INVESTIGATION OF THE MECHANISM OF ACTION OF LADYCARE IN ALLEVIATING MENOPAUSE SYMPTOMS

Dr N. K. Eccles BSc MBBS MRCP PhD

Introduction

Menopause indicates the end of reproductive capacity of women and arises from the cessation of ovarian function. Menopause is a gradual process that occurs for most women between the ages of 47 and 55 years (Greendale et al, 1999). It is confirmed by Absence of menstrual periods for 12 consecutive months confirms it and excludes other obvious pathologic or physiologic causes (Notelovitz, 1989). The peri-menopause, a time of changing ovarian function and precedes the final menses by 2 to 8 years (McKinlay et al, 1992). The clinical manifestations of this transition to menopause are not well understood; however, some symptoms such as hot flashes, begin in the peri-menopause (Greendale et al, 1999; Freeman et al, 2001) and increase as women progress through the menopause (Hardy & Kuh, 1975). The specific symptoms associated with menopause vary among cultures, race/ethnicity, social groups, and persons (Xu et al, 2005). The latter authors found unexpectedly high reports of vasomotor symptoms among women still experiencing regular menstruation. Vasomotor symptoms, such as hot flashes, are known to be associated with variable and lower estrogen levels as women go through the menopause (Greendale et al, 1999). It is thought that the decreased estrogen theory fails to explain why some regularly menstruating women experience hot flashes or why hot flashes are not experienced by all perimenopausal or postmenopausal women (Hahn et al 1998). Menopause can be a challenging stage of life. Hot flashes are associated with a decreased quality of life (Groeneveld et al, 1996) and are a primary reason that midlife women seek medical care (Anderson et al, 1987). According to a recent Gallup Poll, 80 percent of menopausal, post menopausal or surgically menopausal women reported having some symptoms of menopause. Among the women who had symptoms, the most common were: hot flashes (72%), irregular periods (50%), emotional responses (49%), changes in sexual relationship (31%) [http://www.prairiepublic.org/features/healthworks/change/symptoms.htm].

There is strong evidence from randomized controlled trials that oestrogen therapy is highly effective in controlling vasomotor symptoms (Manson & Martin, 2001) and urogenital symptoms (Cardozo et al, 1998). The benefits of HRT to prevent osteoporosis appear to be confined to current or recent users, and it is unlikely that taking oestrogen therapy in the first decade after the menopause protects against fractures later in life (median age of hip fracture is 80 years) [Ettinger & Grady, 1993]. The use of HRT to control menopause symptoms is not without risk. There are definite increased risks of venous thrombo-embolism and endometrial cancer (Grady et al, 1995), and probable increased risks of breast cancer (Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy, 1995) and ovarian cancer (Rodriguez et al, 2001). It increases risk of cardiovascular disease (WHI study, 2002) and cognitive decline (Mulnard, 2000; WHI study 2002).

It is understandable given the above reported side effects why there has been more reluctance recently on the part of women to take HRT and more caution on the part of doctors to issue it so freely.

There is no doubt that menopause can be a challenging time both psychologically and physically for many women. 80% of woman of menopausal age will suffer some degree of symptoms and many of these are majorly intrusive to everyday functioning. Since 2002 when the Women's Health Initiative (WHI) Study was

published, there has been a significant decline in the number of women taking HRT and also doctors have become more careful in prescribing it due to the well-established increased risks of breast cancer, stroke, pulmonary embolus and cardiovascular disease associated with its long-term use. The need for an effective and safer alternative therapy for menopause has become paramount.

The research on LadyCare for menopause was stimulated after women who were wearing the device to relieve period (Eccles, 2005) and who were peri-menopausal reported that in addition to their pain relief that their menopausal symptoms, in particular hot sweats, were improving after wearing the device. A large observational study (referenced below), in 508 women with menopause symptoms, confirmed that menopause symptoms were significantly improved in those wearing the device. Preliminary research (2009) to assess female hormone levels before and after wearing the LadyCare device did not show a clear change in hormone levels that would account for the observed symptom relief.

A large 508 women survey was conducted to investigate the effect of LadyCare on women who complained of menopause symptoms. The data was analysed by an independent third party statistician. The data showed a significant reduction in the majority of common menopause symptoms for one month and even greater effects after 3 months wearing the device after wearing the device daily. The key findings of the survey are summarised below in Figure 1.

- **There was a 50-67% reduction in Anxiety, Feelings of Doom, Sudden weight gain, Muscle tension, Mood swings, Marked fatigue, Vaginal dryness, Difficulty sleeping, Urinary incontinence, Breast tenderness/soreness**
- **There was a 33% reduction in Hot flushes, Irritability, Loss of libido/sex drive, Inability to concentrate, Sore muscles, Lapses of memory**
- **These improvements were noted after one month of wearing LadyCare and the benefits were even more significant after 3 months**

Other observations were:

- 8.1% of women surveyed had had a hysterectomy. This did not seem to affect the response to LadyCare
- 19.1% of the group lost weight. Average weight loss was 14 pounds (6.4kg)
- **NO UNTOWARD EFFECTS WERE NOTED**

Fig 1. Above. Key findings from the 508 women survey on LadyCare. Subjects were recruited from an advertisement in the Daily Mail on a consumer trial basis.

Because sweating is under the control of the autonomic nervous system (ANS), more specifically the sympathetic division (fight-flight/stress reactor system), I proposed a hypothesis that this maybe a likely target for the LadyCare mechanism of action. This hypothesis was developed after a case study experience in Dr Eccles' medical practice (as below).

Case History

A male patient in his 70's that had sought his help with terrible night sweats. The cause of these was not apparent to the Medical profession but the patient had been troubled by these for many years causing him to have to change his bed shirt 4 or times during the night as he was drenched with sweat. He had been offered neurosurgery to try to correct the problem but was not keen on this. Because of the observed benefit with LadyCare in the relief of night sweats in menopausal women, Dr Eccles suggested that the patient should try wearing a LadyCare at night. The next day the patient's son called Dr Eccles to tell him that within 30 minutes of his father wearing the LadyCare in the usual pelvic location, his sweats had stopped completely. Such rapid relief of symptoms in a man needed to be explained by a mechanism other than a change in hormones levels; a mechanism that one would expect to take more time.. Because sweating is under the control of the autonomic nervous system (ANS), more specifically the sympathetic division (fight-flight/stress reactor system), Dr Eccles proposed that this was a likely target for the LadyCare mechanism of action.

