

Comparison the effects of Gabapentin and Propranolol in Patients with essential tremor

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Abstract

Introduction: Essential tremor is the most common abnormal movement in the world .there is no associate neurologic abnormality. Tremor in this disease has low frequency and it's prevalence is 3 to 5 percent in community.

Methods: This prospective study was conducted on 120 patients with essential tremor in neurology clinic of shahid mostafa Khomeini hospital (shahed university) from 2005to 2008. Patients assigned randomly in two groups. 59 patients received propranolol 40 mg 3 times daily for 3 weeks and 61 patients in another group received gabapentin 300 mg 3 times daily for the same duration. Fahn – Tolosa-Marin tremor rating scale (TRS) that is a numerical scale (0-88) was used for evaluation in both groups.

Results: 120 patients completed the study.56 (47%) patients were male and 64(53%) patients were female. Mean age was 43.9(26-59) years old .At the beginning of study the TRS was 38.6±1 and 39.1±1 in patients taking propranolol and gabapentin respectively .at the end of study TRS was 28.4±1 and 25.6±1 in propranolol and gabapentin group respectively. Statistical analysis with SPSS software showed significant difference in both group after treatment. (P<0.0005)

Conclusion: Gabapentin can be used as an effective drug in the treatment of essential tremor it's efficacy is at least equal to propranolol. Due to its lower side effects and better tolerance especially in patients with cardiac and respiratory problems and in older patients this drug can be as the first selection in these patients.

Keywords: Tremor,Gabapentin,Propranolol,Abnormal movement

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Introduction

The term essential tremor has been in regular use since the second half of 20th century. but Burrelli used it for the first time in 1874.⁽¹⁾ Essential tremor is the most common abnormal movement in the world its pathophysiology is unknown.⁽²⁻⁵⁾ there is some belief that this disease is under diagnosed and many patients with this disease don't receive adequate treatment.^(6,7) This type of tremor has low frequency.⁽⁸⁻¹⁰⁾ there is no other neurologic abnormality in this disease and all of the neurologic exam is normal. The inheritance of disease is autosomal dominant with high penetration.⁽¹¹⁻¹³⁾ Essential tremor mostly begins in the arms but may diffuse to other parts and in some patients it appears as head tremor.^(6,14) Both sexes are affected its prevalence is estimated 415 per 100000 population in one study and in other studies its prevalence have been reported 3/09 to 5 percent.^(11;15;16) Etiology of essential tremor is unknown .three associated loci have been found but genes have not been identified.⁽⁶⁾ It often has been considered as a degenerative disorder. Some patients have cerebellar ataxia and degeneration of purkinje cells are sometimes find.^(1; 17) some studies correlate it with 2nd and 3rd chromosome.⁽¹⁸⁾ some studies correlates essential tremor with environmental elements such as harmane,lead and pesticide exposure.⁽¹⁹⁾ All patients with essential tremor feel symptoms subside after alcohol drink but it is temporary.⁽¹¹⁾

propranolol and primidone are other drugs that are effective but their overall effectiveness is not more than 50-60 percent in more studies.^(11;20;21) new drugs such as topiramate and gabapentine are under investigation.^(20;22) This study is designed to compare the effectiveness of gabapentin in comparison with propranolol in patients with essential tremor.

Methods

This prospective study performed from 2005 to 2008 in neurology clinic in Mostafa Khomeini hospital (shahed university). Patients were selected in two groups sixty four patients in group G were treated with gabapentin and sixty patients in group P were treated with propranolol. Selected patients had essential tremor for at least 18 months.all patients between 25 to 60 years old selected randomly in two groups. All patients had symmetrical tremor in upper limbs although tremor of other body parts might be present. Patients had no other neurologic abnormality especially rigidity and bradykinesia and there was no other explanation for tremor. Patients with asthma, cardiac failure and diabetes mellitus were excluded. all patients who received any drugs which may affect tremor , such as acetyl choline, neuroleptics ,lithium, cortico steroids and thyroid hormone supplements, anticonvulsant medication, antidepressants, and drugs used for asthma were not permitted in this study. Patients in group G took

gabapentin 300mg 3 times daily. Initial dose was 300mg daily raised by 300mg every three day to maximum dose of 1200mg daily. Patients in group P received propranolol 40mg three times daily. All patients received drugs for 3 weeks. for evaluation tremor in our patients we used from Fahn-Tolosa-Marin tremor rating scale (TRS) that is a standard scale for evaluation of tremor in clinical medicine this scale has (0-88) points and higher points shows more disability .(23) All patients evaluated at the beginning of study before taking any drug and at the end of study. Study was described for all patients and all patients had informed consent. If there was any drug hypersensitivity or drug reaction study was discontinued. All the data analyzed with SPSS soft ware at the end of study.

