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Relations between pharmacokinetic parameters of carbamazepine and therapeutic response in bipolar patients

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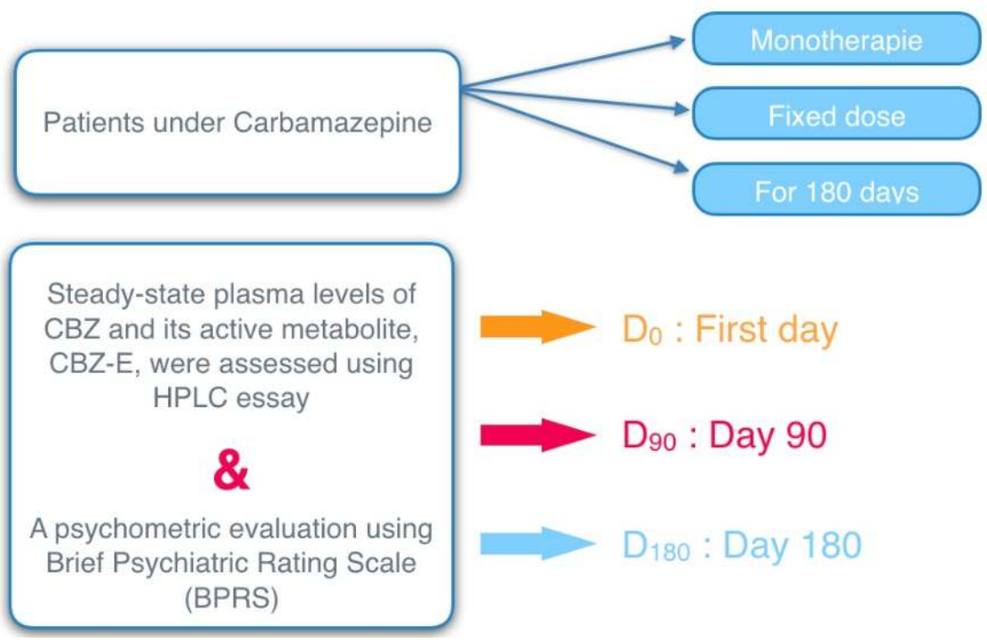
Background & Objective

- Carbamazepine (CBZ), an established therapeutic option in the treatment of bipolar disorder since the early 1970s [1,2], has become less and less prescribed in recent years, mainly because of the high frequency of relapses under this medication, and the difficulties of controlling its efficacy through standardized values of carbamazepine plasma levels.
- Efficient CBZ doses and efficient CBZ plasma levels were quite variable from one patient to an other, making it so difficult to optimize therapeutic response to CBZ using CBZ plasma levels only.
- This study aimed to address the relation between therapeutic response to CBZ in bipolar patients and pharmacokinetic parameters of this medication including CBZ plasma levels, 10,11-epoxide-carbamazepine levels (CBZ-E) and the carbamazepine metabolic index.

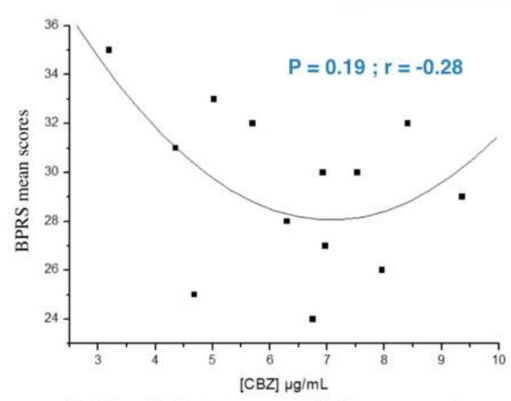
Methods

- A prospective study was conducted. It included all euthymic bipolar patients who were exclusively treated with carbamazepine at a dosage allowing clinical stabilization over a minimum period of one month, due to carbamazepine self-induction properties.