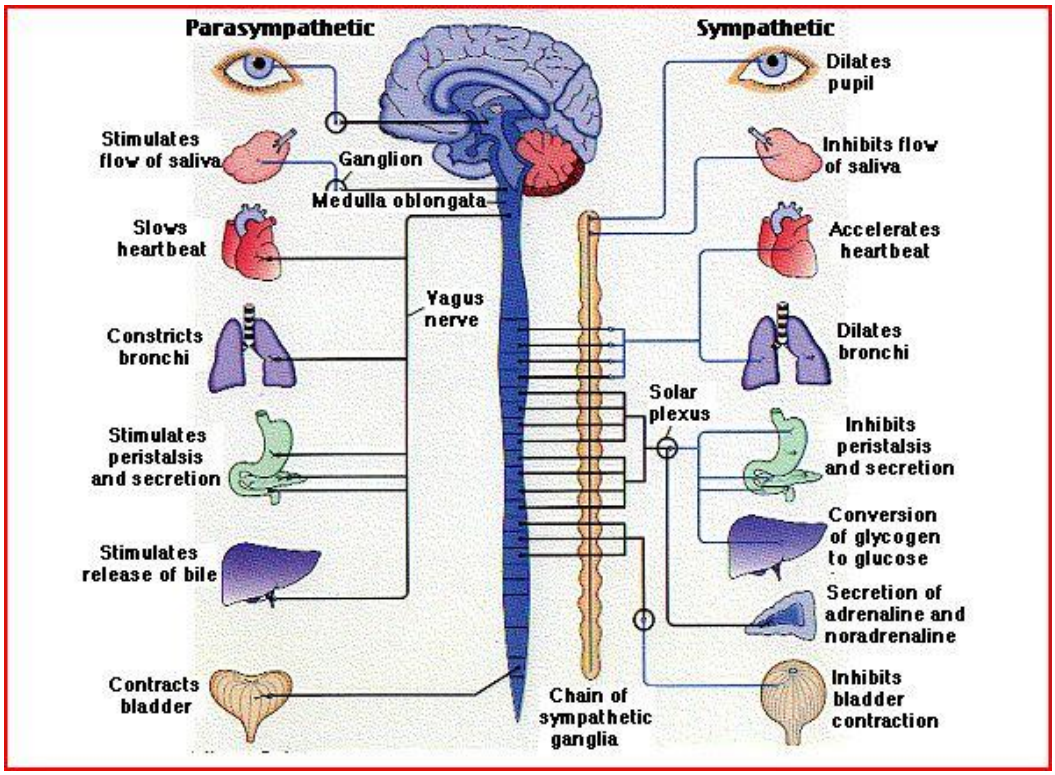

Fig 2 (above) shows the 2 divisions of the ANS, the Sympathetic division which is the fight-flight stress reactor system of the body e.g. When under threat the heart beats faster and the pupils dilate to allow more light for enhanced visual acuity and faster reactions. In contrast, the Parasympathetic division is responsible for REST and DIGESTION. It is the repair and regulatory system of the body and tends to have the opposite effect to the Sympathetic nervous system. For example, the SNS speeds the heart rate while the PNS slows it down. The 2 systems work together to regulate all our organ systems as is illustrated in the diagram above.

I proposed that LadyCare may be acting by somehow re-balancing ANS activity.

METHODS

In order to investigate this hypothesis a study undertaken to measure the ANS activity in 35 police women with menopause symptoms. Because sweats/hot flushes are the most likely symptom to be related to ANS imbalance, all volunteers had to have hot flushes as one of their menopause symptoms.
A recognised non-invasive method for measuring ANS activity is by Heart Rate Variability (HRV). Close inspection and measurement of the heart rhythm reveals that the heart beat from one to the next is not even.

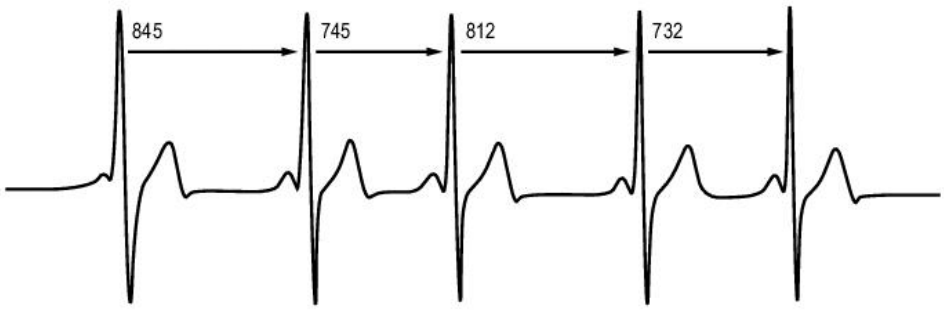

Fig3.

As shown above in Fig 3 the measured time in milliseconds between each beat varies beat to beat. This variation is a reflection of a tonic influence of the SNS (speeding the heart) and PNS (slowing the heart down). Measuring HRV is therefore a convenient way of measuring ANS activity. A 5-6 minute heart rhythm (as shown above) recording is taken from which computer analysis is able to derive quantitative measurements of both SNS and PNS activity. The Nerve Express Apparatus (Version 2.4, Intellewave, Inc, NY) was used for this purpose.

Each subject was required to have hot flushes as one of their menopause symptoms. We did not exclude peri-menopausal women (i.e. not 12 months menses-free) on the basis that we elected to study these as a separate group to those that were

menopausal (last menses > 12 months ago). Inclusion and exclusion criteria were as on the proforma below that was sent to all potential volunteers :

Heart Rate Variability and Menopause Study

Thank you very much for volunteering to take part in this study.

In order to take part the following MUST apply to you:

1) You must be menopausal (this means that your last period was 1 year or more ago)
2) You must have menopausal symptoms (see below for a list of the most common symptoms) and these **MUST INCLUDE hot flushes**
3) You must NOT be on HRT
4) If you are taking any herbal type preparations for menopause symptoms then you must have been on them for at least 3 months
5) You must not have any concomitant medical condition such as unexplained irregular vaginal bleeding
6) You can still take part even if you have had a hysterectomy
7) You must be available to attend during the times specified above i.e. not have planned leave during these times
8) You will be required to attend twice, first in June and one more time in July. We will only need 15 minutes of your time on each occasion

If all of these apply to you then you are eligible to take part. The assessment will involve completing a short symptom questionnaire, which we will send you prior to the test, and then a 6-7 minute heart rate reading which requires you to wear a sensor belt around the chest to enable us to record your heart rhythm. The procedure will be exactly the same on both visits.

<u>Common Menopause Symptoms</u>

Hot flushes
Heart palpitations (feeling your heart racing)
Irritability
Mood swings
Sudden tears
Loss of libido, sex drive
Anxiety
Fatigue
Feelings of doom and dread
Vaginal dryness/Painful intercourse
Inability to concentrate
Trouble sleeping

Urinary incontinence upon sneezing or laughing
Itchy, crawly skin
Sudden weight gain
Hair loss
Stomach problems: indigestion and gas
Painful and sore muscles, tendons and joints
Breast soreness, tenderness
Irregular vaginal bleeding
Disturbing lapses of memory
Increased muscle tension
Bladder infections

Each subject had to fill in a questionnaire that rated all the above 23 of the above mentioned symptoms. Subjects rated 23 different menopause symptoms before and after wearing the LadyCare device for one month. Symptoms are rated 0 to 5. Zero = non-existent, whereas 1-5 indicate a mild to severe symptom. The same questionnaire was employed at baseline, 1 and 3 months.

