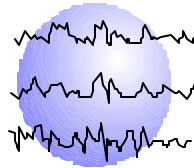


CLINICAL EXPERIENCE WITH FELBAMATE IN ADULTS WITH MEDICALLY INTRACTABLE EPILEPSY

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REVISED ABSTRACT

RATIONALE

Felbamate (FBM) use had dramatically declined since 1994 following reports of FBM induced aplastic anemia and liver failure. FBM prescribing in epilepsy centers has continued due to efficacy in intractable epilepsy patients. Limited published data is available on the clinical experience of FBM use since 1994. This study reflects the experience of the Minnesota Epilepsy Group, P.A. with FBM use in adults with intractable epilepsy.

METHODS

One hundred seventy-two patients (age 16 and older) treated with FBM at Minnesota Epilepsy Group, P.A. were identified. Their records were reviewed. Data were tabulated and analyzed to include patient demographics, efficacy and tolerability. Paired t tests were calculated to compare mean seizure frequency prior to FBM use and at FBM optimization. The responder rate was calculated.

RESULTS

Of the 172 patients reviewed, 82 were female and 90 were male. Mean age at time of starting FBM was 32 years. The mean number of past AEDs failed was 5.5. Mean baseline frequency per seizure type: 7.9 GTCs/month, 35 CPS/month, 27.3 SPS/month, 102.1 tonic seizures/month, 121.2 myoclonic seizures/month and 20.4 atonic seizures/month. Duration of FBM therapy ranged from 1 to 120 months (mean: 39.5) with an average FBM maximum dose 3,769.3 mg/day. The average FBM level was 73mg/dl. Responder rate (³50% reduction in baseline seizure frequency) was 66% with 49% (85/172) having >75% reduction in baseline monthly seizures. The average reduction in baseline frequency per seizure type: GTCs (n=81), 52.3% (p<0.001); CPS (n=115), 24.1% (p=0.007); SPS (n=37), 29.4% (p<0.05); myoclonic seizures (n=18), 63.1% (p=0.03). The average reduction in tonic seizures (n=27), 49.2% (ns) and in atonic seizures (n=8), 63.1% (ns). Thirty-four patients (19.8%) became seizure free. One-hundred two (102) (59.3%) of these patients remain on FBM. FBM was discontinued in 40% of patients. Reasons for discontinuation included intolerable side effects, family/patient requested discontinuation, no perceived benefit in seizure reduction, anticipating pregnancy, and the announcement of the risk of aplastic anemia. Side effects documented included insomnia, behavioral changes, decreased appetite and headache. One patient developed aplastic anemia. No hepatic complications were documented.

CONCLUSION

In adults with intractable seizures including GTCs, CPS, SPS and myoclonic seizures, FBM is significantly effective in reducing mean baseline seizure frequency with some patients becoming seizure free. In this practice it has been tolerated with few discontinuations related to side effects. FBM remains an important treatment consideration in patients with intractable epilepsy.

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METHODS

One hundred seventy-two adult patients (age 16 years and older) prescribed FBM since 1993 were identified. Their records were reviewed retrospectively. Data were tabulated and analyzed to include patient demographics, efficacy and tolerability. Paired t-tests were calculated to compare mean seizure frequency prior to FBM use and at FBM optimization. The responder rate was calculated. Adverse events while on FBM were identified.

RESULTS

Of the 172 patients reviewed, 82 were female and 90 were male. Mean age at time of starting FBM was 32 years. The mean number of past AEDs failed was 5.5. Mean baseline frequency per seizure type: 7.9 GTCs/month, 35 CPS/month, 27.3 SPS/month, 102.1 tonic seizures/month, 121.2 myoclonic seizures/month and 20.4 atonic seizures/month. Duration of FBM therapy ranged from 1 to 120 months (mean: 39.5) with an average FBM maximum dose 3,769.3 mg/day. The average FBM level was 73mg/dl. Responder rate (\geq 50% reduction in baseline seizure frequency) was 66% with 49% (85/172) having $>$ 75% reduction in baseline monthly seizures. The average reduction in baseline frequency per seizure type: GTCs (n=81), 52.3% (p<0.001); CPS (n=115), 24.1% (p=0.007); SPS (n=37), 29.4% (p<0.05); myoclonic seizures (n=18), 63.1% (p=0.03). The average reduction in tonic seizures (n=27), 49.2% (ns) and in atonic seizures (n=8), 63.1% (ns). Thirty-four patients (19.8%) became seizure free. 102 (59.3%) of these patients remain on FBM. FBM was discontinued in 40% of patients. Reasons for discontinuation included intolerable side effects, family/patient requested discontinuation, no perceived benefit in seizure reduction, anticipating pregnancy, and the announcement of the risk of aplastic anemia. Side effects documented included insomnia, behavioral changes, decreased appetite and headache. One patient developed aplastic anemia. No hepatic complications were documented.

