Effect of Transcutaneous Electric Nerve Stimulation (TENS) on Hormones Profile in Subjects with Primary Dysmenorrhoea - A Preliminary Study

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ABSTRACT: ***Background & Objective:*** *Primary dysmenorrhoea (PD) is defined as the occurrence of painful menstrual cramps of uterine origin which occurs in the absence of any underlying disease. The pathogenesis is unclear, but uterine hyperactivity, elevated prostaglandin and leukotrienes levels, and hormonal level fluctuations have all been implicated. The objective of this study was to evaluate the effect of TENS on the hormones cortisol and prolactin in individuals with PD.*

Methods: *Plasma levels of cortisol and prolactin were studied in twenty-one (21) subjects with PD by obtaining blood samples from each subject pre-and post-TENS therapy on the first day of menstruation. The mean age of subjects was 23 (+ 2) years. The Visual Analogue Scale (VAS) was used to assess the pre-and post-treatment pain intensity. The TENS unit was applied for a duration of 30 minutes.*

Results: *A paired t-test showed that there was an overall reduction in the mean cortisol and prolactin from pre treatment values of 28.45µg/dl ((5.27) and 56.81ng/ml ((31.86) to post treatment values of 27.33µg/dl ((5.13) and 53.23ng/ml ((37.63) respectively. However, these differences were not statistically significant (P>0.05). Pain intensity was significantly reduced comparing pre and post treatment VAS scores (P = 0.001).*

Conclusion: *The probable mechanism by which TENS effected alterations in cortisol and prolactin levels and pain reduction in subjects with PD might be through the opioid-modulating analgesia system, which releases B-endorphins and other endogenous opiates in response to pain. This is because there is a close relationship between B-endorphin, cortisol and neurons, which secrete dopamine into the hypothalamic-pituitary-portal system.*

KEY WORDS: PRIMARY DYSMENORRHOEA, TENS, CORTISOL, PROLACTIN.

INTRODUCTION

Dysmenorrhoea is pain occurring at or about the time of the menses. It can be classified as primary or secondary. Primary dysmenorrhoea (PD) is the occurrence of painful menstrual cramps of uterine origin that occur in the absence of any obvious underlying disease (Akin et al, 2004; Proctor et al, 2004). The pathogenesis of PD is unclear, but uterine hyperactivity and elevated prostaglandin and leukotriene levels have all been implicated (Auld and Sinha, 2004). The pain described as spasmodic in nature usually accompanies the beginning of menstrual flow or precedes it only by a few hours (Klein and Litt, 1991). The usual location is the supra pubic area (lower abdominal region), which may radiate to the lower back, sacrum, medial and anterior thighs before or during menses (Auld and Sinha, 2004). The commonly associated symptoms are nausea, vomiting, increased frequency of defaecation, headaches, muscular cramps, irritability, sweating, increased body temperature, dizziness, and syncope (Smith, 1993; Harlow and Park, 1996; Auld and Sinha, 2004).

Secondary or acquired dysmenorrhoea is pain occurring when there has been little or no pain until some disease has occurred in the pelvis. It is commonly associated with pelvic inflammatory diseases, endomentritis and fibroids (Akin et al, 2001). Dysmenorrhoea affects 40% to 70% of women of reproductive age. It is one of the most frequent causes of absenteeism from work and school (Andersch and Milson, 1982). The high prevalence and enormous medical, social and economic consequences of dysmenorrhoea are therefore substantial. This has led to numerous studies of its pathophysiology and treatment (Lin, 1998; Zhang and Li wan Po, 1998, Akin et al, 2004).

While the true cause of PD remains unclear, various hormonal activities have been implicated as causative factors. The increase in prostaglandins in the endometrium following the fall in progesterone in the late luteal phase of the menstrual cycle which results in increased myometrial tone and excessive uterine contraction have been implicated (Andersch and Milson, 1982; Akin et al, 2001). Women with severe

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PD have been shown to have higher plasma concentrations of arginine vasopressin (AVP), than healthy subjects on the first day of menstruation (Stromberg et al, 1981; Chegini and Rao, 1988; Harlow and Park, 1996).

