxation of cavernous smooth muscle, a prime requirement for the initiation and maintenance of penile erection (Saenz de Tejada et al., 1991), is highly susceptible to pharmacological manipulations of NO.

Specifically, it has been established that nitric oxide mediates penile erection as neuronal nitric oxide synthase (Burnett, 2006; Ignarro, 2002; Burnett et al., 1993; Stanarius et al., 2001; Lugg et al., 1995; Gonzalez-Cadavid and Rajfer, 1996; Burnett, 1995) as reported in dog (Trigo-Rocha et al., 1993), rabbit (Holmquist et al., 1991), cat (Wang et al., 1993), and rat (Burnett et al., 1992).The nitric oxide is formed during the conversion of L-arginine into L-citrulline, catalyzed by the enzyme nitric oxide synthase (NOS) (Lowenstein et al., 1994; Forsterman et al., 1994), which has been found almost exclusively in the penile cytosol (Burnett et al., 1992; Garban et al., 1995a; Vernet et al., 1995; Lugg et al., 1995 and Garban et al., 1995b). Only one NOS isoform -the constitutive neuronal type (nNOS), has been identified in the penis and localized in the nerve terminals (Lugg et al., 1995; Gonzalez-Cadavid and Rajfer, 1996; Burnett, 1995; Burnett et al., 1992; Burnett et al., 1993; Keast, 1992).

Scientists have observed that the mechanism of this principal neurotransmitter for erection, involves its release by both nerve terminals and endothelial cells. The smooth muscle relaxation during erection depends upon the promotion of Ca2+ efflux. This relaxation of smooth muscle cells is mediated mainly by nitric oxide, which activates the enzyme guanylate cyclase. This cytoplasmic enzyme increases formation of the second messenger, cGMP. Elevated levels of peripheral cGMP in turn promote the efflux of Ca2+ ions from the cavernosa smooth muscle cells. This induces muscle relaxation, facilitates blood flow into the corpora cavernosa, and thereby helps to maintain penile erection (Burnett, 1995).

Our finding suggests therefore, that the ingestion of mild or high dose potash-tobacco dust combination can induce *Priapism* in a dosage dependent manner. It also indicate that males who are severely addicted to smokeless tobacco (often mixed with some quantity of potash), are likely vulnerable to *Priapism* and its attendant consequences, especially if the addiction to tobacco is not checked.

ACKNOWLEDGEMENT

Our special thanks to all, who in one way or the other contributed to the success of this research, especially the staff of Anthonio Research Center. Our thanks also go to Mr and Mrs Charles Ngwu MD/CEO citadel suit Nigeria Ltd, for their financial support toward the successful completion of this research work.

REFERENCES

Aggarwal, H., Jain, D and Yadav, R (2010): Priapism Induced With Single Oral Dose Of Sildenafil: A Rare Case Report . *Webmed Central Pharmacology.*1(9):WMC00676.

Bagchi, M., Bagchi, D., Hassoun, E.A. and. Stohs,(1994): Smokeless tobacco induced increases in hepatic lipid peroxidation, DNA damage and excretion of urinary lipid metabolites. *Int. J. Exp path.75:197-202*

Burgu, B., Talas, H., Erdeve, O., Karagol, B. S., Fitoz, S and Soygur T. Y (2007): Approach to newborn priapism: A rare entity. *Journal of Pediatric Urology Company.* 3:509-511.

Burnett, A. L., Lowenstein, C. J., Bredt, D. S., Chang, T. S. K. and Snyder, S. H. (1992): Nitric oxide: a physiologic mediator of penile erection. *Science.* 257:401—403.

Burnett, A. L., Tillman, S. L., Chang, T. S. K; Epstein, J. I., Lowenstein, C. J; Bredt, D. S., Snyder, S. H and Walsh, P. C (1993): Immunohistochemical localization of nitric oxide synthase in the autonomic innervation of the human penis. *J, Urol*. 150:73-76.

Burnett, A. L (1995): Role of nitric oxide in the physiology of erection. *Biol Reprod*. 52:485-489.

Burnett, A. L (2006): Nitric oxide in the penis—Science and therapeutic implications from erectile dysfunction to priapism. *J. Sex Med.* 3:578–582.

Dail, W. G., Barba, V., Leyba, L and Galindo, R. (1995): Neural and endothelial nitric oxide synthase activity in rat penile erectile tissue. *Cell and Tissue Research.* 282:109—116.

Du Toit, R. M., Millson, R. C, Heaton, J. P et al (2004): Priapism. Can. J. Psychiatry. 49:868–869.

Forsterman, U., Closs, E. I., Pollock, J. S., Nakane, M; Schwarz, P., Gath, I and Kleinert, H(1994): Nitric oxide isozymes. Characterization, purification, molecular cloning and functions. *Hypertension.* 23:1121-1131.

