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Cannabinoids with children

Good experience with pain, spasticity and in oncology

Time after time, therapists face enormous problems when treating children with chronic pain or a life limiting illness. Most medication is not authorised or available in useable paediatric doses. In addition to this, many medicines cause adverse side effects. In particular, for multi-morbid children who have severe multiple disabilities, many problems, from feeding through to pronounced tetra-spasticity, who, as a rule, already take substantial polymedication, cannabinoids appear to offer an interesting approach.

In spite of the number of case reports (see also case history on the next page) and a constantly increasing number of clinical studies amongst adults, there is almost no data amongst paediatric patients, in spite of the positively reported effects of cannabinoids on muscle tone/spasticity, pain, nausea, loss of appetite, anxiety, sleep disturbance, migraines, etc.

We have since gained long-term experience in our centre for palliative medicine and children pain therapy with the use of cannabinoids and would like to give an account of this in following article.

Available as a prescription drug since 1998

Cannabis contains more than 600 defined substances including a cocktail of at least 63 different active cannabinoids, their main agent, Delta-9-Tetrahydrocannabinol (THC, Dronabinol). The medical use of cannabis has been passed down through the ages. In Asia, reports exist on the medical use of cannabis sativa from the 3rd millennium BC. In recent times, THC has been available as a prescription drug since the amendment to the Narcotics Act 1998 and can be administered on prescription.

Photo caption: Dr. Sven Gottschling, Homburg/Saar

The fact that this relates to a prescription drug, opens up customised dosing possibilities for paediatric patients which are lacking in most proprietary medicinal products with doses tailor-made to adult patients and thus impede a differentiated pain therapy and symptom control, in particular amongst paediatric palliative patients with low body weight. I therefore welcome this prescribed drug from a paediatric point of view.

The main indications for the use of Dronabinol amongst our patients were the treatment of spasticity and pain with severely handicapped children and nausea and vomiting in the field of paediatric oncology in the event of loss of appetite.

Spasticity and pain amongst children

Both animal experiments and smaller studies on adult patients, in particular with multiple sclerosis and the ensuing spasticity have shown that Tetrahydrocannabinol has pain relieving and anti-spasticity effects. On this basis, we have examined this prescription drug for its efficacy on children. We have, up to now, treated 13 children with severe multi-handicap and tetra-spasticity aged from seven months to 17 years and from 7-47 kg. With all children, therapy fractal spasticity existed (Baclofen was either dosed or massive side effects could not be overcome). In the children, these patients had infantile cerebral palsy, leukodystrophy, debilitating diseases and hypoxic brain damage. Four children already had additional treatment with opioids and non-opioids, two further receive merely non-opioids.

All children received a titrated dose of Dronabinol, with children below 10 kg - 2 x 0.5 mg, with children between 10 and 20 kg - 2 x 1 mg, with children above 20 kg - 2 x 2 mg. The maximum dose was 2 x 5 mg depending on the body weight and effect. The average Dronabinol daily dose after the titration phase was 0.2 mg/kg body weight.

Within the framework of the above-mentioned doses, all of the children who have been treated so far showed in part a definite reduction in pain (measured by the FLACC-R scale, see inset) and this was often revealed within the first 48 hours after the start of treatment. The effect with regard to spasticity according to subjective estimates by parents was within the first one to two weeks. Ten out of 13 children showed an improvement in their sleeping-through behaviour with otherwise unchanged medication. Amongst a few children with opioid co-medication, an opioid saving effect was noticed.

Patents from this group receive long-term treatment with Dronabinol. The longest period of use is as revealed by the patient in the case study, which is five years. No “accustoming” effects were noted amongst any of the patients in the sense of necessary dose escalation.

The results are so encouraging that corresponding urgent studies have to be carried out as I can image Dronabinol to be a first line medication for spasticity and pain based on our clinical experience with these patients.

Use in oncology

The best known indication for cannabinoid treatment in oncology is cancer (tumour) cachexia, which, in addition to numerous other causes is linked with a lack of appetite and nausea within the framework of an oncological illness and treatment. It is indisputable that a tumour cachexia goes hand in hand with a clearly worse prognosis of an oncological illness since patients recover slower between chemotherapy treatment, suffer from frequent infections and have to face a worse tumour control through delays in treatment. Based on this reason, treatment for a tumour cachexia is of great importance.

In the field of children’s oncology, cannabinoids have been used in the University Clinic of Homburg for over ten years and experience has since been gained with more than 50 patients from the age of three months. Dronabinol as an oily solution, can still be administered with pronounced mucositis so that in difficult situations the regular taking of this is not a problem.