Prolactin, a stress hormone is secreted by the anterior pituitary gland and regulated by the action of dopamine (Stromberg et al, 1981). Prolactin has been reported to play an essential role in the menstrual cycle as it has been linked to a number of menstrual dysfunctions (De-Cree, 1989). Normal range of prolactin in pre-menopausal women is 1.2-19.5ng/ml (Ganong, 2001). Another hormone that has been implicated in menstrual disorder is cortisol, synthesized by the adrenal cortex and regulated by adrenocorticotropic hormone (ACTH) which is an anterior pituitary hormone (Ganong, 2001). The concentration of cortisol varies with time of day and with phase of menstruation (Kaplan et al, 1994). According to Orth et al, (1992) and Kaplan et al, (1994), the highest concentrations range from 10 - 27ug/dL and are seen in the early morning within the usual time of wakening. Plasma cortisol concentration ranges from 5 - 10ug/dL at 4pm and lowest levels, less than 5ug/dL are observed an hour after the usual time of sleep (Ganong, 2001).

Different methods with varying side effects have been employed in the management of PD. In the 1960s, oral contraceptives were commonly used (Menaker et al, 1962; Mathews et al, 1968). Oral contraceptives reduce the pain of PD by reducing menstrual fluid prostaglandins, as a result of an overall decrease in menstrual fluid volume (Chan and Dawood, 1980). The efficacy of oral contraceptives in the treatment of PD is well recognized and documented, however they have adverse effect on the gastrointestinal tract with prolonged administration (Langrick et al, 1989).

Since the 1970s, oral contraceptives have given way to non-steroidal anti-inflammatory drugs (NSAIDs) in the management of PD. However, it has been reported that only two-thirds of dysmenorrhoeic women respond positively to NSAIDs, and are known to also have associated side effects (Henzl et al, 1998; Langrick et al, 1989). Previous studies have showed that prostaglandin was implicated in the pathogenesis of PD (Flower and Vane, 1974; Pulkkinen, 1979). NSAIDs act by suppressing menstrual fluid prostaglandins through enzymatic inhibition.

In the 1980s, a number of studies involving acupuncture for PD were carried out (Manheimer and Whalen, 1985; Lundeberg et al, 1985; Yuqin, 1994). A preliminary trial reported that 86% of dysmenorrhoeic women treated with acupuncture had complete relief of pain for three consecutive menstrual periods (Manheimer and Whalen, 1985). The use of acupuncture-like TENS has been compared with conventional TENS and there was significant pain relief in both forms of therapy (Manheimer and Whalen, 1985). The use of high-frequency TENS (100Hz), low frequency TENS (2Hz) and placebo-TENS was investigated in a group of dysmenorrhoeic patients (Dawood and Ramos, 1990). It was discovered that patients treated with high, and low frequency TENS obtained pain relief exceeding 50% of its original intensity but in some of the low frequency subjects, the pain relief was augmented by naxolone, a relatively pure opiate antagonist (Lundeberg et al, 1985). A comparative study on effects of acupuncture-like TENS and placebo pill on PD revealed average pain relief of 50% post-treatment (Lewers et al, 1989).

While different methods, with varying side effects and clinical outcomes, have been employed in the management of PD, TENS has been reported to be a safe and effective non-pharmacological means of treating PD (Kaplan et al, 1994). Also hormonal imbalance has been linked as contributing factors to the pain experienced during menstruation (Baker et al, 1999). Considering the recent popularity of TENS in managing PD because of its efficacy and minimal side-effect and the hormonal imbalance reported to be a contributing factor to menstrual pain. This study was therefore conducted to evaluate the effect of TENS on the hormones prolactin and cortisol amongst university undergraduates with PD.

METHODS

Twenty one female undergraduate subjects, age 18 - 26 years participated in this study. The local Ethics Committee approved the study protocol and all patients gave written informed consent.

