Diplomarbeit
Thesis

Hyperbaric oxygenation (HBO) as a supportive measure during sub-acute to late-stage neurorehabilitation after traumatic spinal injuries.

eingereicht von
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Graz, am 12.9.2019…… *Verena Andrea Zajac eh*

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In memoriam Andrzej Zajac

1950-2007

Zusammenfassung

Einleitung:

Verletzungen des Spinalmarks führen zu temporären oder permanenten Funktionsausfällen. Die Symptome umfassen unterschiedliche Ausprägungen motorischer bzw. sensibler Ausfälle bzw. Störungen der autonomen Funktionen distal des Traumalevels. Durch posttraumatische Mediatorkaskaden kann sekundäre Schädigung mit Absterben von Neuronen - in erster Linie infolge von Ödem und Lipidperoxidation - entstehen, die das Outcome drastisch verschlechtern können.

In einer Reihe von Tierexperimenten hat Hyperbare Oxygenation (HBO), Atmung von 100% Sauerstoff unter erhöhtem Umgebungsdruck, durch verschiedenste molekulare Mechanismen zur Niederregulierung inflammatorischer Mediatorkaskaden, zu Ödemreduktion und zur Terminierung der Lipidperoxidation und dadurch zur Verhinderung des neuronalen Zelltods beim spinalen Trauma geführt. Darüber hinaus wurden Steigerung der re-Myelinisierung und Verringerung der der glialen Narbenbildung beobachtet.

Trotz dieser positiven experimentellen Ergebnisse existieren bis dato kaum klinische Studien zur Hyperbaric Oxygenation beim spinalen Trauma. Die wenigen Publikationen beschreiben HBO innerhalb der ersten 24 Stunden nach dem Unfall. Zur HBO in der subakuten und chronischen Phase des spinalen Trauma gibt es de fakto keine klinischen Beobachtungen.

Material und Methoden:

PatientInnen mit subakutem oder chronischem spinalem Trauma, die innerhalb der letzten 10 Jahre in der Druckkammeranlage der klinschen Abteilung Thorax- und Hyperbare Chirurgie der Medizinischen Universität Graz unter intention-to-treat Indikation behandelt wurden, wurden in einer retrospektiven Studie evaluiert. Exkludiert wurden Fälle, die innerhalb der ersten 24 Stunden nach dem Unfall eine HBO erhielten.

Zusätzlich zum ASIA-score zur Beurteilung von Motorik und Sensibilität wurde ein 10-stufiger VAS-score zur subjektiven Beurteilung der Symptomveränderung (Motorik, Sensibilität, Parästhesien) eingesetzt. Die HBO wurde auf 2,2 ata über 90 Minuten an 5 Tagen pro Woche mit Wochenendpausen appliziert. Die Daten wurden aus elektronisch asservierten Krankenakten extrahiert. Der Wilcoxon matched signed rank Test und Spearman´s rank correlation Test wurden für die statistische Auswertung eingesetzt.

Ergebnisse:

12 PatientInnen mit spinalem Trauma (10 Männer, 2 Frauen, Durchschnittsalter: 49,3 Jahre; range: 19 – 69) wurden eingeschlossen. Sowohl Schweregrad als auch Niveau der Verletzung variierten beträchtlich. Die subjektive und objektive Evaluierung ergab während der HBO-Behandlungsserie für jeden einzelnen Patienten/Patientin neurologische Verbesserungen, Verschlechterung wurde in keinem einzigen Fall beobachtet.

Der Spearman's rank correlation Test zeigte eine sehr hohe (92%) negative Korrelation zwischen Dauer der Behandlung und Symptomschweregrad. Für die Kombination der 3 untersuchten Qualitäten war a p=0,000. Für die Einzelfaktoren ergab Spearman's Test 92% Korrelation für motorische Defizite und Behandlungszeit, 81% für sensible Defizite and 74% für Parästhesie. Der ASIA score ergab einen signifikanten Anstieg bei den sensorischen and motorischen Werten (Wilcoxon matched pairs signed rank test: p = 0.0031). Elf PatientInnen hatten Verbesserungen in beiden Qualitäten, ein Patient verbesserte sich nur sensorisch, während die Motorik unbeeinflusst blieb. Bei keinem der Patienten kam es zur Verschlechterung einer der beiden Qualitäten.

	before HBO	after HBO	p (Wilcoxon test)
sensory	78.9+-9.5	92.2+-7.3	**p = 0.0031**
motoric	61.9+-8.9	78.1+-5.9	**p = 0.0031**

Konklusion

HBO scheint beim subakuten spinalen Trauma wirksam zu sein. Da jedoch in dieser retrospektiven Analyse keine Kontrollgruppe vorhanden war, kann nicht ausgeschlossen werden, dass die beobachteten Verbesserungen auch ohne HBO aufgetreten wären. Allerdings ist anzumerken, dass in fast allen Fällen vor Beginn der HBO keine Symptombesserung zu verzeichnen war

Es besteht demnach Bedarf an prospektiv randomisierten Studien an großen Kollektiven um die Wirksamkeit der HBO beim spinalen Trauma weiter zu evaluieren.