Results

In group P (taking propranolol) 59 patients completed the study and in group G (taking gabapentin) 61 patients completed the study. One patient in group G had drug reaction

and one had sleepiness that both of them excluded from study. There was 33 (56%) males and 26(44%) female in group P and in group G there was 31 (51%) male and 30(49%) female. Mean age of patients in group P was 43.3(26-59) years old and mean age in group G was 44.6(27-58) years old. Mean height in group P was 171.3(159-183) cm and mean height in group G was 169.8(165-186) cm. Mean weight in group P was 79.5(66-97) kg and mean weight in group G was 72.3(65-99) kg. At the beginning of study Fahn-Tolosa-Marin tremor rating scale (TRS) in group P was 38.6 ± 1 (29-41) and in group G it was 39.1 ± 1 (29-44) . Statistical analysis shows no difference between two groups at the beginning of study. At the end of study TRS scale in group P was 28.4 ± 1 (22-31) and statistical analysis shows significant difference in comparison with beginning of study .($P < 0.0005$) In group G TRS at the end of study was 25.6 ± 1 (22-30) and statistical analysis shows significant difference in comparison with beginning of study.($P < 0.0005$)

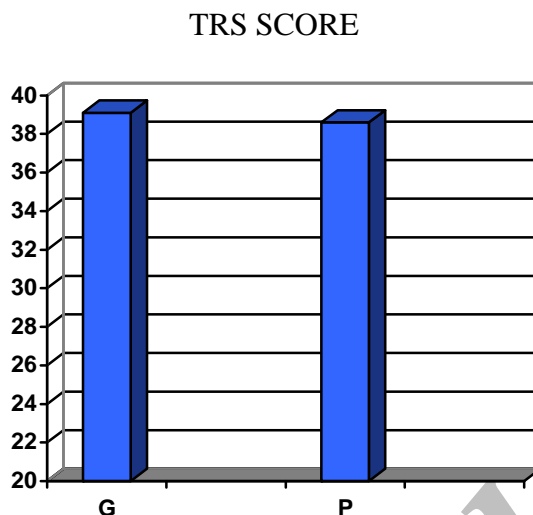


Fig 1: Mean Trs Score Comparison Of Group G And Group P At The Beginning Of Study

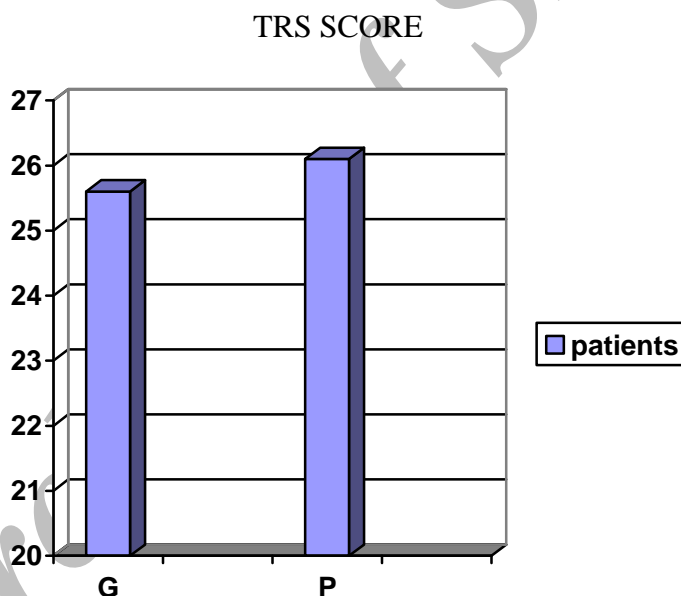


Fig 2: Comparison Of Mean Trs Between Two Group At End Of Study

Discussion

Gabapentin is an antiepileptic drug with a structure similar to GABA which penetrates to blood brain barrier.^(24; 25) Gabapentin does not interact with other drugs and does not induce liver enzymes and it is well tolerated in elderly and patients with asthma or cardiac problems.^(21;26;27) the

origin of essential tremor is unknown but a central mechanism is possible. increased excitability of cell membrane in motor cortex is possibly the underline disorder. Innervations in muscles have reciprocal form and increased excitability of cell membrane produce some oscillations that its presentation in clinic is tremor^(4;28)

Electrophysiological studies also consistent with a central source of tremorogenic oscillation and inferior olive and cerebellum are involved in studies with PET scan.⁽²⁸⁾ Gabapentin as we mention have inhibitory effect like GABA so it can stabilize the cell membrane and inhibit the oscillatory effect of the unstable cell membrane and suppress tremor with this mechanism. This study shows us that gabapentin can be at least as effective as propranolol in treatment of essential tremor.

