Clinical Comparison of the Effects of Gabapentin and Megestrol Acetate on Hot Flashes in Patients with Breast Cancer

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Abstract

Introduction: Hot flash affects approximately 75% of women with breast cancer. Those who experience hot flashes have higher rates of sleep disorders, temper and lower quality of life than women with no hot flashes. The persent study was aimed to compare the effect of megestrol acetate with gabapentin on the severity of hot flashes in patients with breast cancer

Materials and Methods: In a randomized controlled clinical-trial study 120 patient with breast cancer who had moderate and severe hot flashes were randomly assiged into two groups; 40 mg megestrol acetate twice daily and 300mg gabapentin oncedaily for a period of 8 weeks. Demographic data and the severity of hot flashes were recorded before treatment and 8 weeks after therapy. The obtained data was analysed using SPSS V15 withstatistical tests chi-square, Student T- Test and Paired T-Tes.

Results: After 8 weeks of treatment with megestrol acetat a reduction of 64.3% in hot flash frequency and 37.1% reduction in hot flash severity from base line were observed. In the gabapentin group the decrease was 44.8% and 24.6% compared before treatment respectively.(P= 0.005, P= 0.04)

After eight weeks of treatment the number of hot flashes was 3.9±4.0 and 5.8±3.7 in the megestrol acetat and gabapentin groups respectively; the difference was statistically significant (P=0.04). In the megestrol acetat group number of hot flashes was obviously lower than their level in the gabapentin group. After eight weeks of treatment, the serverity of hot flashes was 50.4% and 62.9% in the megestrol and gabapentin groups respectively; the difference was statistically significant (P= 0.005). In the megestrol group severity of hot flash was obviously lower than their levels in the gabapentin group. In the megestrol group frequency and severity of hot flashes were obviously significantly lower than their levels in the gabapentin group.

Conclusion: Megestrol acetat is significantly more effective than the Gabapentin in treating hot flash and can be considered as an effective therapy to reduce the disorder.

Key Words: Hot flashes, Megestrol Acetat, Gabapentin, Breast Cancer

Introduction

The diagnosis and treatment of breast cancer can result in physical and psychosocial impacts with long-term consequences. Hot flashes are more common finding in these patients, with up to 75 % of prevalence in patients with breast cancer.(1, 2)

Hot flash has more implications in patients with past history of breast cancer, because most women who receive chemotherapy are in pre-menopausal cycle of their life will experience the early menopause. In addition, the majority of the patients with past history of breast cancer receive tamoxifen, which might trigger induction of hot flashes. Administration of exogenouse estrogen to prevent the hot flashes should be avoided due to the risk of recurrence of the breast cancer.(3- 6)

Hot flashes are typically experienced as a feeling of sudden redness, heat and sweating in face, neck and chest and may last from seconds to a few minutes or rarely, up to one hour for each occurrence. The hot flash event may be occurred a few times or repeatedly every few minuets, with the frequency increasing over night or during stress. Hot flashes deeply affect all personal life quality, including social activities, job, happiness, sleep, temper and concentration.(1, 3, 7- 9)

Hormone replacement therapy (estrogen alone and with progestron) is usually considered as the best treatment for hot flashes. However, hormonal

therapies may increase the risk of breast cancer, and thus, alternatives therapies are now more recommended.(5, 10- 12)

Several studies have shown that megestrol acetate might provide relief from hot flashes by reducing the frequencies and the severity with having minimal adverse effects.(3, 5, 7, 10, 13)

Moreover, several investigation have shown that gabapentin, as an anticonvulsant, can provide relief from hot flashes through an unknown process that might be associate with side effects, including dizziness and drowsiness.(2, 3, 7, 14, 15- 18)

To the best of our knowledge , previously no study has been investigating the effect of both gabapentin and megestrol acetate together, nor compared them on hot flashes.

This study aimed to investigate the effects of both gabapentin and megestrol acetate on hot flashes in patients suffering breast cancer in Iranian population.

Materials and methods

Patients: In this clinical trial, 120 patients with breast cancer (<50 yo) admitted in Rasoul Akram Hospital who were suffering a moderate or severe hot flash and concurrently were receiving chemotherapy along with tamoxifen were selected. The sample size required for this study was calculated using Altman's nomogram graphical method (alpha= 0.05, power= 80 %). Patients were randomly assigned to two group of 60 in each and received a daily dose of 300 mg gabapentin or 40 mg of megestrol acetate for 8 weeks.