Abstract

Introduction:

Any damage to the spinal cord causes changes in its function that may be temporary or permanent. Symptoms involve variable degrees of loss of motor function, of sensation, or of autonomic function in the regions of the body distal to the level of the injury. Due to inflammation cascades post-trauma, secondary damage with neuronal cell death mainly due to oedema and lipid peroxidation can dramatically worsen the outcome.

In an abundance of animal experiments hyperbaric oxygenation (HBO), denoting breathing of 100% oxygen under elevated ambient pressure, has been found to downregulate inflammatory mediator cascades, to reduce oedema and counteract lipid peroxidation and cell death by a variety of molecular mechanisms. Furthermore HBO supports re-myelonization and minimizes glia-mediated inflammation and glial scar formation.

In spite of the experimental data and a few clinical studies on hyperbaric oxygenation (HBO) treatment during the first 24 hours following spinal trauma, there are hardly any clinical data on sub-acute and late-phase HBO after spinal injuries.

Materials and methods:

Patients who had HBO at the hyperbaric facility of the Division for Thoracic and Hyperbaric Surgery, Medical University Graz within the last 10 years were reviewed. Those who had HBO under intention-to-treat indication for spinal trauma more than 24 hours after the accident were included into the analysis. In addition to the ASIA-score documenting both motoric deficits and sensory deficits, a 10-grade subjective VAS score for motoric, sensible and paraesthesia symptoms had been used. HBO treatment was delivered at 2,2 ata for 90 min 5 times a week with weekend breaks. The data was collected from electronical patients´ charts. For statistical analysis was Wilcoxon matched pair signed rank test and Spearman´s rank correlation test were used.

Results:

12 patients with spinal cord injury (10 males, 2 females; mean age: 49,3; range: 19 – 69) were included into the study. Both degree and level of the injury varied considerably. Both subjectively and by objective evaluation each patient reported improvements during the course of HBO treatments, while none experienced any worsening of symptoms. Spearman's rank correlation test showed a very high (92%) negative correlation between the duration of treatment the severity of symptoms. All 3 symptoms combined had a p=0,000 and when analysed by each individual symptom Spearman's test showed a 92% correlation regarding motoric deficits and treatment time, an 81% correlation regarding sensible deficits and a 74% correlation for paraesthesia. The ASIA score showed a significant increase of both the sensory and motoric score (Wilcoxon matched pairs signed rank test: p = 0.0031). Eleven patients showed an improvement in both scores, one patient was improved in the sensory score and unchanged in the motoric score. In none of the patients a decrease of either score was found after HBO therapy.

	before HBO	**after HBO**	**p (Wilcoxon test)**
sensory	78.9+-9.5	92.2+-7.3	**p = 0.0031**
motoric	61.9+-8.9	78.1+-5.9	**p = 0.0031**

Conclusion:

HBO seems to be effective in subacute spinal trauma. However, since there was no control group, it is not possible to state, whether the patients would have equally improved without HBO within the same time interval. Of note is the fact that in most cases there had been no clinical improvement until HBO was started.

There is definitive need for prospectively randomized studies including large collectives of patients to further elucidate the effectiveness of HBO in spinal cord injury.

Figure 1 a portable chamber on a research boat. Florida 2019 (Photo: Author)

Contents

Glossary and Abbreviations

AGE…arterial gas embolism

ASC…adaptor molecule apoptosis-associated speck like protein

ASIA…American Spinal Injury Association

Ata… atmospheres absolute

BBB score…Basso Beattie Bresnahan locomotor rating scale

CO… carbon monoxide

CNS… central nervous system

CX43…Connexin43

DCI/DCS… decompression illness/sickness

ERS…Endoplasmic reticulum stress

FAST… Focused assessment with sonography for trauma

GCS… Glasgow coma scale

HBO… hyperbaric oxygen

HBO… hyperbaric oxygen therapy

HMGB1…high-mobility group protein box 1

ICP… intracranial pressure

INOS… inducible nitric oxide synthase

IV… intravenous

MEP…motor-evoked potential

NALP3… NACHT domain-leucine-rich-repeat- and pyrin domain containing protein 3

NF-κB…Nuclear Factor κB

NOS… reactive nitrogen species

PO_2… oxygen partial pressure

PP… partial pressure

ROS…reactive oxygen species

SCI…spinal cord injury

VEGF…vascular endothelial growth factor

Tables and figures

Introduction

Traumatic spinal cord injuries

Any damage to the spinal cord causes changes in its function that may be temporary or permanent. Symptoms comprise variable degrees of loss of motor function, of sensation, or of autonomic function in the regions of the body distal to the level of the injury.

The range of symptoms, which are depending on the severity of the damage and its location covers paraesthesia or complete loss of sensitivity, paralysis and incontinence. If the cervical spine above C4 is involved, the phrenic nerve loses its function and breathing becomes impossible. The predominant complications evolving in the later course are muscular atrophy and contraction at the joints, pressure sores, and urinary or respiratory infections.

