Optimising medicines use in older adults with intellectual disability who have epilepsy: challenges and perspectives

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Background

Seizures and intellectual disability

The rate of epilepsy is up to 30 times greater in people with intellectual disability (ID) compared with the general population.[1] Epilepsy in this population is more likely to require polypharmacy and there are challenges associated with communication of need and side effects of medicines.[2] Epilepsy is also difficult to diagnose in this population, and may be misdiagnosed in approximately 25% of cases.[3] Seizures are one of the leading causes of preventable death in adults with ID and are the main cause of potentially avoidable hospital admissions.[4] Seizures which are unrecognised, or those which are inadequately treated or uncontrolled, may have a negative effect on the quality of life.[5] The two main causes of death relating to epilepsy are status epilepticus and sudden unexplained death in epilepsy (SUDEP), both of which are over-represented in adults with ID who have epilepsy.[6,7] In particular, SUDEP is recognised to be associated with duration of unremitted epilepsy.[8] Rates of SUDEP have been reported at 3–9 times higher in this group than in the general population with epilepsy.[9]

There are few high-quality observational/intervention studies of the treatment of epilepsy in ID.[10] A Cochrane review assessing pharmacological interventions for epilepsy in people with ID concluded that the quality of evidence of studies is low to moderate.[11] Guidelines developed have noted a "dearth of high-quality evidence from well-constructed studies".[12]

Seizures in adults with ID are commonly of multiple types and are often resistant to single-drug treatment.[13] Up to 60% of adults with ID may be resistant to anti-seizure treatment, compared with 20–30% in the general population.[1] The incidence of side effects with anti-seizure drugs may be as high as 58% in the general population,[14] however people with ID who have epilepsy are less likely to report anti-seizure drug side effects.[15]

Older people with ID and epilepsy

Generally older people with epilepsy have complex care needs such as managing concurrent polypharmacy, frailty, multiple health conditions and reduced social interaction.[16] This population encounters premature ageing with higher levels of physical and mental health comorbidities, which increases sensitivity to medicines that makes prescribing complex.[17–19] There is a limited evidence base underpinning polypharmacy. For example, pharmacokinetics and pharmacodynamics of anti-seizure drugs and other medicines may alter as adults with ID who have epilepsy age, but little research is currently available.[20]

Older adults with ID who have epilepsy represent one of the most vulnerable groups in society. A recent study on this population has shown that around 50% were taking two or more anti-seizure drugs, yet 40% were still experiencing monthly seizures.[21] Key medication-related issues relating to psychotropic co-medications, anticholinergic and sedative burden emerged, to which anti-seizure drugs may contribute.[21,22]

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Cognitive decline and mortality in older populations are associated with cumulative sedative and anticholinergic medicines.[23,24] The risk of harm through polypharmacy, particularly sedative and anticholinergic medicines, is compounded by the presence of organic dysfunction associated with the ID. This may lead to idiosyncratic responses/increased sensitivity to co-medications, particularly anti-seizure drugs.[17] Given early diagnosis and high prevalence of epilepsy in this population, and the high prevalence of multiple anti-seizure drugs, there may be increased risk of cognitive symptoms from long-term use. Anti-seizure drugs may have effects on behaviour and mood, positive or negative, including behavioural problems and affective disorders.[25] The mood-stabilising anti-seizure drugs, for example, carbamazepine and valproic acid, may have positive effects on mood and are commonly used in bipolar disorder.[26] Other anti-seizure drugs are associated with higher risk of precipitating challenging behaviours in adults with ID, including phenobarbital, topiramate, vigabatrin and zonisamide.[27]

A concern for older adults with ID and epilepsy is the impact upon bone health. People with ID are generally at two times increased risk of inadequate vitamin D levels due to a number of environmental factors and certain genetic disorders.[28] The effect of anti-seizure drugs on bone metabolism is multifactorial and more prominent with known enzyme inducers (phenytoin, carbamazepine and topiramate).[29] In people with ID the high prevalence of prescribing of antipsychotic medication and associated hyperprolactinaemia are both added risk factors for osteopenia and osteoporosis.[30,31] A recent study of people with ID ($n = 575$) in which 41% were on anti-seizure drugs used quantitative heel ultrasound measurements to highlight that a third of the sample was osteopenic and 41% osteoporotic.[32] Less than one-third with objective evidence of poor bone health were receiving treatments such as calcium, vitamin D combinations or bisphosphonate.

