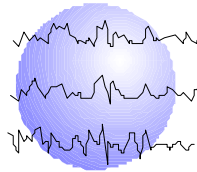


**EFFICACY OF VALPROATE AND LAMOTRIGINE
THERAPY IN PATIENTS WITH MEDICALLY
INTRACTABLE EPILEPSY:
AN “INTENT TO TREAT” RETROSPECTIVE**

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Please consider this information to be preliminary findings.

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REVISED ABSTRACT

RATIONALE: We have previously reported the combination of valproate and lamotrigine to be highly effective as measured by improved seizure control after initiation of the therapeutic regimen. This study applies “intent to treat” methodology to validate our previous observations.

METHODS: All 41 adult and pediatric patients, ages 7-63 (mean = 38.2), with partial seizures who were initiated on valproate and lamotrigine combination therapy at the Minnesota Epilepsy Group Clinic between September 1994 and January 2000 were included in the study. On average, these patients failed 2.9 medications (range 1-5) prior to initiation. For purposes of this study, no other antiepileptic medications were administered while these patients were on valproate and lamotrigine combination therapy.

Average length on valproate/lamotrigine therapy lasted 63.8 weeks (range 12-285). Mean blood level for valproate was 63.0 mcg/ml; mean blood level for lamotrigine was 12.7 mcg/ml. Mean dosages of valproate and lamotrigine were 990.9 mg/day and 321.9 mg/day, respectively.

RESULTS: Fourteen patients (34.1%) were seizure free as a result of the medication regimen. An additional 13 patients (31.7%), although not seizure free, had a seizure reduction of 50% or greater. Combined, 27 patients (65.8%) had a seizure reduction of 50% or greater. Of these 41 patients, 29 successfully remained on the valproate/lamotrigine therapy. For these 29 patients, seizure frequency was reduced from an average of 10.3 seizures per month to an average of 1.6 seizures per month ($p < .05$). Three of the 41 patients had side effects necessitating discontinuation (ataxia, double vision, tremors, and/or shakiness). None had a rash. Nine of the 41 patients discontinued due to lack of perceived efficacy.

CONCLUSION: Valproate and lamotrigine in combination therapy effected a significant reduction in seizures, including 34.1% seizure free and, overall, 65.8% with a seizure reduction of 50% or greater. It is, therefore, a highly effective combination therapy.

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INTRODUCTION

Several new antiepileptic medications have been released in the United States since 1993 when felbamate was the first in a series that has since included gabapentin, lamotrigine (LTG), levetiracetam, oxcarbazepine, topiramate, and zonegran. There has been considerable interest in how these newer medications work with each other as well as with the more established medications. This study assesses the efficacy in an “Intent To Treat Study” of LTG, in combination with valproic acid (VPA), both of which are broad-spectrum antiepileptic drugs for patients with medically refractory epilepsy. Interest in this combination is underscored by the previous work of Brodie, Yuen and the 105 Study Group¹ who demonstrated that when comparing combinations of LTG with carbamazepine, with phenytoin, and with VPA, the lamotrigine/valproate group dramatically improved for partial and tonic-clonic seizure. A more recent study by Gates², et al., reported enhanced efficacy of VPA in combination with LTG.

METHODS

All 41 adult and pediatric patients, ages 7-63 (mean = 38.2), with partial seizures who were initiated on valproate and lamotrigine combination therapy at the Minnesota Epilepsy Group Clinic between September 1994 and January 2000 were included in the study. On average, these patients failed 2.9 medications (range 1-5) prior to initiation. For purposes of this study, no other antiepileptic medications were administered while these patients were on valproate and lamotrigine combination therapy.

Average length on valproate/lamotrigine therapy lasted 63.8 weeks (range 12-285). Mean blood level for valproate was 63.0 mcg/ml; mean blood level for lamotrigine was 12.7 mcg/ml. Mean dosages of valproate and lamotrigine were 990.9 mg/day and 321.9 mg/day, respectively.

CONCLUSIONS

Valproate and lamotrigine in combination therapy effected a significant reduction in seizures, including 34.1% seizure free and, overall, 65.8% with a seizure reduction of 50% or greater. It is, therefore, a highly effective combination therapy.