The causative trauma mechanisms are predominantly traffic accidents, falls, sports injuries or sequelae of violence such as gunshots. In more than 50% of cases the cervical spine is affected, while about 15% each involve the thoracic spine, the junction between thoracic and lumbar spine and the lumbar spine.

Apart from the clinical assessment imaging by X-Ray, computed tomography (CT) and magnetic resonance imaging (MRI) is used for diagnosis and treatment planning.

Grading of spinal cord injuries is done according to the ASIA impairment scale first introduced by the American Spinal Injury Association. The five (A-E) grades of impairment range from the most severe A, (complete injury; no motor or sensory function in the sacral segments S4 – S5) to various degrees of incomplete (from B-D) to normal motor and sensory function. An underlying scoring system involving the function of key muscles on the upper and lower extremities, anal and bladder function as well as sensory evaluation of the dermatomes reflecting the spinal levels allow for an objective evaluation of the extent of the dysfunction. Furthermore, it enables the documentation of changes during therapy and follow-up. SCI are also graded according to the degree of impairment ranging from complete paralysis of all for limbs – quadriplegia and paralysis of the legs only – paraplegia. (1)

Severance of the spinal cord - either complete or partial - following spinal trauma is irreversible. In addition, inflammation mediators cause secondary damage of hitherto unaffected, and not severed parts of the spinal cord, worsening the clinical picture. Patients regarded to have complete SCIs have little to no chances of neurological improvement.

The secondary damage in spinal cord injuries is due to a complex biochemical cascade. It begins mainly with the destruction of the blood-spinal-cord-barrier triggered by resident cells in the injured area which initiate a neuro-inflammation process. The neuroinflammatory cascade is facilitated by chemokines cytokines and their complement activation compounds that stimulate the accumulation of inflammatory haematogenous cells like macrophages, lymphocytes and neutrophils at the site of the traumatic impact. (1)

Those cells generate reactive nitrogen species (NOS), proteases and reactive oxygen species (ROS). It is mainly the resulting oedema, which causes secondary damage. Swelling impairs and eventually cuts off oxygen supply, leading to even more cell death of neurons and glial components.

Glucocorticoids have been used to reduce tissue inflammation and swelling. Though some success has been reported the treatment carries major side effects, mainly inhibition of neuroregeneration which counteract possible benefits. Thus this treatment modality is no longer recommended.(2) Up to this time, no alternative systemic treatment has been established.

Immediate surgery for decompression of confined parts of the spinal cord, for stabilization of the fractured spine and for haemostasis is required in cases of traumatic spinal cord injury associated with unstable or comminute fractures. It has been shown that surgery within 24 hours after the accident is associated with a significantly better long-term outcome.(1)

The principles of hyperbaric oxygenation therapy (HBO)

The lack of oxygen plays a major role in secondary damage after traumatic spinal injuries. According to various experimental studies hyperbaric oxygenation therapy (HBO) might not only be beneficial in acute spinal cord injuries (SCIs) but may also help to recruit non-irreversibly damaged neurons in the later course.(3)

HBO treatment involves of breathing of 100% oxygen under ambient pressure higher than one atmosphere. Under these conditions the amount of oxygen dissolved in the plasma shows a linear increase according to the pressure applied. Thus, the normally dissolved oxygen fraction (paO2) which ranges between 75 and 100 mmHg rises to about 1000 mmHg at 2 ata and to about 2000 mmHg at 3 ata. This considerable amount of dissolved oxygen even obviates the oxygenation via haemoglobin as long as the patient is exposed to HBO. Beyond 3 ata HBO must not be delivered because neurological side-effects are inevitable when the dissolved oxygen fraction is further increased (4)

The high level of oxygen in the plasma and in consequence also in the tissues has a number of pharmacological effects. It causes reduction of oedema, downregulation of mediator cascades, modulation of the blood-brain barrier, mobilization of stem-cells, neuroprotection and neuro-neogenesis, and stimulation of macrophages and leucocytes. The intracellular ATP-reserves are immediately rebuilt, counteracting cell death and apoptosis. HBO causes an increase of the arterial blood-pressure and shows an antibacterial effect the degree of which is dependent on the type of the germ involved.

In addition, the mere increase of pressure causes ectopic gas bubbles to shrink according to the law of Boyle and Mariotte. This effect is used for the treatment of gas embolism.

According to the level of evidence, the following indications for HBO have been established:

- Decompression sickness/illness, DCI
- Arterial gas embolisms AGE
- Gas gangrene and necrotizing fasciitis
- Intracranial abscesses
- Problem wounds
- Burn injury
- Compartment syndrome
- Osteomyelitis
- Sequelae of radiation treatment (radiation cystitis, radiation proctitis, osteoradinecrosis)
- Carbon monoxide and cyanide poisoning

The most common side-effects are problems with pressure equalization in the middle ear or in the nasal sinuses during the pressurization phase of the treatment. If there is no pressure-equalization possible in case of an acute indication for HBO, myringotomy has to be done in order to avoid rupture of the eardrum.