Gonzalez-Cadavid, N. F and Rajfer, J (1996): Nitric oxide and other neurotransmitters of the corpus cavernosum. In: Hellstrom WJG (ed.), Textbook of Andrology: Relevant Issues in Male Infertility and Sexual Dysfunction. New York: Springer Verlag. (in press).

Garban, H. Marquez, D; Cai. L., Rajfer, J and Gonzalez-Cadavid, N. E (1995a): Restoration of normal penile erectile response in aged rats by long-term treatment with androgens. *Biol Reprod.* 53:1365-1372.

Garban, H., Vernet, D., Freedman, A., Rajfer, J and Gonzalez-Cadavid, N.E (1995b): Effect of aging osn nitric oxide-mediated penile erection in the rat. *Am. J. Physiol*. 268:467-475.

Holmquist, F., Stief, C. G., Jonas, U and Andersson, K. E (1991): Effects of the nitric oxide synthase inhibitor NG-nitro-L-arginine on the erectile response to cavernous nerve stimulation in the rabbit. *Acta. Physiol. Scand.*143:299-304.

Ignarro, L. J (2002): Nitric oxide as a unique signaling molecule in the vascular system: A historical overview. *J. Physiol Pharmacol*. 53:503–514.

Keast, J.R. (1992). A possible neural source of nitric oxide in the rat penis. *Neurosci. Lett.*; 143: 69-73.

Lam, E. W. N., Kelley, E. E., Martin, S. M and Buettner, G. R. (2003). Tobacco xenobiotics release nitric oxide. *Tobacco Induced Dis*. 1, 207–211.

Lugg, J. A., Rajfer. J., Gonzilez-Cadavid, N. E. (1995). The role of nitric oxide in erectile function. *J. Androl.*16:2-5.

Lugg, J. A., Rajfer, J and Gonzalez-Cadavid, N. E (1995): Dihydrotestosterone is the active androgen in the maintenance of nitric oxide-mediated penile erection in the rat. *Endocrinology*. 136:1495-1501.

Lowenstein, C. H. J., Dinerman, J. L., Snyder, S. H (1994): Nitric oxide: a physiologic messenger. *Ann. Int. Med.*120:227-237.

Ruan, X., Couch, J. P., Shah, R. V; Liu, H., Wang, F and Chiravuri, S (2007): Priapism — A Rare Complication Following Continuous Epidural Morphine and Bupivacaine Infusion. *Pain Physician.* 10: 707-711.

Saenz de Tejada, I., Moroukian, P., Tessier, J., Kim, J. J., Goldstein, I and Frohrib, D. (1991): The trabecular smooth muscle modulates the capacitor function of the penis. Studies on a rabbit model. *American Journal of Physiology*. 261:1590—1595.

Segraves, R.T (1989): Effects of psychotropicdrugs on human erection and ejaculation. *Arch, Gen. Psychiatry*. 46:275–284.

Seyed, H.H., Hafez, B. and Padideh, G. (2012). Effects of cigarette smoking on priapism induced by quetiapine; a case report. *DARU Journal of Pharmaceutical Sciences*; 20(1): 55.

Stanarius, A, et al. (2001) Immunocytochemical distribution of nitric oxide synthase in the human corpus cavernosum: An electron microscopical study using the tyramide signal amplification technique. *Urol Res.* 29:168–172.

Sood, S., James, W and Bailon, M.J (2008): Priapism associated with atypical antipsychoticmedications: a review. *Int. Clin. Psychopharmacol* 23:9–17.

Thompson, J. W., Ware, M. R and Blashfield, R. K (1990): Psychotropic medications and priapism: A comprehensive review. *J. Clin. Psychiatry.* 51:430–433.

Trigo-Rocha, F., Aronson, W. J., Hohenfellner, M., Ignarro, L.J., Rajfer, J and Lue, T.E (1993): Nitric oxide and cGMP: mediators of pelvic nerve-stimulated erection in dogs. *Am. J.Physiol*. 264:419-422.

Vernet, D., Cai, L., Garban, H., Babbitt, M.L., Murray, F., Rajfer, J and Gonzalez-Cadavid, N. E (1995): Reduction of penile nitric oxide synthase in diabetic BBIWORdEP (type I) and BBZ/WORdP (type II) rats with erectile dysfunction. *Endocrinology*. 136:5709-5717.

Wang, R., Higuera, T. R.., Sikka, S. C.., Minkes, R. K; Bellan, J. A., Kadowitz, P. J., Domer, F. R and Hellstrom, W, J (1993): Penile erections induced by vasoactive intestinal peptide and sodium nitroprusside. *Urol. Res.* 21:75-78.

AUTHORS' CONTRIBUTIONS

Ugbor C.I., was responsible for the design of this work and supply of some literature material. Eloka CCV was responsible for organization of the manuscript. All authors (Ugbor CI., Eloka CCV., Okonkwo LO., Ugwu MC., Ogbodo LA) contributed to the completion of this study and were actively involved in the presentation of this manuscript.