HRV assessment was undertaken at the start and again 1 and 3 months. The measurement took 6 to 7 minutes; the duration of which is determined by the collection of a fixed number of heart beats. The measurement protocol involves approximately 3 minutes with the subject supine (lying on an inflatable mattress) and then the remainder of the assessment in an upright position.

RESULTS

Questionnaire Responses

The mean age in both M and PM groups was as below.

Variable	Status	N	N*	Mean	StDev	Minimum	Maximum
Age	M	16	0	53.44	4.69	45.00	59.00
	PM	15	0	48.47	5.10	35.00	58.00

If we compare responses to all 23 questions then we have a total of 46 test results (2 periods x 23 questions) and some comparisons will lead to spurious significant results (false positives). When using questionnaires it is common practice to produce a total score (aggregate) and use this to compare the two groups. So, for example, adding the scores for all 23 questions might produce a single value with may be considered a measure of overall satisfaction with the treatment.

If we sum the scores we get:

Variable	Status	Mean	StDev	Minimum	Maximum
Sum0	M	38.44	15.64	14.00	58.00
	PM	41.40	14.09	12.00	69.00
Sum1	M	29.81	14.67	6.00	54.00
	PM	30.53	15.21	5.00	67.00

Overall it can be shown that there is a significant reduction in total score ($p < 0.001$) if we ignore menopausal status.