At the therapeutic pressures with a maximum of 3 ata oxygen toxicity is very seldom observed, though in principle it can develop beyond 1,7 ata. Clinically, oxygen toxicity presents as numbness, optical or acoustical hallucinations and tonic-clonic convulsions. If the oxygen is replaced by compressed air, the symptoms are immediately reversible.

The only absolute contraindication for HBO is any untreated pneumothorax.

The therapy is administered in a hyperbaric chamber at pressures up to 3 ata according to schedules defined for the different indications.

There are different types of chambers available. Hospitals prefer large Multiplace chambers that can treat about 6-10 people at a time and can easily accommodate patients lying on stretchers or in hospital beds.

In chambers equipped for the treatment of critically ill patients, hyperbaric physicians and nurses accompany the patients during treatment.

Monoplace chambers are cheaper and allow for the treatment of only one patient at a time. In case of an emergency during the treatment, it will take some time to depressurize the device and to get access to the patient. Nevertheless, some hospitals use them for patients with MRSA infected wounds, since they are easy to clean.

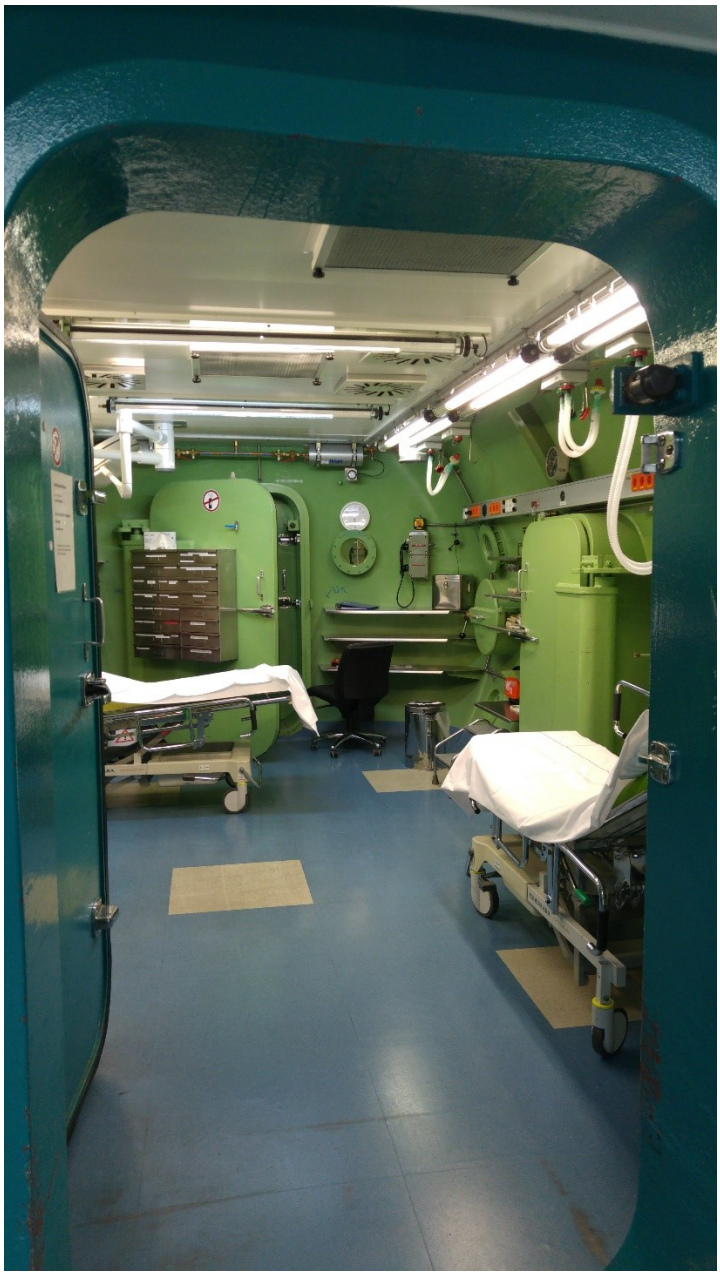

Figure 2 Multichamber ,University Hospital Graz 2018 (Photo: Author)

HBO for spinal cord injuries:

Experimental animal studies:

HBO has successfully been used in experimental cerebral ischaemic strokes in rats as an additional neuroprotective measure. There was a significantly better overall outcome in the rat models. Another study showed a faster post-ischaemic stroke recovery with supportive hyperbaric oxygen treatment in dogs.(5)
Few clinical studies for post-stroke treatment have been conducted up to this time. They also showed an improvement of the outcome.

Based upon these results, the use of HBO has been investigated also for experimental cerebral and spinal trauma.

Following a concussion model (lateral hit of a pendulum against the surgically exposed brain) Kraitsy et al. investigated HBO after experimental cerebral trauma. Half of the animals were subjected to a 3-day course of HBO-treatment (2.2 atm for 1 hour, daily, starting 1-hour post-injury). Changes in motor function over time were assessed with the Rotarod test. It consists of a rotating rod on the top of which the rats are placed. They must keep moving in order not to fall off. In addition, somatosensory evoked potentials, central motor conduction time and histological evaluation were done.