REFERENCES

1. Brodie MJ, Yuen AWC, 105 Study Group. Lamotrigine substitution study: evidence for synergism with sodium valproate? *Epilepsy Research*, 1997;26:423-432.
2. Gates JR, Mulligan KA, Penovich PE, Moriarty GL. Efficacy of valproate and lamotrigine therapy in patients with medically intractable epilepsy. *Epilepsia*, (40)7:143, 1999.

DEMOGRAPHICS AND METHODS

Pt #	Age	Total # meds taken in yr before VPA/LTG initiation	Total Szs/mo prior VPA/LTG	# wks on trial	Cur. VPA Dosage	Cur. VPA Level	Cur. LTG Dosage	Cur. LTG Level	Cur. Szs/mo	Comments
1	27	3		285	375	13.0	650	19.7	0.00	Seizure free
2	52	4	4.16	238	750	49.5	350	14.6	0.00	Seizure free
3	51	3	41.00	119	1750	95.3	250	18.0	5.00	> 50% reduction in seizures
4	40	5	4.50	68	2000	105.0	300	--	0.00	Seizure free
5	28	2	8.00	82	1000	92.4	275	14.8	0.00	Seizure free
6	43	4	10.80	45	750	59.2	400	15.8	3.70	> 50% reduction in seizures
7	41	3	3.00	248	750	46.4	600	22.5	0.00	Seizure free
8	22	4	0.25	44	750	64.0	250	12.8	0.00	Seizure free
9	61	2	0.92	34	500	41.7	200	11.3	0.17	> 50% reduction in seizures
10	23	2	14.17	27	625	64.0	225	11.2	0.00	Seizure free
11	35	2	1.08	44	1250	81.3	400	9.1	0.00	Seizure free
12	20	4	3.00	20	1500	73.1	350	20.5	12.00	Increase in seizures
13	63	1	1.50	56	250	36.2	225	10.0	2.00	Increase in seizures
14	32	4	15.59	19	750	82.4	300	16.0	0.70	> 50% reduction in seizures
15	33	2	1.00	70	750	44.7	300	6.1	0.00	Seizure free
16	44	3	15.00	78	500	37.5	300	6.9	7.00	> 50% reduction in seizures
17	22	2	136.88	99	1250	99.0	650	21.0	0.50	> 50% reduction in seizures
18	40	2	0.25	12	500	50.0	600	20.4	0.00	Sz free (essentially no change)
19	28	3	0.00	54	1500	50.0	250	7.8	0.00	No change
20	28	3	1.50	78	2000	--	200	--	0.00	Seizure free
21	40	4	1.42	21	1500	96.6	200	8.6	1.29	Slight decrease in seizures
22	55	4	15.00	23	1500	93.3	300	10.6	2.50	> 50% reduction in seizures
23	22	3	2.50	42	375	24.9	75	2.5	1.00	> 50% reduction in seizures
24	20	2	1.30	30	750	19.4	300	4.3	2.00	Increase in seizures
25	40	2	3.00	60	1125	84.0	500	15.9	5.20	Increase in seizures
26	38	1	5.00	88	1500	66.8	250	7.5	1.00	> 50% reduction in seizures
27	54	2	0.20	16	1000	68.1	--	12.3	0.00	Seizure free
28	49	2	2.00	32	1500	86.1	350	9.2	1.00	> 50% reduction in seizures
29	16	4	1.30	68	500	84.7	150	9.2	.025	> 50% reduction in seizures
30	40	4	6.00	192	1750	66.4	300	10.0	1.00	> 50% reduction in seizures
31	51	3	0.30	26	750	63.2	200	14.3	0.75	Increase in seizures
32	47	4	4.00	19	1500	82.3	350	14.1	4.00	No change
33	61	3	4.00	26	500	46.2	400	19.2	0.00	Seizure free
34	20	3	39.20	15	1000	44.7	600	4.6	113.00	Increase in seizures
35	7	2	12.00	15	375	70.2	150	10.9	28.00	Increase in seizures
36	53	1	1.00	17	1000	32.2	25	2.1	0.25	> 50% reduction in seizures
37	57	3	2.20	118	1000	38.9	200	9.2	4.50	Increase in seizures
38	44	2	0.25	34	1000	--	150	--	2.60	Increase in seizures
39	55	4	1.90	17	750	80.9	400	24.8	4.20	Increase in seizures
40	35	4	1.80	16	1250	--	500	--	3.00	Increase in seizures
41	28	3	6.00	22	500	58.8	400	22.3	0.00	Seizure free