Inclusion criteria for participation were, subjects who suffered moderate to severe menstrual pain at least the first two days of their period, regular menstrual cycles and those without prior TENS treatment. Subjects were excluded from the study if they had any known or suspected pathologies of the female reproductive system, any cutaneous lesions of the anterior abdominal wall, or had a known or suspected contra-indication to the use of TENS. Subjects were assessed by history and a detailed physical examination by a consultant gynaecologist before inclusion in the study. 103 subjects were recruited for the study out of which 87 met the inclusion criteria. Only 21 out of 87 subjects that met the inclusion criteria consented to participate in the study. 66 declined participation for various reasons, but the commonest is the fact that the study involves the collection of blood sample. This is the major reason for the small sample size of the study.

Instrumentation

- Transcutaneous Electrical Nerve Stimulation (TENS) unit
- Visual Analogue Scale (VAS)
- DSL-10-2000 Active(r) Cortisol EIA Kit
- ELISA Prolactin Kit
- Centrifuge
- Vacutainer bottles
- Sterilized needles and syringes
- Methylated Spirit and cotton wools

Experimental Procedure

An experimental study design made up of a one group pre and post test design was used. All subjects completed questionnaires and were thoroughly examined. The questionnaire was designed to obtain information on age, weight, height, marital status, nature of menstruation whether regular or not, menstrual pain perception and severity among other, adopting the protocol of Dawood and Ramos (1990). Detailed examination was carried out to exclude other gyneacological pathologies aside PD and to establish the painful areas for electrode placement. All subjects were instructed against taken any non steroid anti-inflammatory drugs (NSAID) or any analgesics for the duration of the study and were instructed to report any unusual medical problem to the researchers immediately.

Subjects were also briefed of the experimental procedure prior to the commencement of the study. On the first

day of menstruation between 8.00 AM and 10.00AM, each subject indicated her pain level on a Visual Analogue Scale (VAS). Subjects was then placed in supine on a plinth, for the collection of blood samples from the median cubital vein of the arm and transferred to a labeled vacutainer bottle. This served as the pre treatment blood sample.

Following this procedure TENS was then administered with two pairs of electrodes placed around the painful region which was the suprapubic area in all subjects. A pair of the adhesive electrodes was placed 10cm from the umbilicus on either side, the second pair placed on either side of the pubic symphysis close to each anterior superior iliac spine (Lundeberg et al, 1985). High frequency TENS was applied at 100Hz and 250µs pulse rate and pulse width respectively, the intensity was adjusted to a tolerable level of stimulation. The treatment lasted for 30 minutes. At the termination of TENS therapy, the subjects' pain level was reassessed and a second blood sample (post treatment) obtained. All the blood samples (pre and post TENS) were collected and were subjected to laboratory analysis to determine the cortisol and prolactin levels in each subject using the ELISA method (Chan and Dawood, 1980).

Statistical Analysis

The demographic data of the subjects were summarized using descriptive statistics, namely means and standard deviations. The Student t-test was used to determine if there was any significant differences in the pre-and post TENS prolactin and cortisol values. The Wilcoxon Signed Ranks Test was used to determine if there was any significance difference in the pain levels of the subjects pre- and post TENS therapy. Significance was set at p=0.05.

RESULTS

A total of 21 subjects aged 18 to 26 years with a mean age of 23 (+2)) with PD participated in the study. Previous methods of dysmenorrhoea pain relief used by the subjects indicated that 61.90% of the subjects commonly used analgesic drugs, 38.10% used nothing at all while none has tried the use of TENS previously.

Table 1 shows the pre-and posts TENS therapy cortisol and prolactin levels. There was a slight reduction in the mean cortisol level from 28.45µg/dl (±5.27) to 27.33µg/dl (±5.13) and prolactin level from 56.81ng/ml (±31.86) to 53.23ng/ml (±37.63). However these differences were not statistically significant (p>0.05).

Table 1: Pre and Post TENS Therapy Cortisol and Prolactin levels.

N=21	PRE-TENS	POST-TENS	t	p-value
	X (±SD)	X (±SD)		
Cortisol	28.45 (± 5.27)µg/dL	27.33 (± 5.13)µg/dL	1.04	0.31
Prolactin	56.81 (± 31.86)ng/mL	53.23 (± 7.63)ng/mL	0.64	0.53

Table 2: Pre and Post Treatment Pain intensity change.