CONCLUSIONS

- FBM is significantly effective in reducing seizure frequency in GTC, myoclonic, CPS, and SPS.
- 20% patients became seizure free.
- 1 patient developed aplastic anemia in the entire population treated with FBM over a 10 year period. No patient developed hepatic failure. To ensure safety, an ANA is obtained prior to prescribing FBM. Complete blood count (CBC), platelets, and liver function tests are obtained at initiation of treatment and at regular intervals thereafter (Pellock, 1999).
- FBM is a broad spectrum anti-epileptic medication that remains an important treatment consideration in patients with intractable epilepsy (Li, et al, 1996).

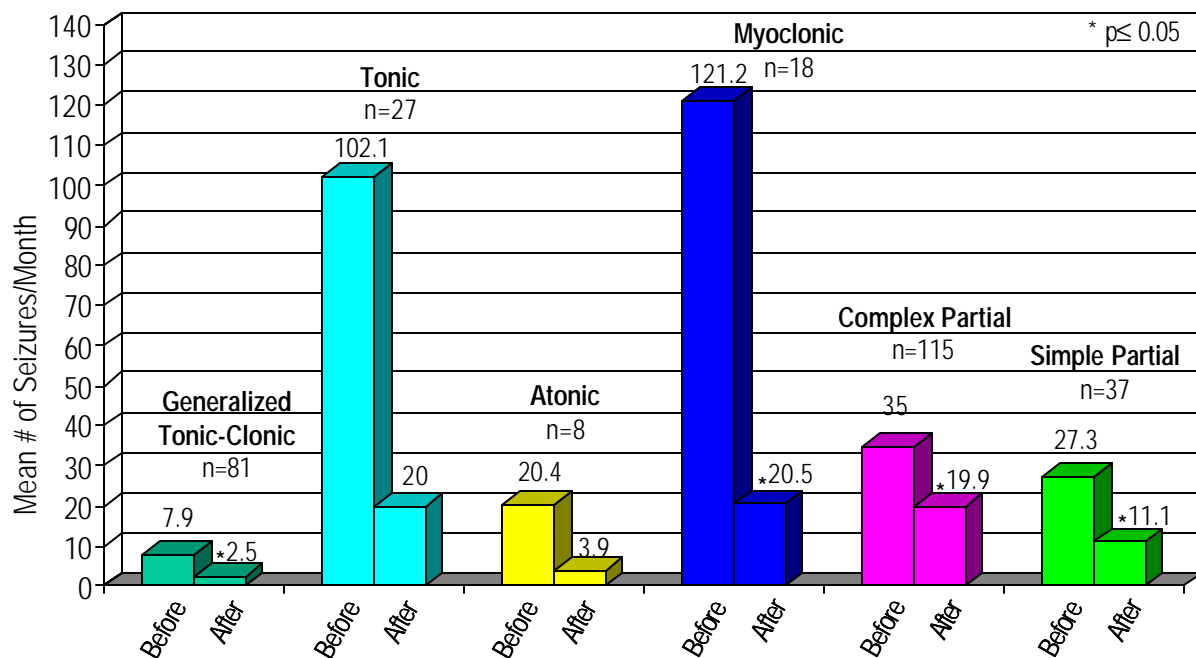
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- LM Li, L Nashef, J Moriarty, JS Duncan, and JW Sander. Felbamate as add-on therapy. *Eur Neurology*, January 1, 1996; 36(3): 146-8.

