Cannabinoid therapy in Epilepsy

The rise in attention of the subject in media, with almost unbelievable anecdotal positive outcomes, is what caught my eye for the subject.

A literature review

An international survey among neuro-paediatrician

Below there is an link to an example of these media portraits on the subject

https://www.nationalgeographic.com/magazine/2015/06/marijuana-science-drug-research-legality/?utm_source=Facebook&utm_medium=Social&utm_content=link_fb20180420news-marijuanascience&utm_campaign=Content&sf187434319=1
Material and method

The aim for the review was to go through literature published the last 5 years, trying to use the PRISMA protocol for a systematical approach.

Inclusion criteria:
- Literature of clinical effects
- Animal trial
- Pharmacological trials (studying cannabinoids anti-convulsive traits)

Exclusion criteria:
- Articles about recreational use of cannabis.
- Articles about cannabinoids used in other field of medicine
- Articles focusing on the psycho-activity of cannabinoid substances

Searches were performed in MED-LINE and EMBASE on three subjects: Cannabinoids, Epilepsy and Child.

The International survey →
A short survey (16 questions) was outlined and sent to neuro-paediatrician in Norway, Sweden, Denmark and Germany. The aim for this survey was to map how much knowledge and clinical experience there was among the specialist care. We used the web-based online survey software Survey Monkey.
Results

62 studies/articles/review were found in our search in both databases, 26 studies were reviewed. 2 RCTs, 6 prospective cohorts, 3 retrospective cohorts, 9 animal/pharmacological studies and 5 international surveys.

- Most of them showed that CBD (Cannabidiol) had a near 50 % seizure reduction effect.
- Some of the patients also reported other positive results like being able to reduce their use of AED:s
- It was also reported better Quality of life with improved Cognitive abilities

- There was also in quite a lot of the studies reported drug-drug interactions between CBD and some of the AEDs (Valproate which lead to elevated liver enzymes, Clobazam increased dose because of CBD). A few patients were discontinued.
- There were however also adverse effects where diarrhea, somnolence, pyrexia, decreased appetite and vomiting. However most of these were mild to moderate.

International web-based survey →
- Unfortunately low response rate of 13,6 % (85/613).
- 96 % of responders had heard of cannabinoid therapy in epilepsy. However, what stands out in the responses is the warrant of studies with good enough evidence of the efficacy and safety.
- Furthermore, over 40 % of the responders had knowledge of self medication with cannabinoids and 69% had patients or families that had requested cannabinoid therapy.
Discussion

Literature review
- Regarding the PRISMA guidelines, one can argue that they were not fully met. (study selection, summary measures)
- The RCT:s were financed by GW-Parmaceuticals.
- The studies were of heterogenous study methods.
- Most of the researchers and clinicians agree that the compound that ought to be used should be almost solely CBD, but unfortunately in a lot of these studies there is not a standardised product.
- had a population of TRE (treatment resistant epilepsy) patients
- Serious adverse events due to interactions with concomitant AEDs that patients used. (were specific studies that looked at this, however more are needed)
- Subjective bias in form of overconfidence in the effect from parents. (Colorado study)
- Most of the study populations had TRE (Treatment resistant epilepsy) and received CBD in addition to their AED (Antiepileptic drug) regime. This makes it hard to differentiate how much effect on the seizures can be credited to CBD and how much might be CBDs interactions with other AED which lead to seizure reducing effect.
- A lot of other positive outcomes were reported which should be lifted, like increased cognitive abilities → enhanced quality of life.

International web-based survey
- The biggest limitation of the survey is the low response rate. Thus, we cannot appreciate the results representability.
- Perhaps the Nordic countries are a bit conservative and the topic too controversial.
- The issues that arise in our survey resonate in the literature.
- The research is making progress though, since 2013 clinical studies have multiplied, and at present there are about 25 ongoing clinical trials studying the effect of CBD-enriched products on seizures, as well as their safety and drug interactions.
Conclusion

Literature study
- Use of cannabis products, especially CBD seems to have an effect on seizure reduction, most shown in people with TRE.
- However, the results vary, and so far, there is not a good enough understanding of adverse event profile, or true efficacy.
- Rigorous prospective placebo-controlled studies of CBD are needed (and underway), where it is also taken in account for drug-drug interactions.
- Still, people with TRE might not have a lot of other options and in these cases CBD should absolutely be considered as a therapeutic option.
- The scientific community has a responsibility to investigate and inform the public, so that people that might treat their loved ones with CBD while still on a AED regime can do an informed choice and tragedies are avoided. Most of the anecdotal "miracle" stories do not report these backsides.

International study
- The results form our survey indicates that even though many of the responders had heard about cannabinoid therapy, this is not widely used in the countries included in the survey.
- The responders warrant studies that confirm true efficacy and safety, (however there are other indications where cannabinoids are being used, MS, palliation, terminal cancer treatment, and the safety profiles of these studies seem to be in accordance to the studies results that are performed on Epilepsy treatment.) There is also a moral aspect to be considered.