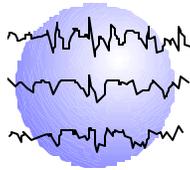


CLINICAL EXPERIENCE WITH FELBAMATE IN PATIENTS WITH MEDICALLY INTRACTABLE EPILEPSY

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ABSTRACT

RATIONALE: Felbamate (FBM) use has declined since 1994 following reports of FBM induced aplastic anemia and liver failure. Limited published data is available on the clinical experience of FBM use since 1994. We previously presented a preliminary report on a limited sample of adult patients treated at Minnesota Epilepsy Group. The current study significantly expands our observations on Felbamate therapy and includes results on pediatric as well as adult patients.

METHODS: 305 patients ages 1 to 73 yrs. treated with FBM were identified and records 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.

RESULTS: Of patients reviewed, 147 female/158 were male. Mean age at start of FBM was 32 yrs. for adults (>16 years) and 6.8 yrs for children (<16 years). The mean number failed AEDs was 5.5. Mean baseline frequency/seizure type/month: GTCs 19 for children/7.9 for adults; CPSs 28.7 for children/27.3 for adults; SPS 9.5 for children/27.3 for adults; tonic seizures 28.7 for children/102.1 for adults; myoclonic 26 for children/121.2 for adults; atonic 10 for children/20.4 for adults. FBM therapy ranged from 1 to 156 months (mean: 36.3) with an average maximum dose of 2,240-mg/day for children/3,769.3-mg/day for adults. The average FBM level was 73-mg/dl for adults/72.3-mg/dl for children. Responder rate (50% reduction in baseline seizure frequency) was 57% for children, 41% of those with >75% reduction. For adults, the responder rate was 66%, 49% having >75% reduction. Average reduction in baseline frequency per seizure type for adults: 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); tonic seizures (n=27), 49.2% (ns) and in atonic seizures (n=8), 63.1% (ns). For children the average reduction in baseline rates were: GTCs (n=34) 83%; CPS (n=48) 77%; SPS (n=18) 82%; tonic (n=25) 70.3%; myoclonic (n=11) 83%; atonic (n=7) 71.8%. 34 adult patients (19.8%) and 22 children (16.2%) became seizure free. 59% of adults and 68% of children remain on FBM. Reasons for discontinuation included intolerable side effects, 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 patients with intractable seizures including GTCs, CPS, tonic and myoclonic seizures, FBM is significantly effective in reducing mean baseline seizure frequency with some patients becoming seizure free. FBM remains an important treatment consideration in patients with intractable epilepsy.

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Introduction:

Felbamate (FBM) use has declined since 1994 following reports of FBM induced aplastic anemia and liver failure. Limited published data is available on the clinical experience of FBM use since 1994. We previously presented a preliminary report on a limited sample of adult patients treated at Minnesota Epilepsy Group¹. The current study significantly expands our observations on Felbamate therapy and includes results on pediatric as well as adult patients.

Methods:

The records of 305 patients treated with felbamate at Minnesota Epilepsy Group since 1994 were reviewed. Patient age ranged from 1-73 years. The variables identified included the number of AEDs failed prior to FBM therapy, seizure frequency by seizure type per month at baseline and at maximum therapeutic dose, percent seizure free and the percent of patients remaining on felbamate. Reasons for discontinuation were also noted. Paired t tests were calculated to compare mean seizure frequency prior to FBM use and at FBM optimization.

Results

Demographic variables are presented in Table 1. There were 158 male and 147 female patients included. The mean age at the initiation of FBM therapy was 32 years for adults (> 16 years) and 6.8 years for children (< 16 years). The mean number of failed AEDs prior to FBM therapy was 5.5.

Baseline seizure frequency rates per seizure type per month are presented in Figure 1 for the pediatric and adult patient groups respectively. Adult patients suffering tonic and myoclonic seizures demonstrated the highest seizure frequency, however, relatively few subjects are included in these two seizure types. Average reduction in baseline seizure frequency per seizure type is presented in Figure 2. Reduction in all seizure types on FBM therapy was significant with the exception of myoclonic and atonic seizures in children and tonic seizures in adults. The overall responder rate as defined by a minimum 50% reduction in seizures was 57% for children and 66% for adults (Table 2). Among responders, 41% of children and 49% of adults had greater than 75% seizure reduction. Seizure freedom was achieved by 16.2% of all children in the study and 19.8% of adults (Table 3). The average daily dose of FBM was 2240 mg for children and 3769 mg for adults.

FBM therapy was discontinued by 60% of the adult sample and by 34% of the children for a total of 50% of the total sample. Of these, the most common adverse events leading to discontinuation reported were insomnia, decreased appetite, and behavioral changes. The total number of patients discontinuing FBM secondary to adverse events is 101 subjects or 33%. 13% of subjects discontinued felbamate following announcement of the

aplastic anemia risk. One patient in the sample developed aplastic anemia. No hepatic complications were documented.

Conclusions:

- In children and adults with intractable seizures, including GTC, CPS, and SPS, FBM is effective in significantly reducing mean baseline seizure frequency with 16% of children and 20% of adults becoming seizure free.
- Myoclonic and atonic seizures in adults and tonic seizures in children were also significantly reduced on FBM therapy.
- The incidence of aplastic anemia in our population was 1/305 (.3%).
- No patient developed hepatic failure.
- FBM remains an important treatment consideration in patients with intractable epilepsy.

