Response to prophylactic treatment in migrainures with epileptic discharges in comparism to migrainures with out epileptic discharges.

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Summary:

Background: migraine is a neurovascular disorder some times associated with epilepsy, in this study we go further in this association and detect subclinical focal epileptic discharges in migrainures. Aim: to study the difference in response to certain prophylactic antimigraine drugs (both propranolol and amytriptylline) between migrainures with focal epileptic discharges and migrainures with out focal epileptic discharges. Patients and methods: we studied 617 patients with migraine with frequent attaches (more than two per week) of ages between 15 and 63 years old, we divided them in to those with focal epileptic discharges and those with out focal epileptic discharges according to the EEG results, we started treatment for them using a fixed regimen (propranolol 20 mg twice daily and amytriptylline 10-25 mg once daily) and follow their response to treatment for three months. Results: we found that 62.45% of those with out epileptic discharges responded to treatment in comparism to only 35.83% of those with epileptic discharges. Conclusion: migraineurs with focal epileptic discharges will be less responder to prophylactic antimigraine drugs (propranolol and / or amytriptylline) than those with out focal epileptic discharges.

Key words: Migraine, epilepsy, Response to prophylactic antimigraine drugs, migralepsy.

Introduction:
Migraine is a disorder of neurovascular origin and it is wide spread in the population with different degrees of severity and frequency\(^7\).

It is well known that migraine and epilepsy share many features and they may associated together in the same person more than can be accepted as happen by chance but whether their association are causally related or have same pathophysiological and or genetic factors is still uncertain\(^8\).

In this study we tried to go further in this association and detect the subclinical focal epileptic discharges in migrainures\(^{13} \& \ 14\) and study the effect of this findings on their response to some of the standard prophylactic anti migraine drugs; excluding drugs that have antiepileptic activity as sodium valproat and topiramat\(^2 \& \ 4\).

**Subjects and methods:**

1- we studied 617 migraine patients (classical or common types only) diagnosed according to international headache society criteria of migraine\(^9\) and having frequent attaches of migraine (two or more than two attacks each week for the last two months) at out patients clinic of al Basra general hospital from April 2007 to October 2010.

2- Range of the age was from 15 – 63 years with average 34 years.

3- We excluded all patients with epilepsy or were having epilepsy in the past.

4- We excluded all patients that have prolonged migraine attacks (attack that continue for more than 3 days without real time of remission) because of the difficulty in the assessment of the response to treatment.

5- We sent all patients to brain imaging studies (CT or MRI) and we included only those with normal results.
6- We sent all patients for EEG examination using EEG machine micromed 2002 in Al Sader teaching hospital under the supervision and assessment of one neurophysiologist using standard bipolar 10-20 system 21 channels.

7- According to the EEG results we divided migraine patients in to two groups:

A. migraineurs with focal epileptic discharges.

B. migraineurs with out focal epileptic discharges.

8- We started treatment for both groups of patients using a fixed regimen of standard anti migraine drugs: propranolol 20mg twice daily and amitryptiline 10 -25 mg daily at night (dose is differ according to the tolerance of the patient).

9- We follow up our patients for three months.

10- All patients that did not tolerate the treatment, were non compliant to treatment or stopped follow up had been excluded from the study.

11- Patients that experienced reduction in the attaches rate by 75% or more from the pretreatment state (comparism between number of attaches per month between pretreatment state and during treatment state) and persist in the same state through the period of treatment (at least one month during the time of the study) considered responder to treatment.

12- Patients that did not experience reduction in the attaches rate by 75% or more from the pretreatment state (regardless the duration and the severity of the attaches) in the first two months of treatment considered as not responder to treatment.

13- We allowed patients to use analgesic drugs to relieve pain during the time of the study but on need only.
14- We considered the bouts of headache that occur in the same day as one attach of migraine (because we allowed the patients to use analgesic drugs during the attach).

Results:

We included in our study 370 patients forming 59.97% of the total number of patients that were at the beginning of the study (617 patients). Two hundred forty seven patients (247) had been excluded from the study.

Table (1) shows the number and percentage of patients that included and excluded from the study and those with focal epileptic discharges.

