Preliminary Report

Application of Gabapentin in Thai Women with Menopausal Syndrome

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Application of 100 mg. three times a day of Gabapentin group,70 women to relieve menopausal syndrome with the following symptoms:Paresthesia,sweating,hot flushes in a comparative study with the amitriptyline group,52 women 10 mg once daily.Analysis of data was done by Chi square which assumed that the Gabapentin is superior to amitripyline as accept alternative hypothesis (H_a) and other reject null hypothesis(H_0) assumed both have the same action.

The result of Chi square showed that the value of calculated Chi square (39.32) is higher than Table Chi square (6.63) at $p < 0.01$ so the authors have to accept that H_a, means that Gabapentin therapy is more significantly effective than amitripyline($p < 0.01$).

In addition, the present study showed that the number need to treat (NNT) of Gabapentin = 2

Keywords: *Gabapentin, Menopause*

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Gabapentin is structurally related to the neurotransmitter gamma-aminobutyric acid (GABA), but evidence shows that it does not act via the GABA ergic system. The mechanism involved in gabapentin's analgesic action is not yet clearly understood, however, a possible mechanism is suggested by recent data on its ability to modulate calcium channels. Evidence shows that gabapentin binds to the δ subunit of voltage-dependent calcium channels, the action of which can block the maintenance of allodynia or mechanical hypersensitivity in animal models of neuropathic pain. It's thought that the binding of gabapentin to the α_2 subunit at postsynaptic dorsal-horn neurons may play a role in the modulation of GABA ergic, glutaminergic, and monoaminergic function and disrupt several processes involved in the development of neuropathic pain.

Pain has specific tract or nerve fibers ,nerve impulse from the pain receptors propagates to neuron at dorsal root ganglion and transmits to neurons or projection neurons at the posterior horn of the spinal cord at this site called 'gate' which contains different type neurons, one of this type is inhibitory neurons the dendrites of which contact the cell membrane of projection nerve cells to inhibit the impulse of pain up to the higher brain center by releasing neurotransmitters : serotonin and gammabutylic acid (GABA) this is the classical pain pathway.

If the nerve fibers or axon opposed with abnormal physiologic or pathologic conditions such as HIV, Multiple sclerosis (MS), Diabetic mellitus (DM), Shingles and post-nerve trauma. The normal function of pain conduction is altered leading to bad interpretation of sensation due to

1. Abnormal synapse of fiber to A delta fiber called rewiring so pain sensation was carried via fiber of touch to a higher center.
2. Abnormal growth of C-fiber at the posterior horn and synapse to A delta, Beta fibers.
3. Abnormal synapse of the sympathetic nerve by production of noradrenalin receptors so the sympathetic nerve will be alerted.
4. C fibers will increase production of Glutamate, exiting neurotransmitter making neuron hyperesthesis.

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5. Wallerian degeneration, each fragments of nerve will produce their own electrical charge at random so stimulate sensation all day and night.

All pathologic phenomena making abnormal sensation and misinterpretation of high centers of the brain, this is called neuropathic pain.

The hall mark of neuropathic pain: Allodynia means feeling of pain after responding to non pain stimuli such as a gentle touch, the other symptom is hyperesthesis which means feeling severe or high intensity of pain after stimulation by small intensity of pain stimulus.

Estrogen has many roles in nerve fibers and functions, Domingul Toran-Allerand demonstrated the new estrogen receptor 'ER-X' at the nerve sheath its main function is to maintain the vitality of nerve fibers. Ito A[1] (2000) , Tamakura T and Yoshimur M[2,3] found that the serotonin receptors decrease in number in ovarectomized rats. Hans Slves (1928) showed that in cases of depletion of estrogen will decrease neurotransmitters : Serotonin, opoid, dopamine GABA leading to feeling of anger, irritability, sleeplessess, and anxiety and in other aspects he found that adrenalin and epinephrine will increase high blood pressure and cause palpitations.

The authors used gabapentin for menopausal syndrome because its action enhances the synthesis of GABA, an inhibitory neurotransmitter by stimulating glutamic decarboxylase for changing glutamic acid to GABA. In another aspect gabapentin can open the chloride channel of the nerve membrane and inhibit glutamate and substance P so the random electrical charges will subside. Gabapentin can block the calcium channel too, so can moderate blood pressure in case of increased noradrenalin.

Material and Method

A total of 122 menopausal women were enrolled in the present study, all of them had at least one symptom and sign of menopausal syndrome: Paresthesia of hand, foot, burning sensation, sweating, hot flushes (Table 1).

Table 1. Number of cases with menopausal syndrome

Symptom and sign	Number of cases
Paresthesia	45
Hot flushes	19
Sweating	5
Mix	1
	70

Results

Application of gabapentin was studied in menopausal syndrome, from a total of 122 cases, 70 cases received gabapentin (100mg) bid and 52 cases took amitripytyline(10mg) once daily. The evaluation was performed after 14, 30 days for relief of paresthesia, hot flushes and sweating.