Statistical analysis between two groups shows no significant difference between group G and group P at the beginning of study but at the end of study statistical analysis shows significant difference in both groups in comparison with starting score

.Although gabapentin is more expensive but it has very low side effect and can be used safely in elderly and also in patients with respiratory and cardiac problems who can not use beta – blockers. This study supports Ondo⁽²⁹⁾ and Gironell studies.⁽³⁰⁾ In these studies they found gabapentin as an effective treatment for essential tremor. Although in most review articles propranolol and primidone are introduced as first choice for treatment but both of them have some complications and also their effectiveness rate is low so further investigation in this disease is needed. According to this study we suggest gabapentin as an effective drug for reduction of tremor in patients with essential tremor especially in older patients.

Reference

- 1- Louis ED, Broussolle E, Goetz CG, Krack P, Kaufmann P, Mazzoni P. Historical underpinnings of the term essential tremor in the late 19th century. *Neurology* 2008 Sep 9;71(11):856-9.
- 2- Elble RJ. Diagnostic criteria for essential tremor and differential diagnosis. *Neurology* 2000;54(11 Suppl 4):S2-S6.
- 3- Elble RJ. Essential tremor is a monosymptomatic disorder. *Mov Disord* 2002 Jul;17(4):633-7.
- 4- Shaikh AG, Miura K, Optican LM, Ramat S, Tripp RM, Zee DS. Hypothetical membrane mechanisms in essential tremor. *J Transl Med* 2008 Nov 6;6:68.:68.
- 5- Elble RJ. Essential tremor frequency decreases with time. *Neurology* 2000 Nov 28;55(10):1547-51.
- 6- Dietrichs E, Kvikstad V. [Essential tremor]. *Tidsskr Nor Laegeforen* 2008 Oct 9;128(19):2210-3.
- 7- Jankovic J. Essential tremor: clinical characteristics. *Neurology* 2000;54(11 Suppl 4):S21-S25.
- 8- Giller CA, Liu H, German DC, Kashyap D, Dewey RB. A stereotactic near-infrared probe for localization during functional neurosurgical procedures: further experience. *J Neurosurg* 2009 Feb;110(2):263-73.
- 9- Ellis TM, Foote KD, Fernandez HH, Sudhyadhom A, Rodriguez RL, Zeilman P, et al. Reoperation for suboptimal outcomes after deep brain stimulation surgery. *Neurosurgery* 2008 Oct;63(4):754-60.
- 10- Elble RJ. Characteristics of physiologic tremor in young and elderly adults. *Clin Neurophysiol* 2003 Apr;114(4):624-35.

- 11- Ropper Ah, Brown RH. Adams and victor's Principles of neurology. 8th ed. McGraw-Hill; 2005.
- 12- Kovach MJ, Ruiz J, Kimonis K, Mueed S, Sinha S, Higgins C, et al. Genetic heterogeneity in autosomal dominant essential tremor. *Genet Med* 2001 May;3(3):197-9.
- 13- Kralic JE, Criswell HE, Osterman JL, O'Buckley TK, Wilkie ME, Matthews DB, et al. Genetic essential tremor in gamma-aminobutyric acidA receptor alpha1 subunit knockout mice. *J Clin Invest* 2005 Mar;115(3):774-9.
- 14- Jankovic J. Essential tremor: a heterogenous disorder. *Mov Disord* 2002 Jul;17(4):638-44.
- 15- Jedynak CP, Diarra E, Verny M. [Tremor in the elderly]. *Psychol Neuropsychiatr Vieil* 2008 Sep;6(3):199-208.
- 16- Sur H, Ilhan S, Erdogan H, Ozturk E, Tasdemir M, Boru UT. Prevalence of essential tremor: a door-to-door survey in Sile, Istanbul, Turkey. *Parkinsonism Relat Disord* 2009 Feb;15(2):101-4.
- 17- Quattrone A, Cerasa A, Messina D, Nicoletti G, Hagberg GE, Lemieux L, et al. Essential head tremor is associated with cerebellar vermis atrophy: a volumetric and voxel-based morphometry MR imaging study. *AJNR Am J Neuroradiol* 2008 Oct;29(9):1692-7.
- 18- Inashkina I, Radovica I, Smeltere L, Vitols E, Jankevics E. Case-control study of patients with essential tremor in Latvia. *Eur J Neurol* 2008 Sep;15(9):988-90.
- 19- Louis ED. Environmental epidemiology of essential tremor. *Neuroepidemiology* 2008;31(3):139-49.
- 20- Lyons KE, Pahwa R. Pharmacotherapy of essential tremor : an overview of existing and upcoming agents. *CNS Drugs* 2008;22(12):1037-45.
- 21- Koller WC, Hristova A, Brin M. Pharmacologic treatment of essential tremor. *Neurology* 2000;54(11 Suppl 4):S30-S38.
- 22- Zaliyeva ZA, Latypova GR. [Topiramate in the treatment of essential tremor]. *Zh Nevrol Psikhiatr Im S S Korsakova* 2008;108(11):39-42.
- 23- Masur H, Papke K, Althoff S, Oberwittler C. Scales and scores in Neurology. 2nd ed. Stuttgart: Thieme; 2004.
- 24- Chadwick D. Gabapentin. *Lancet* 1994;343:89-91.
- 25- Handforth A, Treiman DM. Efficacy and tolerance of long term,high dose gabapentin:additional observation. *Epilepsia* 1994;35:1032-7.
- 26- Louis ED. Clinical practice. Essential tremor. *N Engl J Med* 2001 Sep;345(12):887-91.
- 27- Louis ED. Essential tremor. *Lancet Neurol* 2005 Feb;4(2):100-10.
- 28- Deuschl G, Elble RJ. The pathophysiology of essential tremor. *Neurology* 2000;54(11 Suppl 4):S14-S20.
- 29- Ondo W, Hunter C, Vuong KD, Schwartz K, Jankovic J. gabapentin for essential tremor : amultiple -dose , double blind,placebo-controlled trial. *Mov Disord* 2000;15(4):678-82.
- 30- Gironell A, Kulisevsky J, Barbanj M, Lopez-Villegas D, Hernandez G, Pascual-sedano B. A Randomized placebo-controlled comparative trial of gabapentin and propranolol in essential tremor. *Arch Neurol* 1999;56(4):475-80.