Clinical assessment of hot flash: The clinical assessment of hot flash was performed base on its frequency, severity, and duration and it was classified as mild (not waking up at night, not more than four hot flashes per day, not interfering with activities), moderate (few night awakenings with some loss of sleep, frequent hot flashes during waking hours interfering with work), and severe (waking at night several times with significant sleep loss, hot flashes almost hourly requiring need to sponge off or change clothes) according to the criteria described previously.(19, 21)

Statistical analysis: To determine the quantitative and qualitative parameters, data were analyzed using the Paired *t*-test, Student's *t*-test or Chi square test using (SPSS version 15 SPSS Inc., Chicago, IL, USA). Differences between the means were considered statistically significant if $P < 0.05$.

The description of qualitative data was performed in absolute frequencies and percentages and the quantitative data as mean standard deviation, median, and mode.

Results

No significant difference was found between the average age of gabapentin (42.8± 4.6) and megestrol acetate (42.6± 4.3) groups (P> 0.05). From 120 patients, 18 (15%) were illiterate, 43 (35.8%) patient had a primary education, 30 patients (25%) had a collage certificate and 29 patients (24.2%) had a higher education. No significant difference was found between the education level of two groups (P>0.05). All patients in gabapentin group were married, while one patient in megestrol group was single (P>0.05). In gabapentin group, 3 patient (5%) had no past history of delivery, compared to 8 patients (13.3%) in megestrol group (P> 0.05). The average number of children in gabapentin and megestrol groups was 2.5± 1.7 and 2.7± 1.3, respectively and showed no significant difference between the two groups (P> 0.05). In both groups, the flashing score was the same (3 in 30 patients (50%) and 4 in the remaining patients) (P> 0.05) (Table- 1).

The average hot flash frequency in gabapentin and megestrol groups before treatment was 10± 1.5 and 9.9± 1.7 times, respectively (P> 0.05), and the average of the hot flash severity in both groups was 87.5 % (Table- 1).

The average hot flash frequency in gabapentin and megestrol groups 8 weeks after treatment were 5.8± 3.7 and 3.9± 4.0, respectively. The reduction in the average hot flash frequency in gabapentin and megestrol groups were 44.8 and 64.3, respectively, which show a significant difference (P> 0.04) (Table- 1).

The average of the hot flash severity in megestrol and gabapentin groups decreased to 50.4 % and 62.9 %, respectively (Table- 1). The level of the reduction of the hot flash severity in megestrol group was significantly more than gabapentin group (P= 0.005).

In gabapentin group, the symptoms in 8 patients (13.3%) completely improved, while 40 patients (66.6%) showed a relative improvement and 12 patients (20%) did not respond to the treatment. In megestrol group, these figures were 24 (40%), 34 (56.6%) and 2 (3.3%) patients, respectively, suggesting a significantly higher therapeutic effects for megestrol acetate (P<0.001) (Table- 1).

Totally, the average severity of hot flash in all 120 patients (both groups) before and after treatment was 87.5% and 56.6%, which shows a significant reduction of 30.9% (P< 0.001). The frequency of

Table- 1. Demographic features of patients in both megestrol and gabapentin groups

Parameter		Megestrol group ± SD (n=60)	Gabapentin group ± SD (n=60)	P- value
Age (year)		42.6±4.3	42.8±4.6	NSNS
Marital status	Single	1(1.6%)	0	NS
	Married	59(98.3%)	60(100%)	
History of No-delivery		8(13.3%)	3(5%)	NS
Average of children		2.7±1.3	2.5±1.7	NS
Flashing score	3	30(50%)	30(50%)	NS
	4	30(50%)	30(50%)	
Average of hot flash frequency, before treatment		9.9±1.7	10±1.5	NS
Average of hot flash frequency, after treatment		3.9±4.0	5.8±3.7	0.04
Reduction of hot flash frequency, after treatment (%)		64.3%	44.8%	0.04
Average of hot flash severity, before treatment		87.5%	87.5%	NS
Average of hot flash severity, after treatment		50.4%	62.9%	0.005
Reduction of hot flash severity, after treatment (%)		37.1%	24.6%	0.005
Response to treatment	No response	2(3.3%)	12(20%)	0.0001
	Relative response	34(56.6%)	40(66.6%)	
	Complete response	24(40%)	8(13.3%)	

NS= Not significant

Table-2. The severity of the hot flash in patients before and after treatment.