Figure 1

**AVERAGE MONTHLY SEIZURE FREQUENCIES
BEFORE AND DURING VPA/LTG THERAPY**

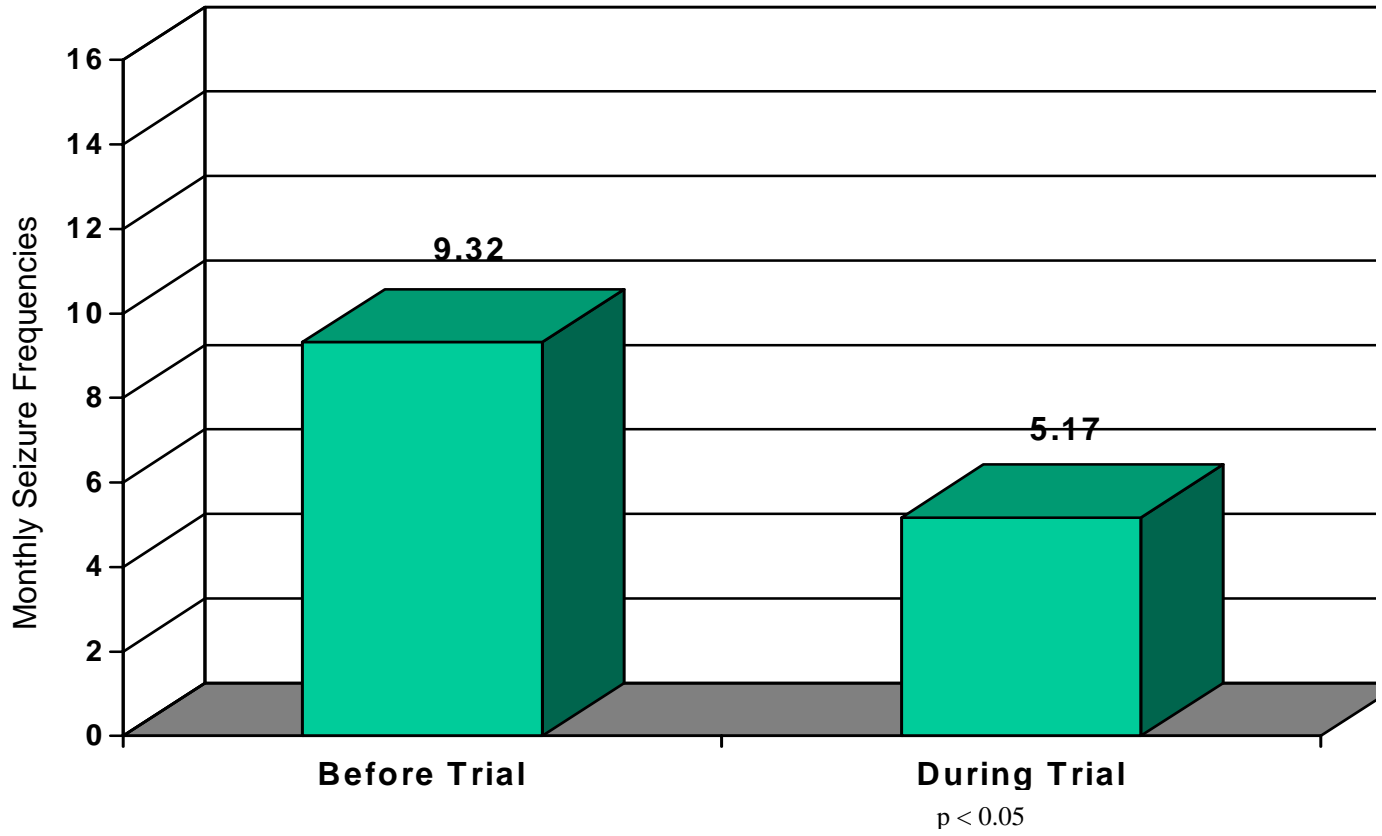


Figure 2

**CHANGE IN SEIZURE FREQUENCY
DURING VPA/LTG THERAPY**

- Seizure Free
- 50% or More Reduction in SF
- Slight Reduction
- No Change