بررسی مقایسه‌ای تاثیر پروپرانولول با گاباپنتین در بیماران مبتلا به لرزش فامیلیال

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چکیده

زمینه و هدف: لرزش فامیلیال شایعترین اختلال حرکتی در جهان است. پاتوفیزیولوژی آن ناشناخته است و هیچ اختلال نورولوژیک دیگری همراه این بیماری دیده نمی‌شود. لرزش در این بیماری با فرکانس پایین بوده و شیوع آن بین ۳ تا ۵ درصد می‌باشد.

روش بررسی: این مطالعه بین سالهای ۱۳۸۴-۱۳۸۷ در درمانگاه نورولوژی بیمارستان شهید مصطفی خمینی بر روی ۱۲۰ بیمار مبتلا به لرزش فامیلیال بصورت آینده نگر انجام شده است. بیماران در دو گروه بصورت تصادفی قرار گرفته‌اند. ۵۹ نفر از بیماران تحت درمان با پروپرانولول به میزان ۴۰ میلی گرم ۳ بار در روز به مدت ۳ هفته قرار داشته‌اند و ۶۱ بیمار نیز به همین مدت تحت درمان با گاباپنتین به میزان ۳۰۰ میلی گرم ۳ بار در روز قرار داشته‌اند. جهت ارزیابی بیماران از مقیاس (TRS) Fahn-Tolosa-Marin که یک مقیاس عددی استاندارد (۰-۸۸) برای سنجش لرزش می‌باشد استفاده شده است.

یافته‌ها: در نهایت ۱۲۰ بیمار مطالعه را به پایان رساندند از این تعداد (۴۷٪) ۵۶ نفر مونث و (۵۳٪) ۶۴ نفر مذکر بودند میانگین سنی بیماران (۲۶-۵۹) ۴۳٫۹ سال بوده است. در ابتدای درمان مقیاس TRS اندازه گیری شده در گروه تحت درمان با پروپرانولول 38.6 ± 1 و در گروه تحت درمان با گاباپنتین 39.1 ± 1 بوده است در انتهای درمان این اعداد به 28.4 ± 1 و 25.6 ± 1 برتیب در گروه تحت درمان با پروپرانولول و گاباپنتین تغییر یافته است. مطالعات آماری انجام شده با نرم افزار SPSS تفاوت معنی دار در هر دو گروه در مقایسه بین شروع و پایان مطالعه را نشان می‌دهد. ($P < 0.0005$)

نتیجه گیری: گاباپنتین به عنوان یک داروی موثر در درمان لرزش فامیلیال بوده و میزان اثربخشی آن حداقل با پروپرانولول برابری می‌کند. با توجه به عوارض کمتر این دارو و نداشتن عوارض قلبی عروقی و تنفسی و تحمل بهتر آن در این موارد بخصوص در افراد مسن می‌تواند در این موارد بعنوان داروی انتخابی نیز مطرح گردد.

واژگان کلیدی: لرزش، گاباپنتین، پروپرانولول، اختلالات حرکتی