If you ask if the change in score depends on menopausal status then:

```
Two-sample T for totaldiff1

Status   N     Mean   StDev  SE Mean
M       16    -8.62    6.39      1.6
PM      15   -10.87    9.18      2.4

T-Value = 0.78  P-Value = 0.440  95% CI difference:  (-3.66, 8.14)
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Thus scores for both PM and M groups fell over time, and there is no evidence to suggest that the reduction depends upon status. In other words both menopausal and peri-menopausal subjects experienced a reduction in overall symptom score and there was no statistical evidence that menopausal or peri-menopausal status affected this outcome.

Summary results for total/overall symptom scores:

Variable	N	N*	Mean	StDev	Minimum	Median	Maximum
Qsum0	31	0	39.87	14.73	12.00	39.00	69.00
Qsum1	31	0	30.16	14.69	5.00	30.00	67.00
Qsum3	20	11	27.75	13.66	4.00	28.00	54.00

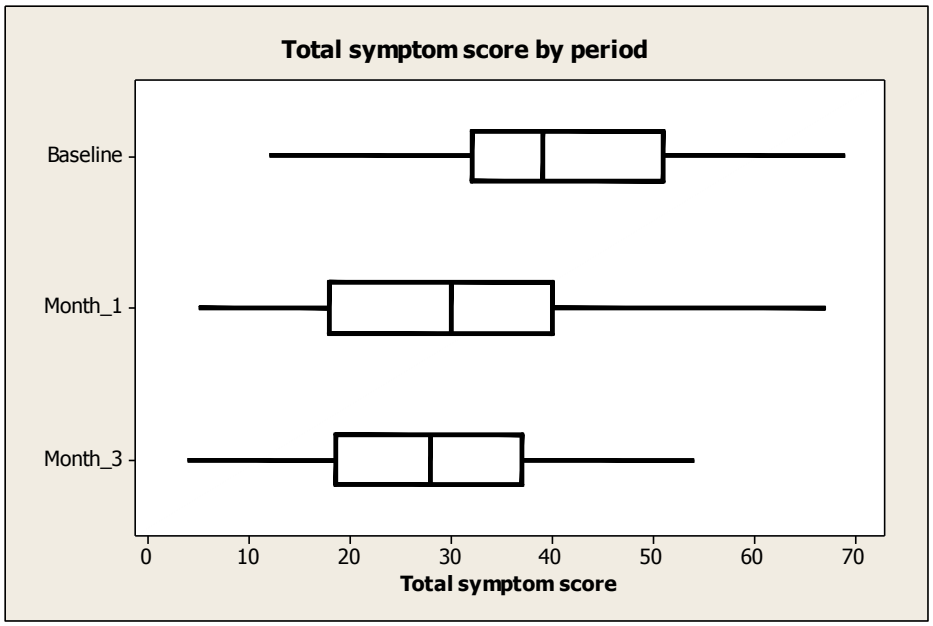

Fig 4 (above). Total Symptom Score over 3 months

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[Qsum0        31   39.87   14.73      2.65
Qsum1        31   30.16   14.69      2.64
Difference   31    9.71    7.81      1.40

T-Value = 6.92   P-Value < 0.001 95% CI reduction: (6.84, 12.57)

Paired T for Qsum0 - Qsum3

              N    Mean   StDev   SE Mean
Qsum0        20   43.05   14.95      3.34
Qsum3        20   27.75   13.66      3.05
Difference   20   15.30    8.50      1.90

T-Value = 8.05   P-Value < 0.001 95% CI for reduction: (11.32,
19.28)


Paired T for Qsum1 - Qsum3

              N    Mean   StDev   SE Mean
Qsum1        20   32.25   15.93      3.56
Qsum3        20   27.75   13.66      3.05
Difference   20    4.50    7.44      1.66


 T-Value = 2.71   P-Value = 0.014 95% CI for reduction: (1.02,
7.98)
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Independently of menopausal status, statistically significant reductions in overall symptom scores were seen at one and three months.

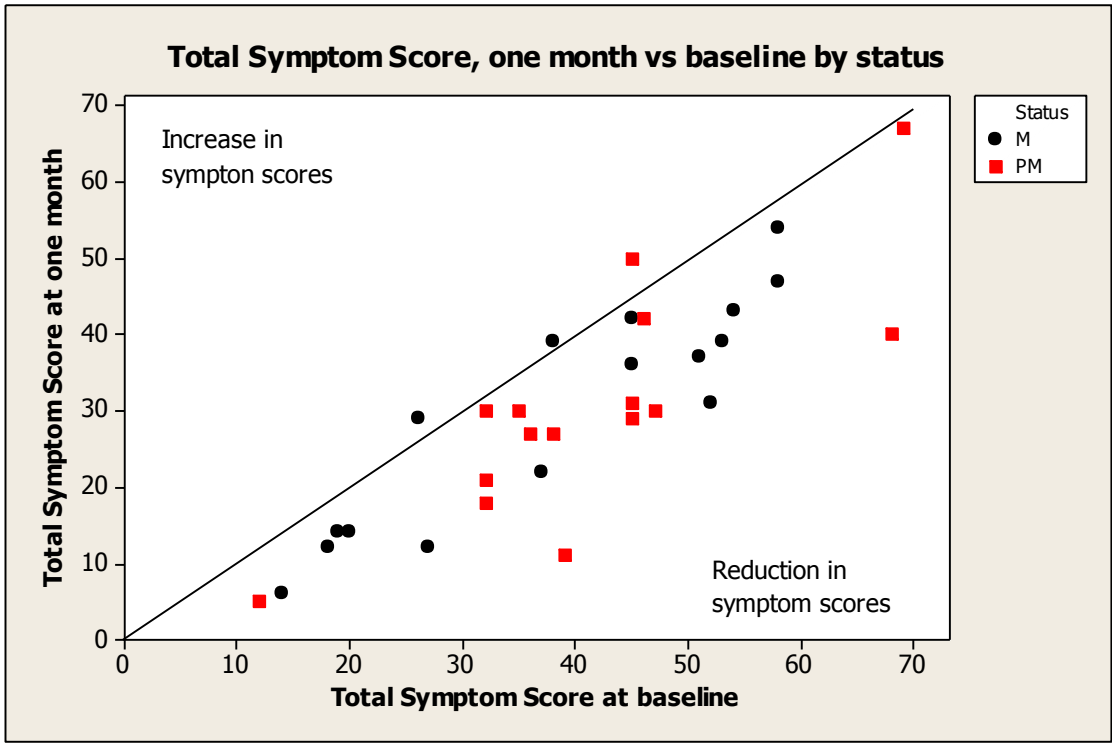

Fig 5. (above). Change in overall symptom scores after wearing LadyCare for after ONE month. Change in score is indicated vs baseline scores. M = menopausal subjects, PM = Peri-menopausal subjects.

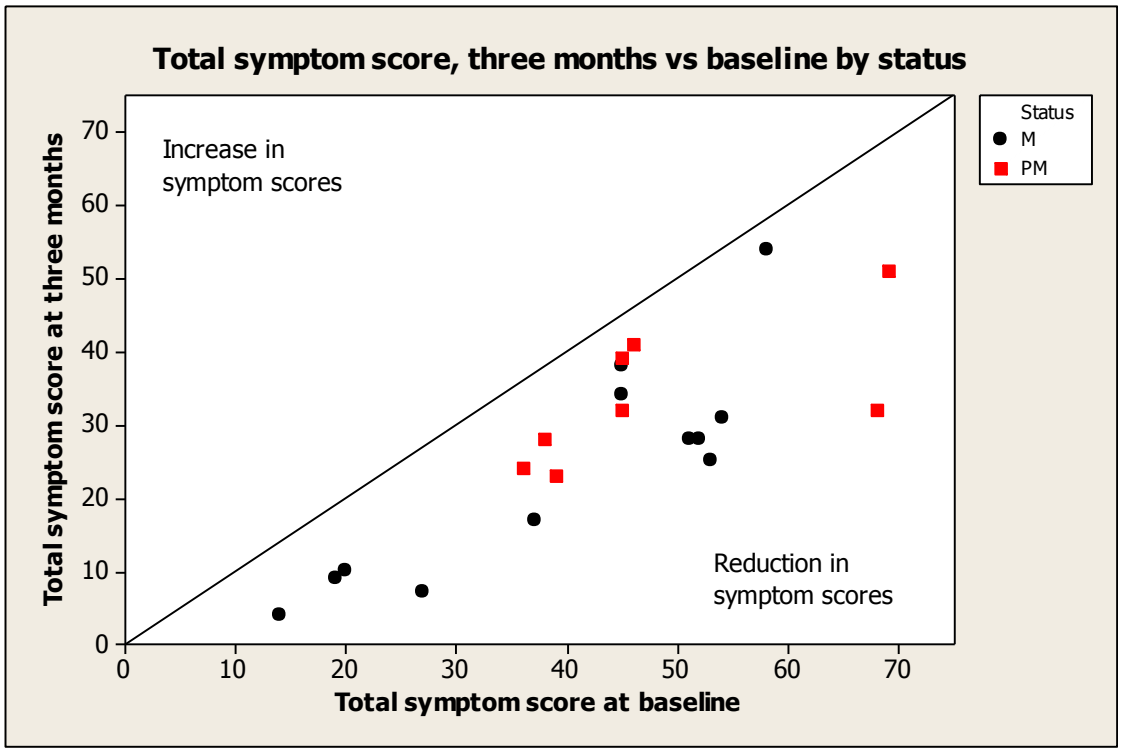

Fig 6. Change in overall symptom scores after wearing LadyCare for after THREE months. Change in score is indicated vs baseline scores. M = menopausal subjects, PM = Peri-menopausal subjects.

Emotional Symptom and Hot flush sub analysis

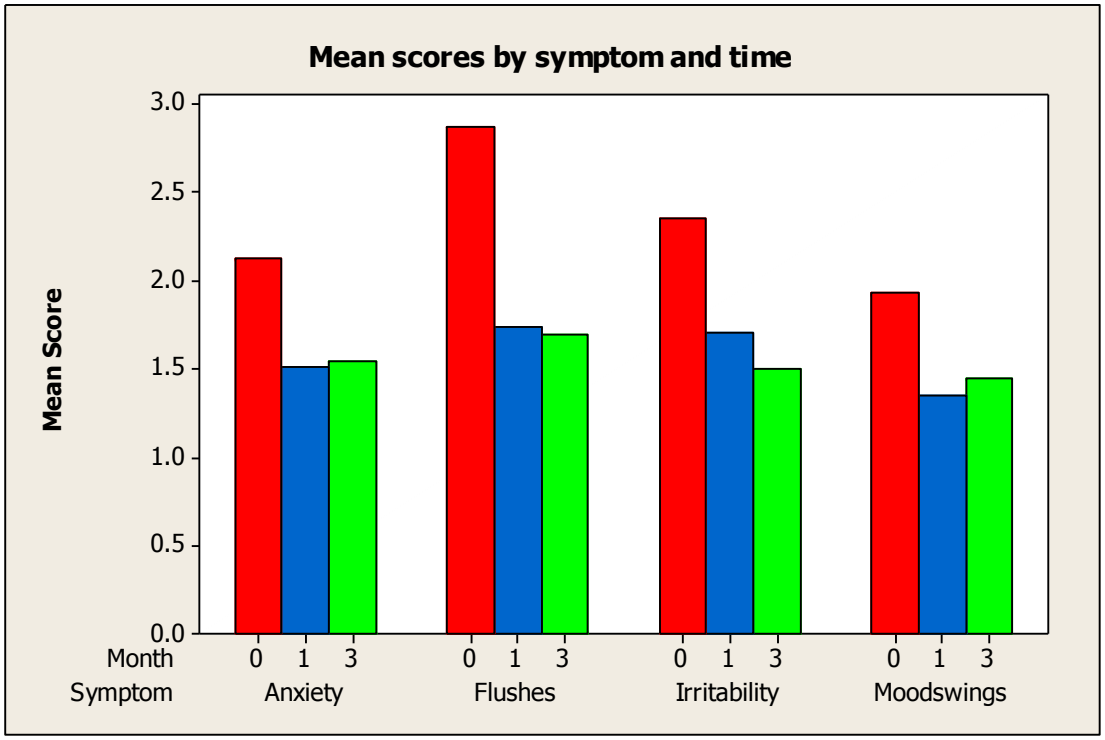

Fig 7 (above). Sub-analysis of several emotional symptoms and hot flushes at baseline, 1 and 3 months. Note that the means scores plotted above are for those subjects who provided data and thus may be biased if patients were lost to follow-up differed significantly from those included in the analysis.

Individual symptom tests:

Analysis of Variance for Anxiety,

Source	DF	Seq SS	Adj SS	Adj MS	F	P
Subject	30	130.4553	131.7401	4.3913	10.53	0.000
Time	2	8.2309	8.2309	4.1155	9.87	0.000
Error	49	20.4358	20.4358	0.4171		
Total	81	159.1220				

Dunnett Simultaneous Tests
Response Variable Anxiety
Comparisons with Control Level
Time = 0 subtracted from:

Time	Difference of Means	SE of Difference	T-Value	Adjusted P-Value
1	-0.6129	0.1640	-3.736	0.0010
3	-0.7315	0.1950	-3.752	0.0009

Overall evidence of changes in scores with time for ANXIETY symptoms ($p < 0.001$). Scores at 1 month ($p = 0.0010$) and 3 months ($p = 0.0009$) significantly lower than those at baseline.

Analysis of Variance for Flushes, using Adjusted SS for Tests

Source	DF	Seq SS	Adj SS	Adj MS	F	P
subject	30	104.1057	104.1774	3.4726	5.09	0.000
Time	2	25.3914	25.3914	12.6957	18.60	0.000
Error	49	33.4419	33.4419	0.6825		
Total	81	162.9390				

Dunnett Simultaneous Tests
Response Variable Flushes
Comparisons with Control Level
Time = 0 subtracted from:

Time	Difference of Means	SE of Difference	T-Value	Adjusted P-Value
1	-1.129	0.2098	-5.381	0.0000
3	-1.215	0.2494	-4.870	0.0000

Overall evidence of changes in scores of HOT FLUSHES with time ($p < 0.001$). Scores at 1 month ($p < 0.0001$) and 3 months ($p < 0.0001$) significantly lower than those at baseline.

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Analysis of Variance for Irritability, using Adjusted SS for
Tests

Source   DF    Seq SS   Adj SS  Adj MS     F      P
subject  30   69.8862  69.6355  2.3212  3.94  0.000
Time      2   10.4849  10.4849  5.2425  8.90  0.001
Error    49   28.8484  28.8484  0.5887
Total    81  109.2195

Dunnett Simultaneous Tests
Response Variable Irritability
Comparisons with Control Level
Time = 0  subtracted from:

      Difference       SE of           Adjusted
Time    of Means  Difference  T-Value   P-Value
1        -0.6452      0.1949   -3.310    0.0034
3        -0.8726      0.2316   -3.767    0.0009
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Overall evidence of changes in scores of IRRITABILITY with time (p = 0.001). Scores at 1 month (p = 0.0034) and 3 months (p = 0.0009) significantly lower than those at baseline.

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Analysis of Variance for Moodswings, using Adjusted SS for Tests

Source   DF    Seq SS    Adj SS  Adj MS     F      P
subject  30  114.0528  115.1102  3.8370  5.40  0.000
Time      2    6.8591    6.8591  3.4296  4.83  0.012
Error    49   34.8075   34.8075  0.7104
Total    81  155.7195

Dunnett Simultaneous Tests
Response Variable Moodswings
Comparisons with Control Level
Time = 0  subtracted from:

      Difference       SE of           Adjusted
Time    of Means  Difference  T-Value   P-Value
1        -0.5806      0.2141   -2.712    0.0177
3        -0.6403      0.2544   -2.517    0.0289
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Overall evidence of changes in scores of MOOD SWINGS with time (p = 0.012). Scores at 1 month (p = 0.0177) and 3 months (p = 0.0289) significantly lower than those at baseline.

BASELINE SYMPATHETIC NERVOUS SYSTEM AND PARASYMPATHETIC NERVOUS SYSTEM ACTIVITY

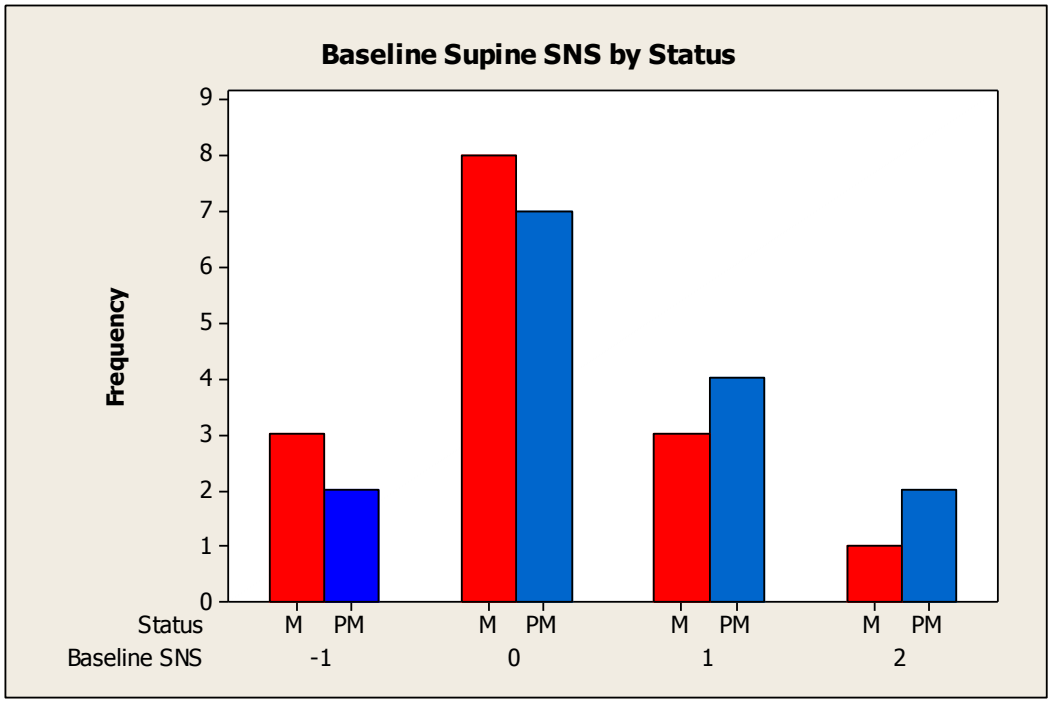

Fig 8. Measurements of SNS activity (supine) in the study group. Zero represents neutral activity. Note the trend to more sympathetic dominance in both M and PM subjects

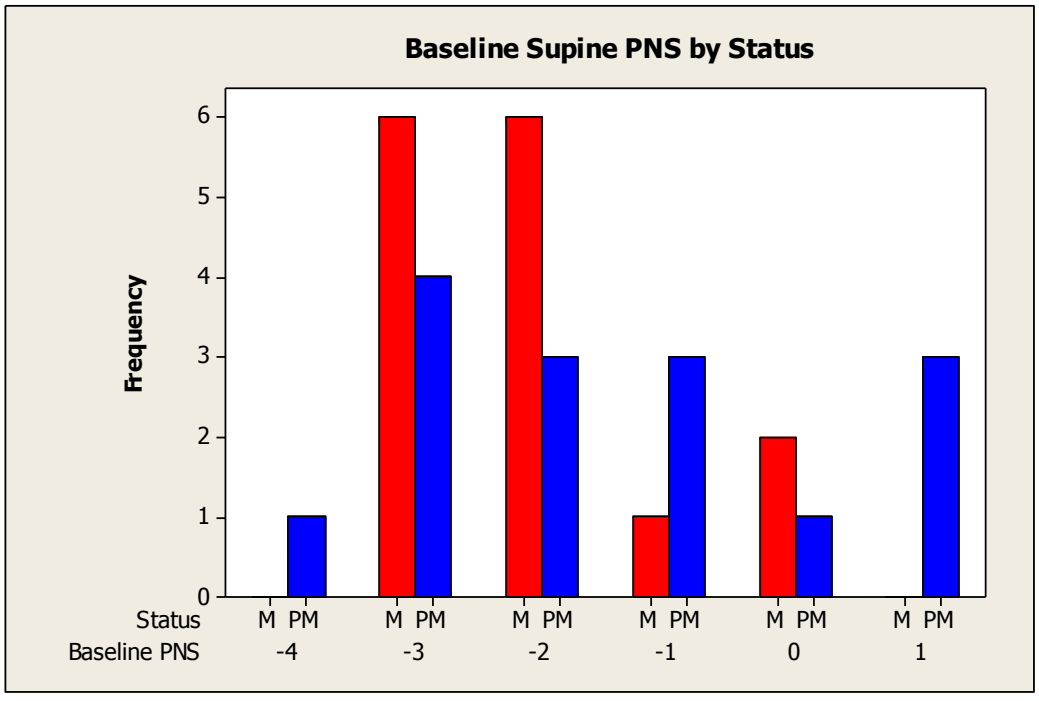