The data was analyzed by Chi square, two by two tables. Hypothesis was assumed as the following:

$\mathbf{H_0}$: Gabapentin and amitryptyline (TCA) are not different in relieving menopausal symptoms and signs.

$\mathbf{H_A}$: Therapeutic of gabapentin is superior to amitryptyline in relieving menopausal syndrome.

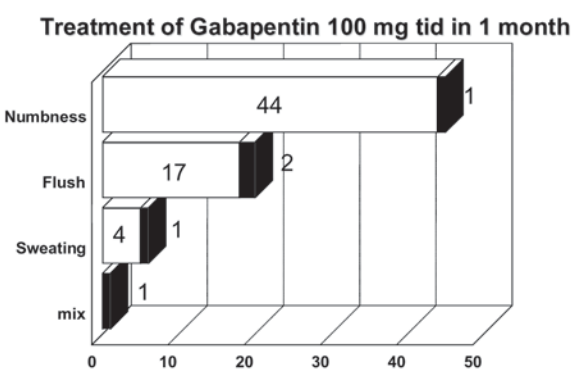

Fig. 1 Shows the efficacy of Gabapentin after 1 month: White column symptoms and signs are relieved, the black column means failure of treatment

Total cases = 122 : Gaba.= 70 and TCA= 52

	TCA	Gaba.	
Relief [1]	11(10.74)*	56 (38.44)	67
Fail	41(23.44)	14(31.55)	55
	52	70	122

1 response 14-30 days

* calculated expected value

Fig. 2 Work sheet of two by two tables: Total cases=122, Gabapentin group=70 and TCA group=52

NNT (Number Need to Treat)

	Outcome A benefit	Outcome B nonbenefit	
Predictor (+) Gaba	56 (a)	14 (b)	70 a+b
Predictor (-) TCA	11 (c)	41 (d)	52 c+d
	a+c	b+d	

$$NNT = \frac{1}{AR\ (\text{Attributable Risk})} = \frac{1}{(56/70\ a/(a+b) - 11/52\ c/c}$$

NNT= 2

Fig. 3 Calculation of the number needs to treat

Calculated Chi square = 39.32 at degree of freedom =1
From table Chi square = 6.63 at degree of freedom=1 and confidential=0.01
So calculated Chi square values are greater than Table Chi square (39.32 > 6.63)

Interpretation: Reject null hypothesis (Ho) and accepted alternative hypothesis (Ha)

That means the gabapentin is more effective than amitryptyline in relieveing menopausal symptoms and signs.

Discussion

Gabapentin is the drug for neuropathic pain

This is the first report (pilot study) of the clinical application of gabapentin (Neurontin(R)) for menopausal syndrome. It is a rather safe and satisfactory medication in this situation and superior to TCA and has a low risk of CHD. However the large scale study is going on and in the future gabapentin will replace estrogen in menopausal syndrome.

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การประยุกต์ใช้ กาบาเพนติน รักษาสตรีวัยหมดประจำเดือนที่มีอาการแสดงของการหมดประจำเดือน

ณรงค์ บุณยะรัตเวช, ทวี ทรงพัฒนาศิลป์

รายงานการศึกษาเบื้องต้นเปรียบเทียบในการใช้ยา กาบาเพนตินขนาด 300 มิลลิกรัมต่อวันกับยาแอมมิทิปพายลีนขนาด 10 มิลลิกรัมต่อวัน เพื่อบำบัดอาการและอาการแสดงของการหมดประจำเดือนในกลุ่มสตรี70และ52 คนตามลำดับที่มีอาการ ซา หรือ เหงื่อออกมาก หรือ ร้อนวูบวาบตามตัว

การวิเคราะห์ข้อมูลใช้ ไคว์สแควร์ โดยตั้งสมมุติฐาน(H_0)ว่าการใช้ยา กาบาเพนตินได้ผลไม่แตกต่างจาก ยาแอมมิทิปพายลีน และ สมมุติฐาน (H_a) ว่ายา กาบาเพนตินได้ผลดีกว่า ยา แอมมิทิปพายลีน จากการคำนวณค่าไคว์สแควร์ที่ได้จากการศึกษามีค่าเท่ากับ 39.32 สูงกว่าค่าไคว์สแควร์ที่ได้จากตารางมาตรฐานคือมีค่าเท่ากับ 6.63 แสดงว่ายอมรับ H_a หมายความว่ายากาบาแพนติน บำบัดอาการของการหมดประจำเดือนดีกว่า อย่างมีนัยสำคัญ ($p<0.01$) นอกจากนี้ได้หาค่าของ กาบาแพนตินมีค่า NNT=2

โดยสรุปยากาบาแพนติน น่านำมาใช้แก้อาการวัยหมดประจำเดือนร่วมกับยาอื่นที่ไม่ใช่ฮอรโมน