Pre-TENS VAS	Post-TENS VAS	Z	P-value
6.50 ± 1.73	1.50 ± 2.08	-3.409	0.001* (p<0.05)

KEY: Pre = pre treatment, Post = post treatment, VAS = visual analogue scale

Table 2 shows the pre-and post TENS application pain level on the VAS pain scale. There was a significant reduction (p<0.05) in the pain levels of the subjects from a value of 6.5(±1.7) to 1.5 (± 2.1) post TENS therapy.

DISCUSSION

It was observed in this study that there was a slight reduction in the mean values of cortisol and prolactin level post-treatment, but the differences were not statistically significant (p>0.05). However there was a clinically significant reduction in pain severity post TENS therapy. This agrees with the study of Rodriguez et al, (1992) who reported similar results in women with post-operative pain following hysterectomy using TENS.

The reason for the lack of significant difference in cortisol and prolactin levels may have been attributed to the small sample size. Most of the subjects new nothing about TENS before the study and are doubtful about its effectiveness and also they do not want their blood sample taken. Because of these most eligible subjects declined participation. A large sample size may revealed a significant difference in the hormonal level post TENS therapy. Also blood sample was not obtained during TENS therapy because the study of Kaplan et al (1994) have revealed a significance difference in the hormonal level when blood was obtained during TENS administration.

Al-Damluji and Gaillard, (1987), asserted that the novelty and unpredictability of an acute situation is an important determinant of the degree of adrenocortical responsiveness. Although the subjects in this study were aware of the experimental procedure and the discomfort of venepuncture, all subjects had never used TENS prior to this study. Thus the experimental procedure and treatment may have represented a stressor sufficient to elicit an elevation in pre-treatment cortisol and prolactin levels of subjects (Al-Damluji and Gaillard 1987; Denegar et al, 1989). This study also revealed a reduction in the mean post-treatment prolactin levels though the difference was not significant. This result supports the study of Rodriguez et al, (1992) who recorded slightly lower concentration of prolactin in response to high frequency TENS in hysterectomized women with post-operative pain.

The fact that women experienced significant reduction in pain levels following TENS treatment is an affirmation for the commonly seen trend in the literature concerning TENS as an analgesic agent in some painful conditions (Akin et al, 2001; Proctor et al, 2004). The ability of high-frequency TENS to achieve this reduction in pain level may be explained by its effect on the opioid-modulating analgesia system (OMAS). The application of TENS stimulates the release of endogenous opiates (like B-endorphin) which produce analgesia (Hughes et al, 1984). Apart from modulating pain, B-endorphins also exhibit a close relationship with cortisol and prolactin (Dent et al, 1981; Plosker et al, 1990). B-endorphin shares a common precursor with ACTH, and ACTH regulates cortisol secretion (Plosker et al, 1990). B-endorphin also lies in close proximity to neurons which secrete dopamine into the hypothalamic - pituitary portal system. Thus, the modulation of dopamine by B-endorphin indirectly regulates prolactin secretion (Plosker et al, 1990). The mean menstrual phase cortisol and prolactin levels

in this study were above normal range for premenopausal women. This result is contrary to the study of Baker et al, (1999), who reported that only in the luteal phase does the mean prolactin secretion for dysmenorrhoeic subjects rise above the normal range. Elevated prolactin and cortisol recorded in this study may be due to the discomfort of venepuncture pre and post TENS application apart from the menstrual pain, since the two hormones are stress related (Stromberg et al, 1981; Kaplan et al, 1991)

CONCLUSION

This study concluded that high frequency TENS significantly reduced the pain levels in dysmenorrhoeic women without significantly affecting serum levels of cortisol and prolactin level. The study also gives further evidence that women with PD have disturbed hormonal status, in particularly cortisol and prolactin.

A potential limitation to this study is the small sample size because most subjects with PD declined participation. Large randomized controlled trials are needed in future study. Eligible subjects should be encouraged to participate by giving incentives. Also a control group was not included because the study is a preliminary one, a control group with placebo treatment may be used in future study.

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