Fig 9. Measurements of PNS activity (supine) in the study group. Zero represents neutral activity. Note the trend to parasympathetic deficiency in both M and PM subjects. Comparing this data with Fig 8 above suggests a SNS dominance in these subjects.

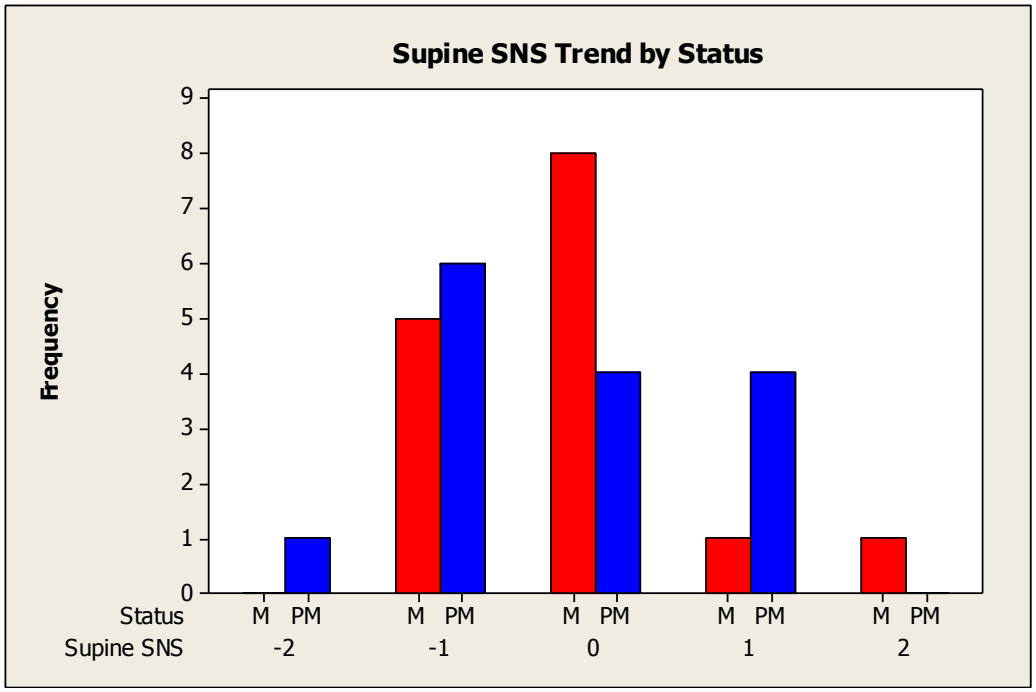

Fig 10 A

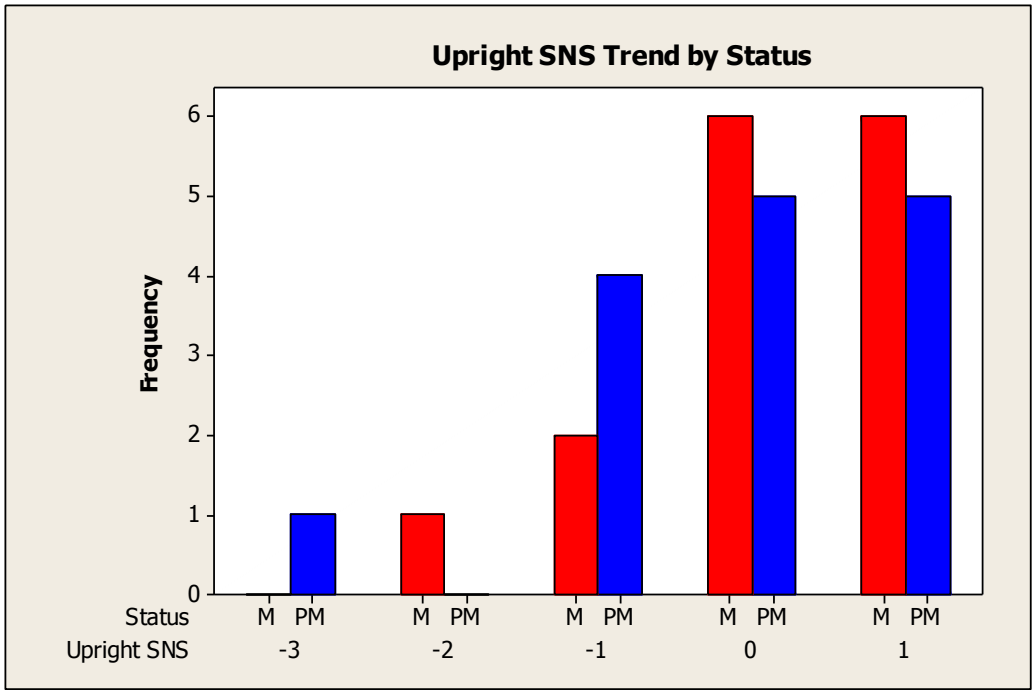

Fig 10B

Fig 10 A &B. Illustrates the expected shift to sympathetic dominance when subjects move from a supine to an upright position. This shows that the measurements made are consistent with the expected physiological changes and support the use of this technology for its ability to measure sympathetic and parasympathetic activity. A comprehensive overview of this technique for this purpose can be reviewed elsewhere. Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology. Heart rate variability
Standards of measurement, physiological interpretation, and clinical use. ***European Heart Journal (1996) 17, 354-381***

Pulse Rate Differences

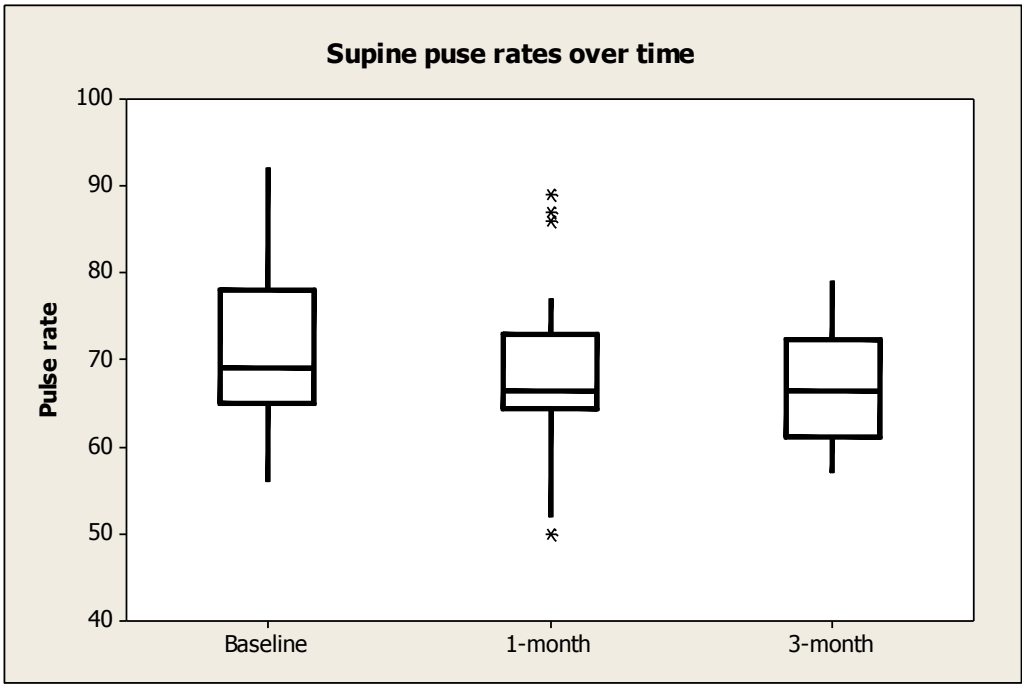

Fig 11. Supine Pulse rate variations from baseline to 3 months

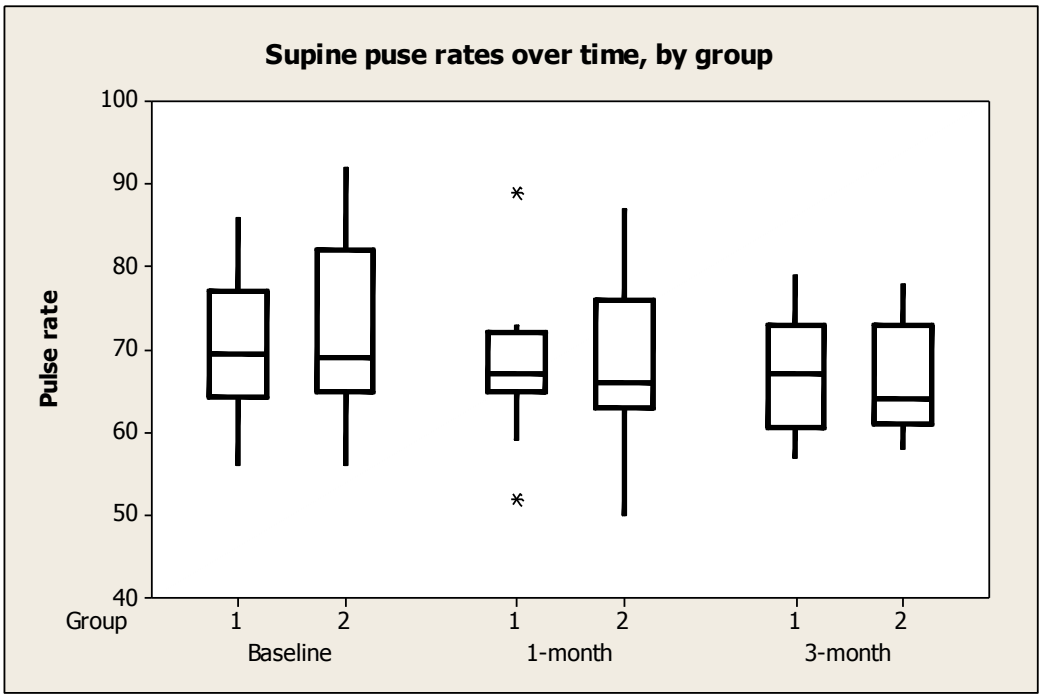

Fig 12. Supine Pulse rate variations from baseline to 3 months by Group

Supine pulse rates, Mean (Standard Deviation)

Time point	Group 1, Menopausal (n = 16)	Group 2, Peri-menopausal (n = 15)
Baseline	69.9 (7.8)	71.5 (10.9)
1 – Month	67.5 (8.2)	67.7 (10.2)
3 – Month[+]	67.0 (7.4)	66.6 (7.2)

[+] n_1 13, $n_2 = 7$

A repeated measures analysis of variance indicates that there is evidence of a statistically significant change in pulse rates over time (p = 0.013), with the change being independent of group (menopausal) status:

Analysis of Variance for supine,

Source	DF	Seq SS	Adj SS	Adj MS	F	P
Time	2	203.80	231.74	115.87	4.82	0.013
Group	1	20.02	6.22	6.22	0.26	0.613
Time*Group	2	12.57	24.92	12.46	0.52	0.599
Subject(Group)	29	4826.34	4826.34	166.43	6.92	0.000
Error	46	1106.71	1106.71	24.06		
Total	80	6169.43				

Pulse rates at 1 month post (p = 0.016) and 3 – months post (p = 0.004) were significantly lower than baseline levels.

This analysis indicates that there is a significant change in supine pulse over time for both groups. Overall, all individuals saw a reduction in pulse levels. There is no evidence of any difference between menopausal and peri-menopausal groups.

AUTONOMIC NERVOUS SYSTEM ACTIVITY CHANGES BEFORE AND AFTER LADYCARE

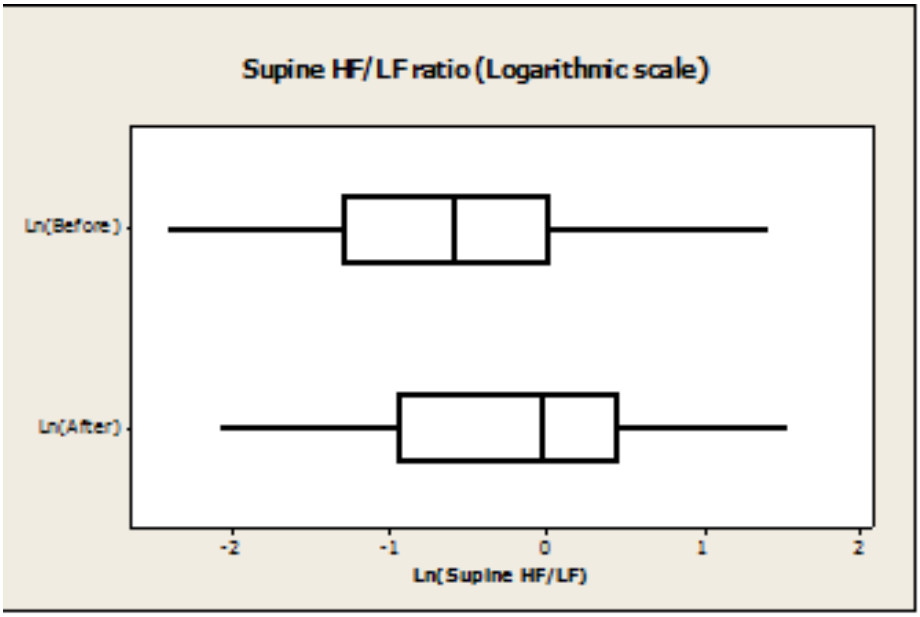

Fig 13. HF/LF ratios before and after LadyCare at 3 months. HF is a measure of parasympathetic activity and LF a measure of sympathetic nervous system activity. The shift to a greater HF/LF ratio is statistically significant (P-Value = 0.017). This was exactly the same at 1 month analysis – see below (p = 0.024).

Ignoring status i.e whether PM or M subjects:

Paired T for LnBefore - LnAfter

	N	Mean	StDev	SE Mean
LnBefore	30	-0.685	0.905	0.165
LnAfter	30	-0.235	0.944	0.172
Difference	30	-0.450	0.969	0.177

T-Value = -2.54 P-Value = 0.017

95% CI for mean difference: (-0.812, -0.088)

Evidence of a significant increase in this ratio over time

Paired T for LNbefore - LNAfter3

	N	Mean	StDev	SE Mean
LNbefore	20	-0.486	0.862	0.193
LNAfter3	20	-0.044	0.793	0.177
Difference	20	-0.443	0.804	0.180

