Preliminary Report

Application of Gabapentin in Thai Women with Menopausal Syndrome

Narong Bunyaratavej, MD*,
Thawee Songpatanasilp, MD**

* Department of Orthopaedic Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University
** Department of Orthopadics, Pramongkutklao Hospital

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 amitriptyline as accept alternative hypothesis (H1) and other reject null hypothesis (H0) 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 H1, means that Gabapentin therapy is more significantly effective than amitriptyline (p < 0.01).

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

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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 GABAergic 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 subunit at postsynaptic dorsal-horn neurons may play a role in the modulation of GABAergic, 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.
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 hallmark of neuropathic pain: Allodynia means feeling of pain after responding to non pain stimuli such as a gentle touch, the other symptom is hyperesthesia 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, opioid, dopamine GABA leading to feeling of anger, irritability, sleeplessness, 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

<table>
<thead>
<tr>
<th>Symptom and sign</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paresthesia</td>
<td>45</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>19</td>
</tr>
<tr>
<td>Sweating</td>
<td>5</td>
</tr>
<tr>
<td>Mix</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>70</td>
</tr>
</tbody>
</table>

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 amitriptyline(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:

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

$H_A$: Therapeutic of gabapentin is superior to amitryptyline in relieving menopausal syndrome.
**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 relieving 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®) 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.

**References**