<table>
<thead>
<tr>
<th>Total No. of patients included</th>
<th>No.Included in the study</th>
<th>%</th>
<th>No.Excluded from the study</th>
<th>%</th>
<th>No. of patients with focal epileptic discharges</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>617</td>
<td>370</td>
<td>59.96</td>
<td>247</td>
<td>40.63</td>
<td>183</td>
<td>29.65</td>
</tr>
</tbody>
</table>

This table shows that 59.96% of our sample of patients had been included in the study and 40.63 of patients had been excluded from the study, and 37.92% of our patients has positive epileptic discharges.
Table (2): shows the number and percentage of patients that did response to treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Gender</th>
<th>Responding</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Group A</td>
<td>173</td>
<td>M</td>
<td>72</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>101</td>
<td>41</td>
</tr>
<tr>
<td>Group B</td>
<td>197</td>
<td>M</td>
<td>85</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>112</td>
<td>79</td>
</tr>
</tbody>
</table>

This table shows that 35.83% of patients in group A responded to the treatment and 62.43% of group B responded to the treatment.

Table (3): shows the number and percentage of patients that did not respond to treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Gender</th>
<th>Not responding</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Group A</td>
<td>173</td>
<td>M</td>
<td>72</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>101</td>
<td>60</td>
</tr>
<tr>
<td>Group B</td>
<td>197</td>
<td>M</td>
<td>85</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>112</td>
<td>33</td>
</tr>
</tbody>
</table>
The table above (table 3) shows that 64.16% of group A and 37.56% of group B did not respond to the treatment.

**Discussion:**

There was a significant difference in the response to treatment between both groups of patients.

In group B [62.43%] of patients respond to treatment in comparison to only [35.83%] in group A and this difference comprise both sexes and because the two groups had been matched regarding age, gender and absence of associated diseases so this difference can be attributed to the presence of focal epileptic discharges in group A and absence of them in group B.

In general female patients showed better response to treatment than male patients in both groups which may be attributed to the antidepressant effect of the amytriptylline and/or the anxiolytic effect of propranolol or to real better response of female patients to the prophylactic treatment.

[40.63%] of our patients had been excluded from the study, [55%] of them because of development of side effects and 45% of them because of poor compliance to treatment or stopped treatment.

This study showed that [29.65%] of migraineurs are having focal epileptic discharges which is much higher than that of normal people (3% only). (16)

and this finding strength the idea of possible association between migraine and epilepsy.

It is important to note that only 10 patients of group A had been excluded from the study (forming 5.46% from total number of patients in this group) in comparism to 237 patients from group B (forming 54.60% from total number of
patients in this group) and this might be attributed to the way of the explanation that we did it to the patients with focal epileptic discharges (we told them that they may have a special type of migraine and they need a good follow up to see the response of the treatment).

**Conclusion:** migraineurs with focal epileptic discharges will be less responder to prophylactic antimigraine drugs (propranolol and / or amitriptylline) than those with out focal epileptic discharges and so better to choose another type of therapy to them as topiramate or sodium valproat. EEG may play an important role in the management of migraine. And although migraine in general has common clinical manifestations but it may has different underling pathophysiological mechanisms.

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المقدمة: الشقيقة من الأمراض الشائعة في العالم ويعتقد إنها اضطراب عصبي وعائى في أن واحد، كما يعتقد أن لها ارتباطًا قوياً بمرض الصرع، وفي هذه الدراسة حاولنا أن ندرس أهمية وجود الفعاليات الصرفية عند مرضى الشقيقة. الهدف: دراسة احتمالية الفرق في الاستجابة للأدوية الوقائية من مرضى الشقيقة بين مرضى الشقيقة الذين لديهم فعاليات صرعة بورية والذين ليس لديهم فعاليات صرعة بورية. طريقة إجراء البحث: 616 مريض بالشقيقة تم دراستهم في هذا البحث تراوحت أعمارهم بين 5 سنين و63 سنين وقد تم إجراء تخطيط الدماغ لهم وقسموا إلى قسمين: أول عنده فعاليات صرعة بورية والثاني ليس عنده فعاليات صرعة بورية. ثم أعطوا جرع محدد من الأدوية الوقائية من الشقيقة (بورترول) حسب 20 ملغ مرتان يومياً وأميبيريتيلين حسب 10-15 ملغ مرة واحدة يومياً) وتتم متابعة حالاتهم لمدة ثلاثة أشهر. النتائج: وجدنا 45.62% من المرضى الذين ليس لديهم فعاليات صرعة بورية قد استجابوا للعلاج مقارنة بنسبة 83.35% فقط قد استجابوا للعلاج من المرضى الذين لديهم فعاليات صرعة بورية.

المستنتاج: مرضى الشقيقة الذين لديهم فعاليات صرعة أقل استجابة للأدوية الوقائية من الشقيقة مقارنة بالمرضى الذين ليس لديهم فعاليات صرعة.

مفتاح البحث: الشقيقة، الصرع، الاستجابة للأدوية الوقائية من الشقيقة، الشقيقة، الصرفية.