T-Value = -2.46 P-Value = 0.024 95% CI difference: (-0.819, -0.066)

Discussion

Many of the police women in the study were skeptical that a device attached to their underwear could make any difference to their symptoms. However, 70% of the women in the study reported reduction of their menopause symptoms one month after wearing LadyCare continuously. Although all of the women volunteers had menopause symptoms, approximately half of them were in fact peri-menopausal and not menopausal i.e. They were not 12 months free of periods. It is well known that women can experience menopausal symptoms well before the onset of cessation of their periods. Data for menopausal women and peri-menopausal women was separated for analysis.

The current data add further support to previous reports (Eccles, 2008. http://www.ladycare-uk.com/effects-of-ladycare-on-menopause-symptoms.php) that both physical and emotional symptoms of menopause are relieved by the wearing of the LadyCare device. It is possible that the relief of the physical symptoms is responsible for the reported emotional improvements but we also cannot exclude that autonomic nervous system changes found in this study might not directly impact on improved emotional symptoms.

Having established what seemed to be a fairly consistent benefit to women with menopause symptoms from the previous large survey and continual feedback from

patients, the obvious question was how LadyCare could possibly be working. I postulated that the rapidity of effect in some women (and in the male case study cited above), as early as within 24 hours that it was unlikely to be a hormonal mechanism as this would almost certainly take longer. We set out in this study to investigate a more plausible mechanism that might involve autonomic nervous system changes. Because sweating is under the control of the autonomic nervous system (ANS), more specifically the sympathetic division (fight-flight/stress reactor system), it was proposed that this was a likely target for the LadyCare mechanism of action.

There are 2 divisions of the ANS, the Sympathetic division (SNS) which is the fight-flight stress reactor system of the body e.g. when we perceive a threat the heart beats faster and the pupils dilate to allow more light for enhanced visual acuity and faster reactions. In contrast, the Parasympathetic division (PNS) is responsible for REST and DIGESTION. The latter is the repair and regulatory system of the body and tends to have the opposite effect to the SNS. For example, the SNS speeds the heart rate while the PNS slows it down. The 2 systems work together to regulate all our organ systems. I proposed that LadyCare may be acting by somehow re-balancing ANS activity.