The results indicated a time dependent biphasic progression of central nervous damage that can be rescued by HBO treatment. A rapid decline in the status of the animals was manifested in a significant decrease of motor function within 1 week after injury as evaluated by rotarod testing. The ability of the injured rats to remain on the rotating rod for longer time periods was significantly augmented by HBO treatment.

The fast improvements in motor function were not mirrored in the results obtained by somatosensory evoked potentials (SEP). Within the first two weeks following injury and treatment a slight increase in the central motor conduction time (CMCT) occurred, that was comparable in both groups. However, after three weeks of HBO treatment the CMCT was significantly reduced.

At the same time the CMCT in severely injured control animals increased considerably, indicating repeated treatment with HBO to contribute to subsequent regenerative processes. Immunohistochemical analysis indicated the improvement in CMCT to be correlated to a decrease in demyelination in the cortex ipsilateral to the trauma (8).

Cristante et al showed in their study of experimental spinal trauma in rats, that animals receiving HBO therapy had significantly better motor function recovery. There was no significant difference in outcome between rats starting HBO right after the injury and those, who had their first treatment 24 hours after the injury. Although, considering the higher metabolical rate of the small rodents, the effect of a 24 hours delay cannot be compared to the one in humans, the authors concluded that HBO after more than one day delay in humans could still be beneficial.(2)

Murakami et al. did a study on ischaemic damage after experimental spinal injury (clipping) in rabbits. The group receiving HBO 30 minutes after the trauma showed significantly better neurological (5-grade muscle strength score) improvement than the group in which HBO- treatment was begun 6 hours after the injury, and the controls. (5)

Yaman et al conducted an elaborate SCI study with rats. They evaluated the motor improvements, measured the nitrite levels in the serum and assessed histological tissue samples. They divided 40 rats into five groups of 8 individuals; the first “sham group” underwent anaesthesia and paraspinal surgery but the researchers did not induce damage to their spines. (6)

The rats from groups 2 to 5 underwent a total T9 laminectomy, their spinal cords being clipped for 10 seconds at that level. Those latter 4 groups were further divided into post-trauma treatment groups. The 8 rats in group no. 2 had no HBO therapy after the injury. Group no. 3 received hyperbaric treatment starting 1 hour after the surgery, group no. 4 started HBO 6 hours post-surgery and group no. 5 had hyperbaric oxygen 24 hours after the trauma. All animals in the treatment groups had 2 HBO therapy sessions per day for day for 5 days at 2,4 ata for 90 minutes.

Motor function was evaluated using an inclined plane test. The animals were put on a plank which was steadily lifted up on one side until the angle was too steep for the rats

to keep their footing. The angle at which the animal was still able to stand for at least 5 seconds was documented on day 1, 3 and 5 post-trauma. In addition, the same 5 grade muscle strength scale as used in human neurological examination was used.

All rodents from group 2-5 were paraplegic right after the surgery. There were significant differences in the plane tests between the group 2 (injury but no hyperbaric treatment) and group 3 which had HBO within an hour following the trauma. All HBO treatment groups improved steadily over the 5 days. A significant difference between the non-HBO trauma group and the ones receiving treatment was only shown for groups 2 and 3. Accordingly, group 3 was the only one that had significant improvements from day 3 to day 5 post-trauma.

When evaluating the rats by the muscle strength grade system all HBO groups performed significantly better than group 2. Again, the improvement was the better, the sooner HBO was started. Though all HBO treated animals improved on a daily basis, only group 3 showed significant changes compared to each previous exam.

On day 6 after the surgery, all animals were sacrificed and histological tissue samples from the spinal cord were taken. Evaluation was based on a 3-grade system (1- minimal necrosis and bleeding, 2 moderate damage, 3 – heavily damaged tissue. There were no significant differences for bleeding between the trauma-only group and the HBO-groups. However, there was statistically significant less necrosis in group 3 compared to group. Concerning signs of inflammation group 3 and 4 both did significantly better when each was compared to the second group.(6)

Another experimental study in rats investigated the effect of repeated HBO treatments compared to one single therapy session. The injury was induced by dropping a 10g weight on the surgically exposed spinal cord. There were seven study groups. Group 1 was the sham collective, undergoing surgery but no but no weight-drop crush procedure, group 2 had weight drop injury, but no HBO treatment. The other 5 groups did receive HBO at 2,8 ata, each session lasting one hour. Groups 3, 4 and 5 only underwent a single HBO treatment 30 minutes, 3 hours and 6 hours, respectively, after the injury respectively. Groups 7 and 6 had one HBO daily for one week, with group 6 starting treatment 6h after the injury and group 7 commencing HBO 24h post-trauma.