Figure 1 **Demographic Information**

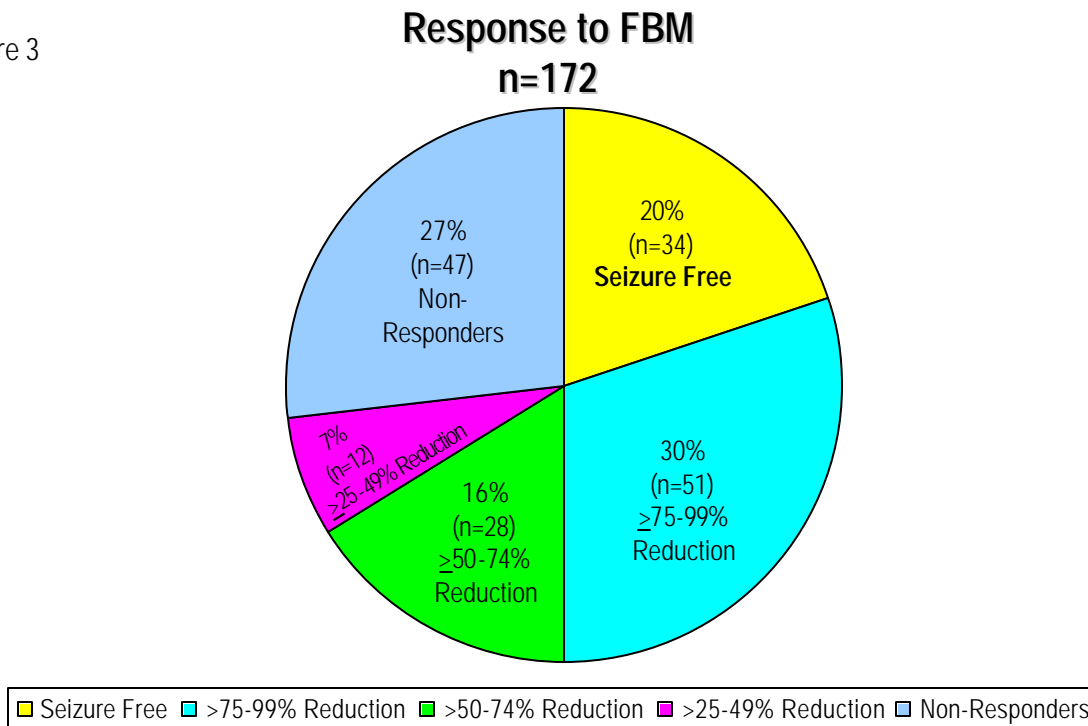
Number of Patients	172
Male/Female	90/82
Mean Age at Start of FBM (SD)	32 yrs (13.1 yrs)
Mean Weight at Start of FBM (SD)	75.7 kg (21.7kg)
Mean Weight with FBM Tx (SD)	73.0 kg (20.0 kg)
Mean # Failed AED's (SD)	5.6 (2.8)
Concomitant # AED's (SD)	1.6 (2.3)
Mean Maximum Dose of FBM (SD)	3,769.3 mg/day (1,520.2 mg/day)
Mean FBM Level (SD)	73.1 ug/ml (26.7 ug/ml)
Duration of FBM Tx (SD)	39.5 mos (36.9 mos)

Figure 2 **Mean Seizure Frequency/ Month According to Seizure Type**



There was a statistically significant reduction in seizure frequency/month in generalized tonic-clonic (GTC), myoclonic, complex partial seizures (CPS) and simple partial seizures (SPS). A statistically significant reduction was not demonstrated in tonic or atonic seizures.

Figure 3



Of those who responded, 34 patients were seizure free, 51 patients achieved a $\geq 75\%$ -99% reduction in seizure frequency while 28 patients experienced a $\geq 50\%$ -74% seizure reduction. Twelve (12) patients decreased seizure frequency $\geq 25\%$ -49%. Forty-seven (47) patients failed to demonstrate a reduction ($>25\%$) in seizure frequency.

Figure 4

Adverse Events on FBM

	# of Patients	%
Insomnia	61	35.5
Behavioral Changes	30	17.4
Decreased Appetite	27	15.7
Headache	18	10.5
Abdominal Pain	12	7.0
Fatigue	12	7.0
Nausea	10	5.8
Blurred Vision	5	2.9
Vomiting	3	1.7
Constipation	2	1.2
Rash	1	0.6
Aplastic Anemia	1	0.6

One patient first developed leukopenia while taking methsuximide (MSM), phenytoin (PHT), gabapentin (GBP), phenobarbital (PB), and trimethoprim/sulfamethoxazole concomitantly with FBM. FBM was discontinued. Aplastic anemia developed after FBM was rechallenged in 7/94. The patient had a positive anti-nuclear antibody (ANA) (DW Kaufman, et al, 1997).

This was the only case of aplastic anemia in the adult and pediatric patient population treated with FBM since 1993 at the Minnesota Epilepsy Group P.A. No patients developed hepatic complications. Insomnia was the most frequently reported adverse effect. Behavioral changes to include aggression were reported. Decreased appetite with an average weight loss of 2.69 kg was documented.