

Epileptic seizure induced by fennel essential oil

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ABSTRACT – An epileptic seizure is reported in a 38-year-old woman, known to be an epileptic patient. Although she was under antiepileptic treatment and had well-controlled epilepsy, she developed a typical generalised tonic-clonic seizure and remained unconscious for 45 minutes following ingestion of a number of cakes containing an unknown quantity of fennel essential oil. Involuntary diarrhoea accompanied her epileptic seizure. This reported case recalls the fact that fennel essential oil can induce seizures and that this oil should probably be avoided by patients with epilepsy. Labelling of products with fennel essential oil should refer to the risk of seizures, particularly for patients with epilepsy. An awareness programme should involve all stakeholders affected by this issue.

Key words: seizure, epilepsy, essential oil, fennel

The use of volatile plant oils, including essential oils (EOs) known under the generic term of “aromatherapy”, is on the increase among the global population. Since the beginning of the 21st century, it has become apparent that EOs have undergone a renewal of popularity (Vigan, 2010). Recent growth in aromatherapy sales have been accompanied by an unfortunate increase of accidental poisoning from these products (Janes *et al.*, 2005). However, EOs can be harmful in other circumstances since they can be found in cosmetics, drugs and food. They are natural substances, but contrary to the belief that they are safe because they are natural, these substances may produce many serious side effects, which can place the individual consumer at great risk (Woolf, 1999).

Several plant-derived essential oils have been known to have epileptogenic properties. This is especially true for fennel (*Foeniculum vulgare* P. Mill) essential oil (FEO) in patients with epileptic syndromes (Burkhard *et al.*, 1999). Based on one recent case notified to the Moroccan Pharmacovigilance Centre, we would like to recall the danger of FEO, in particular, to the public, health professionals in general, neurologists (mainly epileptologists), aromatherapists, caregivers, and regulatory agencies, since this problem has so far been underestimated.

Case study

A 38-year-old woman, known to be an epileptic patient with well-controlled epilepsy treated with

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lamictal (lamotrigine) at 300 mg per day, ingested around five or six cakes containing an unknown quantity of essential oil of fennel. The cakes were made at home with fennel essential oil acquired commercially. Two hours after intake, she suddenly developed a typical generalised tonic-clonic seizure and remained unconscious for 45 minutes, although under antiepileptic treatment. Involuntary diarrhoea accompanied her epileptic seizure. The patient's last seizure had been three years before and she was under clinical follow-up.

Discussion

Essential oils are complex mixtures of substances from vegetable matter. They are derived from the volatile part of the plant, *i.e.* the odorous part, hence the term "aromatherapy". Fennel (*Foeniculum vulgare* P. Mill, Apiaceae/Umbelliferae) is an important crop plant of considerable medicinal value. The essential oil of fennel is used to flavour different food preparations and in perfumery.

The main chemical components of FEO are trans-anethole, estragole or methylchavicol, fenchone and limonene (Miguel *et al.*, 2010). This composition can change after extraction depending on the method of extraction and the storage conditions of the raw plant material. As with other EOs, this composition depends not only on the part of the plant used to derive the essential oil, but sometimes on the soil, in terms of acidity and nutrients, and even on the time of harvest (Vigan, 2010). On the other hand, during distillation, undesirable compounds, pesticides and similar products used for plant growth can sometimes be found in the essential oil. Therefore, the precise composition can only be determined by chemical analysis (Vigan, 2010). These factors can affect the quality of the essential oil available on the market. Unfortunately, advice regarding the amount of product to be used in food and precautions for the general population and patients at risk is lacking on the packaging labels of FEO products marketed both locally and *via* the internet. The nomenclature is also confusing regarding the subspecies *F. vulgare* Mill. ssp. *Capillaceum* (= *F. vulgare* Mill. ssp. *vulgare*) and *F. vulgare* Mill. ssp. *Piperitum*; the subspecies *capillaceum* includes three varieties: *azoricum* Mill. Thell. (Florence), *dulce* Mill. Thell. (sweet) and *vulgare* Mill. Thell. (bitter) (Miguel *et al.*, 2010). Also, different parts of the plant can be used (bulbs, leaves, stalks and fruits or seeds) which may not be identified on the packaging of products.

Evidence in the literature showing that herbal medicines, in this case essential oil, have pharmacological effects and may lead to adverse interactions when co-administered with prescription medicines,

has grown. However, there is not enough information or adequate analysis to estimate the magnitude of the problem. Pharmacokinetic and pharmacodynamic mechanisms account for herbal medicine/drug interactions. Herbal Medicines may affect absorption, metabolism, distribution, and excretory mechanisms. A pharmacokinetic interaction can occur in general when treatment combinations (either between drugs, herbal medicines, or both) are co-administered and one affects the metabolism of another; for example, by inhibition or induction of the specific CYP enzymes involved in drug metabolism (Skalli *et al.*, 2007). A study to investigate the possibility of a drug/herbal medicine interaction between ciprofloxacin and fennel (*Foeniculum vulgare*) in a rat model has been conducted and a significant interaction between ciprofloxacin and fennel was observed. Absorption, distribution and elimination of ciprofloxacin were all affected (Zhu *et al.*, 1999).

Diarrhoea presented by the patient may be attributed to limonene which is known to cause diarrhoea and transient proteinuria (Bonnard *et al.*, 2004). In heavy doses, fenchone may have narcotic effects and may result in convulsions, hallucinations and mental imbalance (Burkhard *et al.*, 1999). Patients suffering from epilepsy or with a history of epilepsy, such as the case reported above, are at high risk and this explains the epileptic seizure of our patient where clinical diagnosis excluded any other cause of the seizure other than the ingestion of a theoretically large amount of FEO. Other EOs, such as eucalyptus with the toxic constituent 1.8-cineole and wormwood with the toxic constituent α or β thujone, are known to cause seizures and dementia (Janes *et al.*, 2005). In children, fenchone has been suggested to influence convulsions (Janes *et al.*, 2005).

The pathophysiology of fenchone epileptogenic effects is unknown. Nevertheless, eucalyptol and camphor constituents of rosemary essential oil on the cerebral cortex of the rat *in vitro* have shown an inhibitory effect on cellular respiration in rat brain slices with loss of tissue gradient for sodium and potassium, leading to a significant increase in cellular excitability (Steinmetz *et al.*, 1987). Fenchone, a cyclic monoterpene ketone, isomeric with camphor, could act similarly. Camphor is known to be contraindicated in children who have had febrile seizures or who present a risk of convulsions (Galland *et al.*, 1992). Fennel essential oil can be present in limited amounts in natural flavourings, which implies that the use of EOs in food should be regulated. The safety of EOs for human consumption has not undergone the rigorous scientific testing typical of regulated drugs, especially in vulnerable populations, such as patients with chronic pathology, in this case epilepsy, children or pregnant women.

Conclusion

Fennel essential oil is rapidly absorbed and demonstrates primary neurotoxicity; people suffering with epilepsy or a history of epilepsy are at high risk and should avoid such oil. Physicians (neurologists and epileptologists) should ask their patients about the use of FEO in order not to overlook diagnoses of pathologies linked to toxic principles of this essential oil. A particular awareness to users (the public, caregivers, etc.) and to prescribers (aromatherapists) about this danger is needed because of the life-threatening risks associated with ingestion. To date, fundamental well-founded studies to evaluate the toxicity of all FEO components and establish non-adverse effect levels are lacking because of the great complexity of effects of EOs. Rigorous legislation is expected to follow soon. □

Disclosure.

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