Most patients benefit from this treatment and report a better control of nausea/vomiting with chemotherapy in addition to an improvement in the actual target parameter appetite loss/weight loss and an improvement in the falling asleep and sleeping-through behaviour. Anxiolytic effects are also reported by patients such as very pleasant muscle relaxation with often mobility restricted and regularly muscle-tensed patients.

With oncological patients, treatment often lasts several months, in part, there is on-off medication spanning over weeks, adapted to blocks of chemotherapy sessions. Neither in the resting phase nor with regard to patients, whereby the medication is terminated after months (often after the end of intensive chemotherapy) did we experience any problems when stopping the medication (e.g. in the sense of withdrawal symptoms).

No serious side effects

We did not observe any side effects within the framework of normal daily dosing for our patients between 0.1 and 0.25 mg/kg body weight (e.g. in the sense of neuro-psychiatric symptoms, lack of drive or cognitive deficits) with long-term use. In addition, with oncological patients the cannabinoid treatment is only intended for a limited amount of time or can be continued within the framework of palliative care without any problems.

In one case study this led to incorrect dosing with one patient at home, who had taken a single dose of 50 mg with a body weight of 50 kg instead of the prescribed 5 mg. The father, who had administered this dose, had not read the dosing instructions properly and thought mg was ml. This patient suffered from massive anxiety, hallucinations and vegetative symptoms for three days such as e.g. racing heart. Nevertheless, this situation was controllable at home and the patient had the courage to re-start the treatment after the symptoms had subsided which showed the desired clinical effects after a period of time.

Hardly any problems with the prescription

With regard to costs, we have had no problems with sponsors for our paediatric oncological patients up to now, however, based on our experience. with the most severely handicapped, sponsors should be notified in advance. As a rule, written medical justification is required. Up to now, the acceptance of costs has not be refused in any one case.

Our experience with Dronabinol with children is very encouraging. It remains to be hoped that our observations will provide evidence in the future in corresponding qualitative high quality clinical studies.

Caption: Spasticity and pain amongst children can be controlled in part with multi-handicapped by using Dronabinol over a long period of time.

Bibliography

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Facts from experience

- Cannabinoids have a wide range of effects and cover, as a rule, several painful symptoms even with the most severely handicapped or oncologically ill children.
- Treatment, based on our experience, produces few side effects and there is very good treatment compliance.
- In the daily doses used by us between 0.1 and 0.25 mg/kg body weight no dose escalation is necessary in long-term use.
- Based on the availability as a prescribed drug, Dronabinol does not pose any problems for the paediatric field and can be individually dosed.

A case study

Noah was four years old when he came to the centre for palliative medicine and child pain treatment in Homburg. He was suffering from a complex brain malformation, heart defect, vascular defects, multiple operative corrected intestinal malformation (oesophagus atresia, external duodenal stenosis). In addition to this, he had problems with electrolyte balance and suffered from cramps which were difficult to control. In spite of this Noah, at the age of 4, was still well motor developed and could even ride a scooter.

After a status epilepticus subject to reanimation at the age of four, Noah was almost deaf, blind and severely tetra spastic upon initial presentation. In addition, he had a painful hip joint subluxation on both sides. He is tracheotomised and has a PEG.[1]

Noah has extensive polymedication, which includes Baclofen in addition to the (unretarded) administration of Tilidin/Naloxon three times a day in underdosing. Based on the large quantity of medication the only sleep window for Noah and his mother was the time between the last medication around 2.30 am and the first at 6.00 am.

In order to enable a restful night's sleep we terminated the night-time medication and changed to a retarded opioid and administration of an unretarded opioid adapted to the situation on an as-needed basis. A clear improvement in pain and unrest was noted afterwards.

Since, however, there was still pain (measured with the FLACC-R scale (face, legs, activity, cry, consolability) and marked spasticity, we extended the medication to Dronabinol. We began with 2 x 1 mg with this patient who weighed 20 kg then after a few days increased this to 2 x 2 mg. Very quickly (within the first 48 hours) there was an improvement in the tetra spasticity and the pain value reduced.

For the past five years, the patient has been on stable Dronabinol treatment, without a dose escalation being necessary (the dose is now 2 x 2.5 mg with a body weight of 27 kg). Baclofen has since been phased out. Noah is now in a permanent stable condition with half of the body weight related opioid dose previously required five years ago. He is visibly content under this treatment.

Caption: Our most severely handicapped patient, Noah, has been stable on Dronabinol for fives years and is visibly content.

[1] The meaning of this is unclear and needs full explanation of the abbreviation for translation.