Reference:

1. Dickens DL, Koch S, Folland C, Carlson B, Penovich PE, Gates JR. Clinical experience with felbamate in adults with medically intractable epilepsy. *Epilepsia* 44(9):105, 2003. [abstract].

Table 1

Demographics

Number of Patients	305
Sex: Male	158
Female	147
Mean Age at Start of FBM	
Adults (≥ 16 yrs)	32
Peds (<16 yrs)	6.8
Mean # of Failed AEDs	5.5

Figure 1

Mean Baseline Frequency/Seizure Type/Month

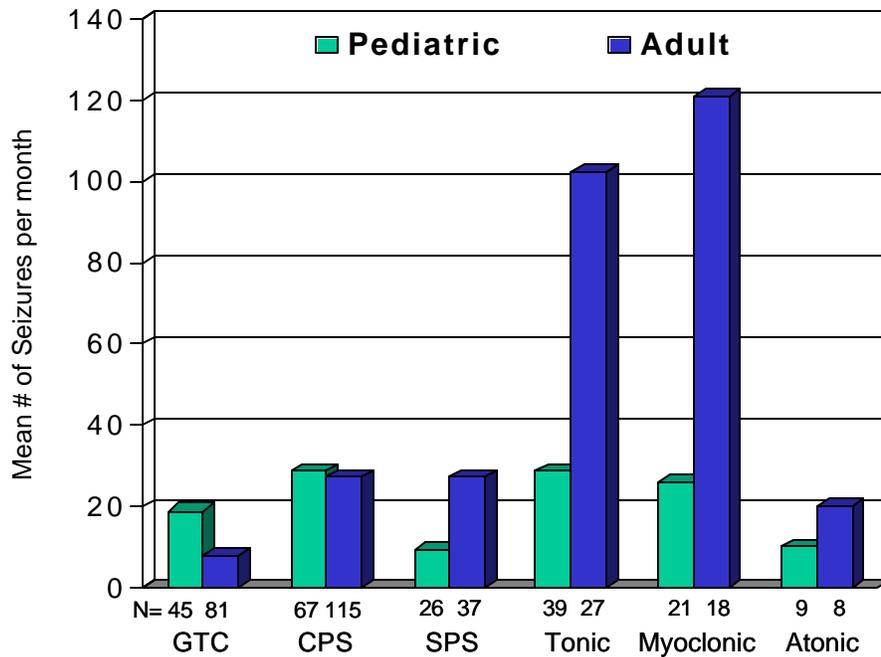


Figure 2

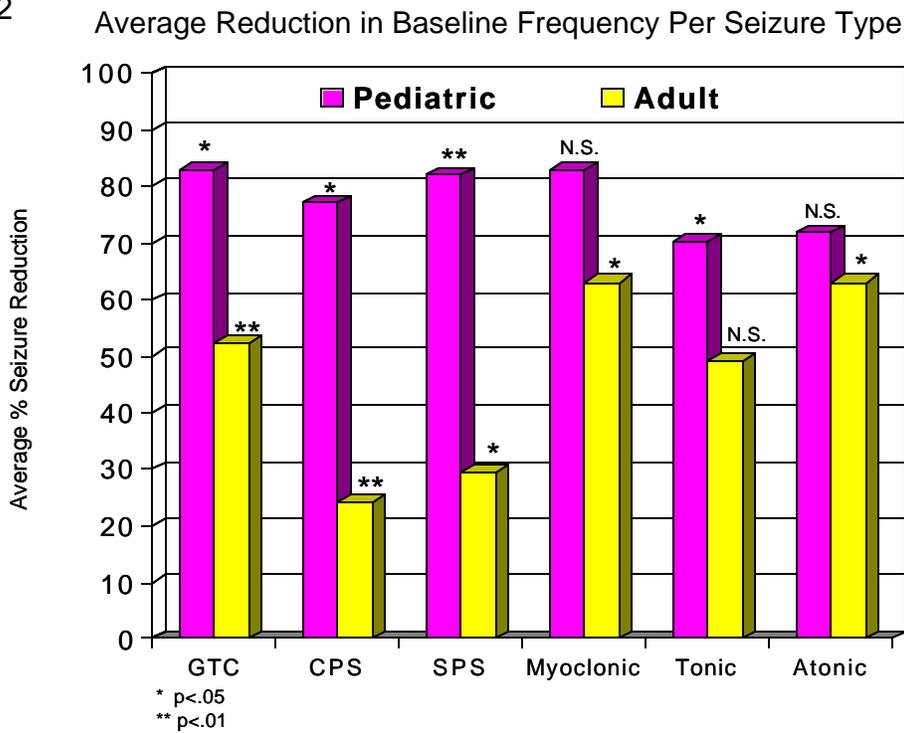


Table 2

Responder Rate

	> 50% reduction	Responders with >75% reduction
Children	57%	41%
Adults	66%	49%

Table 3

FBM Therapy

	Children	Adults
Dose	2,240 mg/day	3,769 mg/day
% Seizure Free	16	20
% Remaining on FBM	66	40