Group	Stage	Severity of hot flash			
		Severe	Moderate	Mild	no hot flash
Megestrol acetate	Before	30(50%)	30(50%)	0	0
	After	2(3.3%)	21(35%)	13(21.7%)	24(40%)
Gabapentin	Before	30(50%)	30(50%)	0	0
	After	5(8.3%)	29(48.3%)	18(30%)	8(13.3%)

hot flash in 120 patients reduced from 9.9± 1.6 reduced to 4.8± 3.9 after treatment, which shows a significant reduction of 5.1± 0.6 (54.5%) (P< 0.001). Generally, 32 patients (26.7%) out of 120 showed a complete response to the treatment and 74 patients (61.7%) showed a relative improvement, and the symptoms of the remaining 14 patients (11.7%) did not improve following treatment.

Patient's age and education level were found not to be related to the treatment results (P> 0.05). However, there was a significant link to the marital status (P= 0.02).

As shown in Table- 2, 50% of the patients in both megestrol and gabapentin groups had a severe hot flash before treatment, which this was reduced to 3.3% in megestrol group and 8.3% in gabapentin group. Forty percent of the patients in megestrol group had no sign of hot flash, while in gabapentin group, only 13.3% of the patients had no hot flash after treatment.

Discussion

The outcome of the current study shows that both gabapentin and megestrol acetate significantly reduced the frequency and severity of hot flashes (both P< 0.001).

In the current study, After 8 weeks of treatment with megestrol acetat a reduction of 64.3% in hot flash frequency and 37.1% reduction in hot flash severity from base line were observed. In the gabapentin group the decrease was 44.8% and 24.6% compared before treatment respectively.(P=0.005 , P= 0.04)

Eight weeks after treatment, 24 patients (40%) in megestrol acetate group had no hot flash and only 2 patients did not respond to the medication. These figures in gabapentin group were 8 (13.3%) and 12 (20%) patients, respectively, indicating a significantly better therapeutic effect for megestrol acetate, compared to gabapentin (P< 0.001).

Guttso et al. (2005) showed that administration of 900 mg gabapentin per day for 12 weeks significantly decreased the frequency (45%) and severity (54%) of hot flashes, compared to the placebo group, which were 29% and 31%, respectively.(20) Despite the different dosage used between that study and the current study, they shared similar results.

Pandya and his colleagues (2006) has also shown that the average of hot flash frequencies at weeks 4 and 8 post treatment in the gabapentin group receiving 300 mg/day were 28% and 30% and in 900 mg/day gabapentin group were 41% and 44%, compared to 18% and 15% in the control group. A significant difference in the results between the treatment and control groups after both 4 and 8

weeks was found (P= 0.0001 and P= 0.007, respectively), suggesting gabapentin as the selective drug for treatment of the hot flash in women with breast cancer.(16)

In another study, after treatment with 300 mg/tid gabapentin a reduction of 55% in hot flashe frequency was observed.(21)

The findings from our study was in concordance with above studies, suggesting the ability of gabapentin in reducing the hot flash frequency and severity, when used at low dosage. The slight differences between the results may be caused by the differences in the dosage and duration of the administration of the gabapentin between the studies.

In a study, investigating the effect of 20 mg/bid of megestrol acetate for 4 weeks in 1992-3, the frequency and the severity of the hot flashes at the end of trial reduced up to 74% and 83%, respectively (P< 0.001).(5)

Our result using megestrol acetate was similar to those from Goodwin et al. (2008) of which, in the patients receiving 20 and 40 mg of megestrol acetate, the frequency of the hot flashes decreased to 65% and 48% , respectively, after 3 months (P< 0.0001), suggesting a significant improvement in the frequency and severity of the symptoms following administration of megestrol acetate.(22)

Conclusion

The outcomes of the current study suggest a more significant effect for megestrol acetate in reducing the frequency and severity of hot flashes, compared with gabapentin in patients with breast cancer.

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