The current study investigated ANS activity in 35 British police women with menopause symptoms. Because sweats/hot flushes are the most likely symptom to be related to ANS imbalance, all volunteers had to have hot flushes as one of their menopause symptoms. A recognised non-invasive method for measuring ANS activity is by Heart Rate Variability (HRV). Close inspection and measurement of the heart rhythm reveals that the heart beat from one to the next is not even. The measured time between each heart beat varies beat to beat. This variation is a reflection of a tonic influence of the SNS (speeding the heart) and PNS (slowing the heart down). Measuring HRV is therefore a convenient way of measuring ANS activity. A 5-6 minute heart rhythm) recording is taken from which computer analysis is able to derive quantitative measurements of both SNS and PNS activity.

We have demonstrated that before the use of the LadyCare device that there seems to be a pre-existing autonomic imbalance in favour of a dominant sympathetic nervous system which may be augmented by a parasympathetic nervous system deficit. This is not the first demonstration of this autonomic imbalance in menopausal women (Hautamäk et al, 2011; Bhat et al 2005). It is known that oestrogen has a stimulatory effect on the sympathetic nervous system whilst progesterone has a stimulatory effect on the parasympathetic nervous system (Dzugan, 2010). A disproportionate fall in both of these hormones at and before menopause is likely to lead to an autonomic nervous system imbalance. Our results confirm the presence of such an imbalance.

The current study shows a significant shift of autonomic nervous system activity after wearing of the Ladycare device; the net result being greater PNS activity and reduced SNS activity. An SNS predominance in menopausal and peri-menopausal women is a logical explanation for the vast majority of common symptoms. A shift away from this SNS dominance after wearing of the LadyCare device, demonstrated in this study, also represents a novel but logical explanation of the observed effectiveness of LadyCare in reducing the common symptoms associated with

menopause. Consistent with this change in ANS activity was the observed statistically significant reduction in supine pulse rate in subjects at one and three months.

These findings represent a novel discovery and mechanism of action for the LadyCare device. The results suggest a physiological mechanism of action for the device. Given the favourable physiological effects observed concurrent with significant symptom relief, it would seem that the LadyCare device can provide an effective, non-invasive solution for menopause symptom relief. In the face of the long term detrimental effects of synthetic hormone replacement, the non-hormonal mechanism of action of LadyCare demonstrated here represents a feasible alternative solution for women suffering from the autonomic nervous system imbalances associated with menopause and peri-menopause.

A residual question remains given the finding of a shift towards greater PNS activity with LadyCare. How or why should wearing this device in the pelvis lead to a stimulation of PNS activity? When one considers the anatomy of the ANS and the fact that the PNS nerve roots exit the spinal cord in two specific regions i.e. the cervical region and sacrum, it is conceivable that the magnetic field of the LadyCare device in the pelvic region somehow specifically stimulates the PNS nerves where they exit the spinal cord.

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