Motor function was assessed using the BBB score (Basso Beattie Bresnahan locomotor rating scale) which is commonly used in those animal studies. The rats from group 3 and 4, who had undergone a single HBO session after 30 minutes or 3 hours, respectively, showed statistically significant improvements compared to the rats of group 2 who were injured, but did not receive HBO. The group of rats who had had a single HBO session 6 hours post-trauma showed no major differences compared with group 2. However, if group 6 (start of HBO after 6 hours, but daily treatment for one week) was compared to group 2, there was a measurable improvement for the former. There were no differences between group 2 and group 7, who received multiple HBO treatments as well, but started therapy after 24 hours.(5)

Dayan et al did an experimental study in rats focusing on neuroregeneration after SCI. They evaluated 8 groups with 6 animals each. Group 1 served as sham and had no intervention at all, group 2 had spinal injury, but did not receive any hyperbaric treatments. Group 3 was a sham group receiving pre-surgery HBO but no trauma, group 5 had HBO after the injury and group 7 served also as sham was administered HBO both pre- and post-surgery without spinal trauma. Group 4 suffered SCI and received pre-operative HBO only, group 6 were injured rats who received HBO after the trauma and group 8 had SCI and underwent both pre- and post-operative HBO. All hyperbaric treatments were delivered at 2,8 ata for 60 min. once a day.

The pre-surgery HBO started 5 days before the operative procedure. Post-surgery HBO but continued until day 7 post-trauma. The Basso Beattie Bresnahan locomotor rating scale was applied to test the motor functions. The BBB score showed that the injury groups receiving post-surgery or pre- and post-surgery hyperbaric treatment showed a statistically significant difference to the group of rats who had SCI but had no HBO sessions. Pre-trauma HBO exposure only had no effect according to this study. Rats who only had pre-injury HBO performed about the same as the SCI rats who did not receive any hyperbaric treatment at all. (3)

Huang et al also did a rat-model experiment based on the hypothesis that after traumatic spinal injuries NO has a major part in the biochemical cascades causing secondary damage and that HBO might reduce the NO build-up. They used 3 groups

consisting of 12 individuals each, one being used as the control/sham group, one being injured according to the weight-drop method but not receiving HBO treatment and one SCI group that received HBO for 24 days post-trauma at 2 ata for 100 minutes starting 30 minutes post-injury. The BBB score showed that the rats receiving HBO performed significantly better than the SCI group who had no HBO treatment. PCR was used to assess the amount of iNOS mRNA expressed in the samples and a diazo-colouring method and nitrate reductase was applied to quantify the amount of NO and iNOS in the serum. The results showed that the iNOS mRNA expression was distinctly lesser in the HBO group compared to the untreated SCI group. The same was true for the iNOS protein expression and the serum NO levels.(7)

Geng et al investigated the anti-inflammatory effects of hyperbaric oxygenation in a rat model focusing on the role of macrophages in secondary injury mechanisms. Marcophages can be divided into two categories. M1 (classically activated) macrophages are believed to be damaging to healthy tissue. They are associated with increased concentrations of cytokines that promote inflammation.
M2 – or alternatively activated macrophages - are thought to be protective on the other hand since they assist matrix remodelling and stimulate angiogenesis.

They divided the rats into 3 groups; A the control/sham group, B the SCI normal air group (1ata – normobaric treatment), and C the SCI hyperbaric oxygen group (2,8 ata for 90 mins, every 12 hours, 6 treatments total). The SCI was established by clipping the exposed T11 segment of the spinal cord for 10 seconds. They took samples for immunostaining on day 3, 7 and 14 post-surgery. iNOS and CD16/32 positive stains are associated with the M1 phenotypes. Arginase and CD 206 positive stains are associated with the M2 “protective” phenotypes. The samples of the hyperbaric oxygen group showed both significantly higher levels of arginase 1 and CD 206 and significantly lower levels of iNOS and CD16/32 than the normobaric air group samples. This seems to support the idea that HBO does have a positive anti-inflammatory effect. (8)

The team of researchers around Geng et al further elucidated the anti-inflammatory effects of hyperbaric oxygenation therapy in combination with stem cell transplantation after SCI. They used 75 rats, which were evenly distributed between 5 groups, a control group, a group receiving saline injections instead of stem cells (“vehicle group”), a HBO-

only group, the stem cell transplant group who received no HBO treatment and the combination group who received both stem cells and hyperbaric treatments. They analysed the cytokines levels (TNF-α, IL-1ß, IL-6, IFN-α) after week 1, week 3 and week 6. The rats treated with HBO only as well as the group who got stem cell transplants in addition to HBO showed significantly decreased levels of cytokines compared to the stem cell-only and vehicle group. (9)

Liu et al focused on the role of Endoplasmic reticulum stress - ERS in secondary damages after traumatic spinal injuries. They researched the attenuating effects of HBO on ERS by inhibition of c-Jun N-terminal kinase and up-regulating the glucose regulated protein 78 (GRP 78). They used an experimental animal model with 72 rats divided into a control/sham group, another one who had spinal trauma induced by the weight-drop method, but received no treatment and an SCI group that underwent HBO