Applying theory to practice

General guidance

The need to understand broad ID-specific prescribing principles is crucial when applied to older adults.[33] The approach to treatment must be person centred in collaboration with the individual and their family or caregivers. The treatment plan should follow available and up-to-date best practice guidelines, the evidence base, and be tailored to the individual's needs. A paternalistic approach to treatment needs should be avoided. Reasonable adjustments by clinicians and services are essential to achieve success, and this includes longer clinic appointments.

Pretreatment consideration

Prior to initiating treatment, it is important to establish a baseline assessment of an individual's symptoms and behaviour. This may include a formal functional analysis supported by behavioural specialists. Without this evidence it will be challenging to establish treatment outcomes and measure success. An agreement on treatment goals with patients and carers should be established before commencement. These goals are likely to be more varied for people with ID and include impact of side effects and quality of life outcomes. Objective outcome measures (specific for the condition being treated) reviewed at regular intervals will help guide treatment. The impact of treatment is not just observing a reduction in the targeted clinical symptoms but should include wider psychological and social factors that all influence quality of life.

Treatment consideration

Medication should be initiated at the lowest possible dose, with slow titration. There is evidence that adverse effects of anti-seizure drugs in people with epilepsy and ID are dose dependent and associated with rapid titration.[10] This approach maximises the likelihood of establishing the therapeutic window, a balance between efficacy and adverse effects. In a heterogeneous aging population with concomitant medications and genetic influences metabolism needs to be considered on an individual basis, not just based upon titration regimes extracted from large randomised control trials which do not consider the subtleties of real-word practicalities. A lengthy titration period needs to be combined with good counselling information for patients, their families and caregivers to maximise success. A good practice principle is to only change one medication at any point and allow time for evaluation. This reduces the ambiguity of attributing success and failure. Individual factors to consider include cognitive function, genetic syndromes, frailty, physical,

neurodevelopmental and mental health comorbidities, and concurrent medications.[33] Medication should be reviewed regularly and medicines which may lower the seizure threshold, for example, certain antipsychotics or antidepressants, should also be considered.[34]

When choosing medication it is essential to consider the side-effect profile of the drug and the influence it might have on the existing regime.[2] Some anti-seizure drugs, particularly older ones like phenytoin, phenobarbital and topiramate, are associated with adverse cognitive effects, which need careful consideration in people who already have cognitive deficits. Other anti-seizure drugs have well-established drug–drug interactions which could potentially lead to serious consequences. Carbamazepine will reduce serum warfarin levels, and a drug that is more commonly prescribed with advancing age. The symptoms of drug toxicity or adverse effects may be vague and difficult to illicit when assessing people with ID. Therefore, increased vigilance is required along with regular monitoring of blood parameters and anti-seizure drugs serum levels where indicated. The development of newer molecules, particularly the third and fourth generation anti-seizure drugs, have focused on developing more favourable profiles with minimum drug interactions and less impact upon cognition and behaviour. There is developing evidence of its use in people with ID.[35–38]

Other medicines optimisation considerations

The guiding principles of a generic prescribing approach are encapsulated in the NHS England Stopping over medication of people with a learning disability, autism or both (STOMP) campaign.[39] Core aims are to encourage healthcare professionals to engage with people, their families and caregivers for regular review of their medication. The complexity of polypharmacy and physical and psychiatric comorbidities observed in older adults with epilepsy and ID require shared decision making, at times involving pharmacists and other secondary care clinicians.[33] As people with epilepsy and ID age they have increased risk of communication, swallowing and mobility problems.[40] Communication problems may reduce assessment reliability. A swallowing problem may influence the formulation of medication. Treatment failure may result not from the wrong treatment choice, but an inappropriate formulation.

Special populations within the ID cohort, particularly those with recognised genetic disorders such as Down syndrome, might need added consideration. People with Down syndrome are at risk of early dementia. At times dementia first manifests as new seizure activity or seizures may develop during the dementia process.[41] Associated negative changes to cardiac function, thyroid, vision, bowel activity and gait all influence treatment choice in a person with Down syndrome with late onset seizures. A similar approach to other genetic syndromes needs to be considered based on their unique symptom profiles. Where possible, assessment of common metabolic and electrolyte biochemistry and bone health should preclude the decision to continue prescribing of anti-seizure drugs.

Improving holistic care

Implementing changes requires accessible relevant evidence-based training regularly for non-ID specialists, including the multidisciplinary team in primary care.[42] The post-anti-seizure drug prescription monitoring responsibilities may depend upon an individual's situation and local service provision, but both GPs and pharmacists should be included. The development of tailored training content, and clinical and operational pathways relevant to that local area would help support engagement and role clarity.[43] Local and regional toolkits can be produced to allow easy access to the principles of monitoring medication in older adults with epilepsy and ID, including where and how to access more information and support.

Conflict of interest statement

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