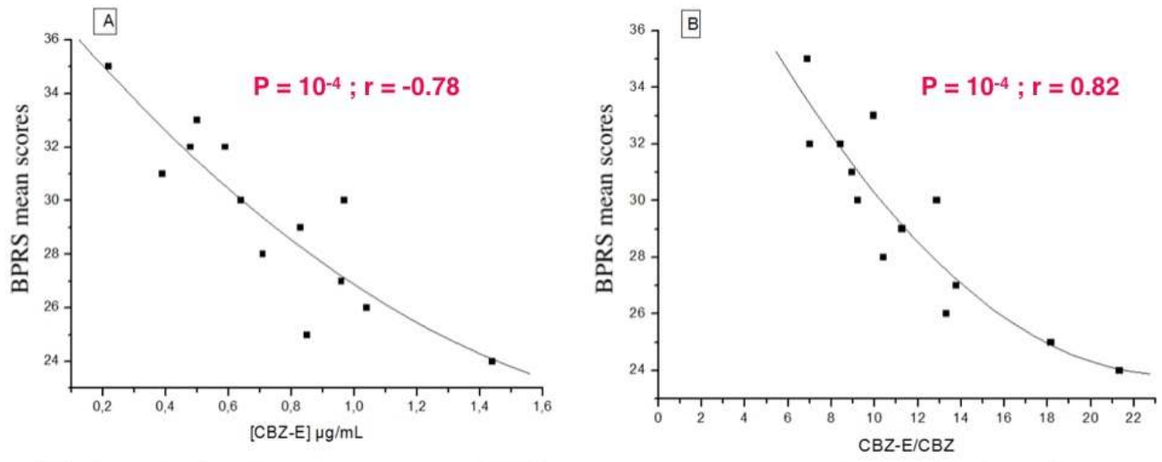


Results & Discussion

- Thirteen patients, three women and 10 men, with bipolar I disorder were recruited, with a mean age of 43.85 ± 10.73 years.
- **Table 1** illustrates CBZ plasma levels, CBZ-E plasma levels, the CBZ metabolic index and BPRS scores in the recruited bipolar I patients.
- Our study showed that optimum therapeutic response was observed among bipolar patients who had a plasma CBZ level of 7 µg/ml and a plasma metabolite level of 1.44 µg/ml, simultaneously.
- Our findings are consistent with those showing no significant role of CBZ plasma levels in the prediction of therapeutic efficacy in bipolar patients [3,4]. Both CBZ and CBZ-E plasma levels should be fixed to achieve an optimum therapeutic response in bipolar I patients, taking into consideration the carbamazepine metabolic index.
- In order to reach the pharmacokinetic conditions required for optimum efficacy, inhibitor drugs of epoxide hydrolase, such as valproic acid [5], or inducer drugs of epoxide hydrolase, such as phenobarbital [6], might be co-administered with CBZ in order to adapt the plasma level of CBZ-E.



Relationship between mean BPRS scores and carbamazepine (CBZ) plasma levels



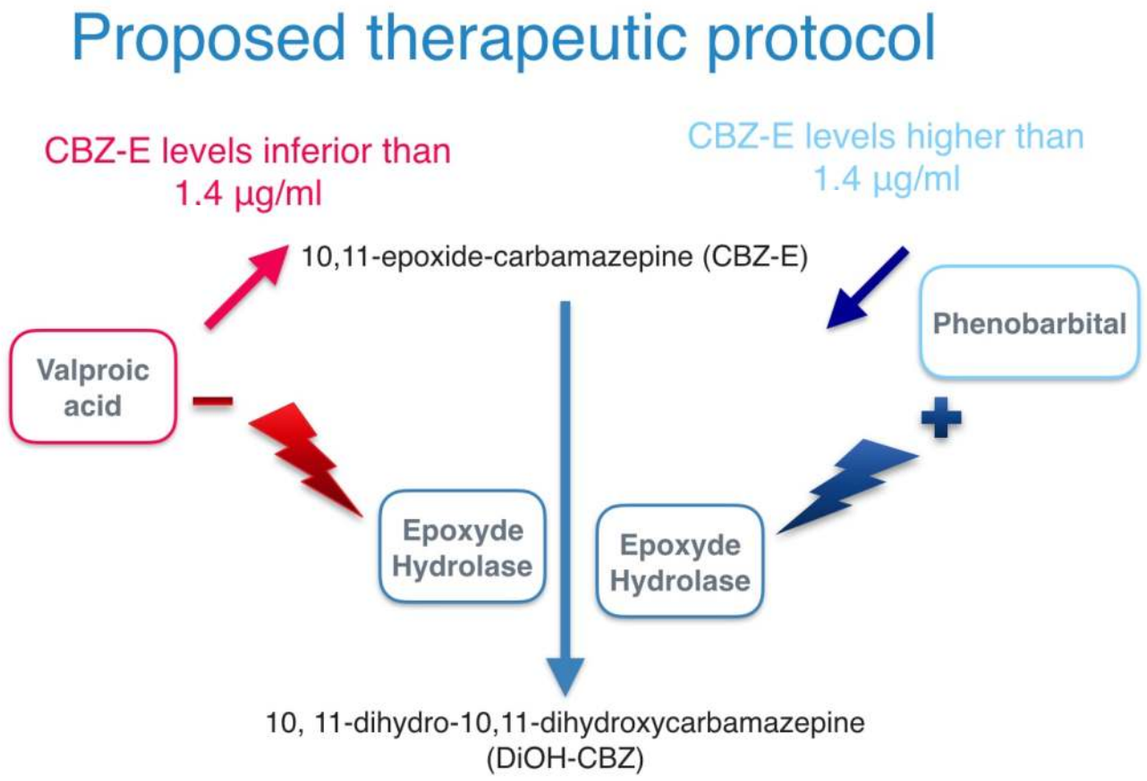
(A) Correlation between mean BPRS scores and mean plasma levels of 10,11-epoxide-carbamazepine (CBZ-E);

(B) Correlation between mean BPRS scores and carbamazepine metabolic index

Table 1: CBZ plasma levels, CBZ-E plasma levels, the CBZ metabolic index and BPRS scores in the recruited bipolar I patients (n=13)

Patient	Mean levels of CBZp (µg/ml)	Mean levels of CBZ-Ep (µg/ml)	CBZ-E/CBZ (%)	BPRS mean scores
1	6.30	0.71	11.269	28
2	8.41	0.59	7.015	32
3	4.35	0.39	8.965	31
4	5.70	0.48	8.421	32
5	5.02	0.50	9.954	33
6	3.19	0.22	6.896	35
7	4.68	0.85	18.162	25
8	6.75	1.44	21.333	24
9	6.93	0.64	9.235	30
10	7.80	1.04	13.333	26
11	7.36	0.83	11.277	30
12	7.53	0.97	12.881	30
13	6.97	0.96	13.773	27

CBZp: carbamazepine plasma levels; **CBZ-Ep:** plasma levels of 10,11-epoxide-carbamazepine; **CBZ-E/CBZ:** carbamazepine metabolic index; **BPRS:** Brief Psychiatric Rating Scale



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