The HBO group had daily hyperbaric sessions at 2 ata for one hour starting 6 hours after the injury. The motor function as well as the biochemical changes were evaluated on day 1, 3, 7 and 14. Like most other teams, the investigators used the BBR score to quantify the changes in motor function. The rats in the HBO group showed markedly more improvement on day 7 and 14 when compared to the untreated SCI group. The immunohistochemical analysis showed that the c-Jun N-terminal Kinase levels in the HBO group were lower compared to the SCI group and the glucose regulated protein 78 expression was higher in the HBO group thus confirming the hypothesis that ERS could be attenuated by HBO.(10)

Liang et al tried to elucidate the role of HBO in NACHT domain-leucine-rich-repeat- and pyrin domain containing protein 3 inflammasome (NALP3). NALP3 together with caspase 1 and adaptor molecule apoptosis-associated speck like protein (ASC) are responsible for a cytokine spike after traumatic spinal events thus playing a major role in inflammation. (7)

Using 120 rats they analysed the NALP3 expression rates in the four different groups; a control group, a sham group that underwent HBO but had no trauma, a spinal injury group that received no further treatment and a SCI group that underwent HBO. Spinal injury was inflicted by the weight drop method at T10. The rats undergoing HBO therapy

received 2 HBO sessions per day for the first 3 days following the trauma at 2ata for one hour and 1 HBO session per day for the time left thereafter. The NALP3 levels were quantified using RT-qPCR and Western Blots.
The NALP3 concentrations were significantly lower in the HBO-treated SCI group compared to the injury-only group on days 1,3 and 7, but not any longer 2 weeks post-injury.(11)

A further study in rats focused on the effect of HBO in modulating the vascular endothelial growth factor (VEGF) and Connexin43 (CX43). CX43 plays a major functional role in Gap junctions. Those junctions provide a passage for a number of second messenger proteins, ions and various metabolites, thus being involved in secondary damage mechanisms following SCI. VEGF, on the other hand, is important in neo- and re-vascularization and neuro-regeneration. 96 rats were evenly distributed into for groups; group 1 served as control, group to had sham-surgery but HBO as well, group 3 was SCI- only, group 4 had spinal cord injury and underwent HBO.

The hyperbaric treatment consisted of 60-minute sessions at 2ata twice a day for days 1-3 and once a day for the remaining time. The SCI was generated using the weight drop method at T10 level. The PCR and Western blot analysis revealed that the VEGF levels in the SCI / HBO group were significantly higher when compared to the injury-only group. On the contrary, the CX43 levels were significantly lower in the SCI / HBO group compared to the injury group on day 3,7, but things switched around on day 14 when the CX43 levels were lower in the injury-only group.(12)

Yang et al investigated the role of high-mobility group protein box 1 (HMGB1) and Nuclear Factor κB (NF- κB) in secondary damage cascades after spinal trauma.
NF- κB induces an inflammatory cascade by activating various factors like TNF-α. HMGB1 is a component in a number of cells including macrophages and monocytes. It is therefore also a major player when it comes to post-acute inflammatory responses. A large group of 160 rats was divided into 4 groups; the first group had injury (weight-drop at T10) only, the second had SCI and hyperbaric treatment, the third served as controls and the fourth had sham surgery without inflicting trauma. HBO started 6 hours after the injury and involved of 70-minute sessions at 2,5 ata two times a day for days 1-3 followed by one session per day thereafter.

The Western blot showed that the HMGB1 concentrations were significantly reduced in the HBO treated group when compared to the SCI-only group on days 7 and 14. There were also significantly lower levels of NF- κB protein in the HBO-group on days 3, 7 and 14.(13)

Predicting outcomes in human trials based upon the results of experimental animal studies has always proven to be difficult. Very often, promising data from experimental studies cannot be reproduced in human clinical trials.

Further problems when designing clinical trials in SCI arise due to the given inhomogeneous nature of the injuries in a clinical environment. Standardization is difficult because of these factors. What is more, there are only few chambers worldwide which can accommodate patients with acute or subacute spinal cord injury and even fewer are located in a practicable distance to a trauma centre.(14)

Therefore, the aim of the thesis was to retrospectively analyse the course of patients who had intention – to – treat - HBO in the post-acute phase following spinal injury – i.e. more than 24 hours after the event.

Material and methods

This thesis was designed as a retrospective study based upon patients with subacute and chronic spinal cord injury who had HBO as an intention-to-treat between 2009 and 2018. The total number was 12 (10 males, 2 females; mean age: 49,3; range: 19 – 69). In order to avoid a bias by a-priori downregulating the mediator cascade, patients who had their first HBO treatment within 24 hours after the accident were excluded from this study.
Patient records (neurological examination, surgery notes and previous histories) were collected through the hospital's digital MEDOCS database.

Neurological assessment
Neurological assessment was done according to the ASIA-classification. The sensory qualities were checked by pin-prick.

In addition, a VAS-score had been used by which each patient stated his or her subjective neurological condition (motor function, sensibility and paraesthesia) ranging between 10 describing the overall subjective situation at the beginning of HBO-treatment and 0 indicating total lack of symptoms. In patients the general condition of whom did not allow its application, the VAS-score was omitted.

