

The patient voice: valproate, topiramate and MHRA regulation

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BACKGROUND

- Valproate is a known serious teratogen for women during pregnancy associated with malformation of the unborn foetus.
- The evidence of harm in men and boys is contested and contradictory.
- Valproate is the most clinically effective treatment for many forms of generalised seizures, including the most dangerous ones.
- Valproate and topiramate use is increasingly restricted in the UK by government regulations, such as those of the MHRA. There was little consultation with people with epilepsy where valproate is an option or choice.
- Views of people with epilepsy and their families affected by these changes, and their unintended consequences are largely unstudied.

AIM

This is a qualitative study of the views and lived experience of the valproate and topiramate regulations in 21 people with epilepsy and their families.

METHODS

A qualitative analysis was conducted on the views of 21 people with epilepsy and their families who shared their lived experience with the Royal Free London NHS Foundation valproate PPP service review or the SUDEP Action Charity "Share your experience" Register and gave written consent.

Themes explored include informed consent, shared decision making, negative consequences of avoiding valproate or topiramate (including SUDEP), missed opportunities and disruption of belief systems. Overarching themes were developed and refined based on independent reviews.

Ethics:

Approved by Royal Free Governance committee as part of Valproate and topiramate audits.

Approved by SUDEP Action Charity.

Participants or next of kin gave informed consent for anonymised publication.

RESULTS

Three themes emerged:

Direct and indirect negative consequences of avoiding Valproate and topiramate, including death and injury.

- Included 5 deaths
- Highlighted by all respondents

"He was not offered a medication for children, even those at risk of death. Where is there any concern and care for my son's safety and the right to his life?"

Missed opportunities

- Loss of vocational, social & relationship opportunities

"Continually asked to put hypothetical child above my own well being"

Disruption to belief systems of patients, and to their relationship with clinicians and the medical system as a whole.

"It feels as if we are being limited to just a couple of medications: limiting our lives, our ability to live a life because we are not considered intelligent enough to choose for ourselves"(S)

Name (age range, years)	Health status	Unintended Harms & risks following MHRA legislation
1. Emma (25-30)	GGE Uncontrolled 7 unsuccessful medications but not valproate	Death (SUDEP) without option of valproate
2. Jo (15-20)	JME-uncontrolled Not on valproate	Multiple unsuccessful medication trials Multiple injuries Risk of SUDEP
3. Stan (45-50)	Seizure free x 20 years on valproate	Risk of valproate withdrawal as declines to sign PPP form
4. Louise (20-25)	Severe ID Epilepsy with no tonic clonic seizures x 7 years on lamotrigine & valproate	Family stress Less time for other discussions
5. Becky (35-40)	JME-seizure free on valproate x 20 years Healthy child while on valproate	Risk of valproate withdrawal as declines to sign up to PPP
6. Tess (25-30)	GGE uncontrolled Valproate avoided- 6 unsuccessful ASM trials	Multiple injuries Depression Unemployment
7. Meg (25-30)	GGE uncontrolled	Death (SUDEP) of patient and unborn child
8. Hannah (25-30)	GGE (Tonic-clonic seizures) No seizures since valproate	Waited 4 years for valproate 20 tonic clonic seizures x 4 years on various medications Risk of SUDEP Delayed education & career due to uncontrolled seizures
9. Tom (20-25)	GGE On Valproate since 14 years, seizure free	Risk of valproate withdrawal if declines to sign up to PPP
10. Rupert (20-25)	GGE Unsuccessful medications x 3 years Now seizure free on multiple medications including valproate	Multiple facial injuries while uncontrolled Risk of valproate withdrawal if declines to sign up to PPP
11. Caitlin (25-30)	Epilepsy in remission – 6 years Valproate x 7 years Uncontrolled seizures of Lamotrigine & side effects	Head injury & near drowning while avoiding valproate Unable to complete university year due to seizures Anxiety due to valproate supply stopped Risk of permanent valproate withdrawal if declines to sign up to PPP
12. Kristi (45-50)	JME, seizure free x 40 years on valproate Healthy baby born while taking valproate	Risk of permanent valproate withdrawal if declines to sign up to PPP
13. Faye (35-40)	GGE Seizure free on valproate, then stopped because married (not patient choice) Child with autism (not taking valproate during pregnancy) Now seizure free on valproate	Life threatening Seizures and injuries Risk of SUDEP Anxiety Years of poor seizure control off valproate
14. Sandy (45-50)	Migraine and Temporal lobe epilepsy Autism 2 children with autism (one on no medication, one on clobazam) Symptoms controlled on pregabalin & topiramate after multiple trials	Risk of permanent topiramate withdrawal if declines to sign up to PPP Anxiety
15. Sarah (40-45)	Migraine and mixed focal generalised epilepsy Best seizure control on valproate and felt most alert	Denied valproate as wishes to become pregnant Risks of status epilepticus, injuries and SUDEP
16. Helena (40-45)	JME Seizure free on valproate since 2020 Pregnant on valproate & had miscarriage	Risk of valproate withdrawal as declines to sign up to PPP
17. Sue (40-45)	JME Seizure free for >10 years on valproate	Seizure free on valproate Healthy child on valproate
18. Rachel (15-20)	GGE Multiple tonic clonic seizures on lamotrigine, levetiracetam, zonisamide, perampanel, phenobarbitalone Seizure free on valproate/ lamotrigine Cognition & social life improved	During time not taking valproate- multiple injuries, missed many months of schooling During time not taking valproate -risk of status epilepticus, SUDEP, depression, anxiety & social isolation for patient & family
19. Sabina, 45-50	GGE Cerebral palsy Seizure free on valproate for >30 years 2 healthy children in 20s born while on valproate	Perceived coercion Breach of privacy Threat to work, family life, injuries and SUDEP as risk of valproate withdrawal as she declines to sign up to PPP
20. Mark (20-25)	GGE Seizure free for >5 years on valproate Valproate stopped 6 months before death	Death (SUDEP) Advised on risks of valproate for males
21. Graham (0-5)	Severe epilepsy and autism	By not offering Valproate straight away we lost the choice to see if his seizures could be stopped or reduced or his epilepsy stopped from worsening ... and Graham died

CONCLUSION

The voices of people with epilepsy and families support the necessity that regulations are implemented and aligned to protect human rights and true informed decision-making.

Person-centred care, fair access to anti-seizure medications and proper safety checks and balanced discussions are essential before restrictions of life-saving medicines.