Hyperbaric oxygenation (HBO)
HBO was administered in a large walk-in-drive-in multiplace hyperbaric chamber. The facility accommodates patients able to walk, as well as those relying on a wheelchair or patients lying in hospital beds. The design with large doors allows the transfer of the patients into the chamber with the patient lying in bed – there is no need to disconnect any lines. Depending on their general condition, patients were accompanied by an attendant, by a specially trained nurse or by a hyperbaric physician.

The hyperbaric protocol was 2,2 ata for 90 minutes.

Statistics

Statistical analysis comprised descriptive statistics, Spearman´s rank correlation test and the Wilcoxon signed rank test using STATA version 15 (Stata Corp., College Station, TX, USA). $P < 0.05$ was considered to indicate statistical significance.

Case histories

Patient 1

Trauma mechanism, history and on-site findings

A 24-year-old male fell from a 3,5m high roof unto solid ground. He had no relevant diseases in his history. He was alert and oriented, complaining about severe pain in the lower back. After initial assessment at a peripheral hospital (data not available) he was transferred to the University Hospital Graz the day after the accident.

In-hospital neurological / clinical findings

On clinical examination, the patient complained about severe pain in the lumbar area. Sensory function was normal at the first assessment. Patellar tendon reflexes were intact on both sides, yet there was bilateral Achilles reflex absence. Otherwise, the initial examination showed no motoric deficiencies. There was perianal paraesthesia, no anal sensation and no voluntary anal contraction was found. The patient had to be catheterised because of urine retention. ASIA score was 100 motor and 100 sensory, impairment calculation: D

Radiological findings

The routine roentgenogram showed a fracture of the L1 vertebral body with a height reduction of more than 50%. CT revealed a large bone fragment protruding into the spinal canal causing a significant obstruction.

Surgery

L1 laminectomy and a dorsal TH 12 to L2 spinal fusion were done the day after the accident.

Postsurgical course

The anal contraction improved. Urinary retention and perianal paraesthesia, however, persisted on day 2, though the paraesthesia was markedly improved by day 3.

Interval between trauma and first HBO

The patient was referred for HBO therapy the day after the injury.

Neurological findings before first HBO

The ASIA score was 100 motor with impaired but no longer absent anal contraction. The sensory score was 100, unchanged. The patient was mobile with the help of crutches.

Neurological findings during and after HBO therapy

The patient subjectively felt an improvement of anal contraction after the first HBO session. On the 3rd day the paraesthesia improved significantly.
On day 16 he reported further improvement regarding perianal sensibility. Thereafter, the sensibility remained unchanged (ASIA sensory: 111, motor: 100)

On the subjective VAS-score he indicated 5 after the first, and 4 after the second, third and fourth week of treatment.

The total number of HBO-treatments was 29.

Final outcome

Six weeks after surgery the patient had no residual neurological deficiencies (ASIA motor: 100; sensory: 112).

Patient 2

Trauma mechanism, history and on-site findings

A 58-year old female patient fell down a flight of 20 stairs. She had no relevant diseases in her history. When the paramedics arrived, she still had some feeling left in her legs, but could not move them. Emergency transport to the University Hospital Graz was done.

In-hospital neurological / clinical findings

On arrival at the hospital the patient was alert, oriented and able to speak. She had a gaping 1,5cm wound in the occipital region, and no other visible injuries than a mild swelling in the dorsal cervical/thoracal area.

She was able to move her upper extremities but no movement of the legs was possible. There was no voluntary anal contraction possible and the bladder function was absent. Sensibility was in a large part intact with some mild sensibility loss in the plantar area of both feet.
ASIA score was 50 motor and 100 sensory, impairment calculation: A

Radiological findings
CT showed a comminuted L1 fracture with severe narrowing of the spinal canal, a fracture of the ankle (Weber A) and calcaneus fracture on the right side.

Surgery
The orthopaedics team performed a laminectomy at L1, a kyphoplasty and dorsal spinal fusion from T12 to L2. The Weber A fracture was treated conservatively with a plaster cast.

Postsurgical course
Surgery and the postsurgical course were uneventful. With the exception of the possibility of dorsal flexion of the left foot, no neurological improvement was noticed.

Interval between trauma and first HBO
Hyperbaric oxygenation was started on day 8 after the accident.

Neurological findings before first HBO
Only dorsal flexion at the left ankle was possible (ASIA grading: 2), incontinence and bladder dysfunction were unchanged, sensibility at the left side below the trauma level had slightly deteriorated. (ASIA motor score: 52, sensory score: 96).

Neurological findings during and after HBO therapy

The first HBO session had to be discontinued because the patient was unable to equalize the pressure in the middle ears. After paracentesis, the therapy was accomplished uneventfully. During the first week no neurological changes were documented.

On day 10, the patient reported sensibility improvement in her right foot and on day 11, the dorsal flexion of her left foot was markedly stronger (ASIA grade 4).

Final outcome

For the 25th treatment session she came down from the ward by herself, needing no further help with the wheelchair. Sensibility at both legs improved further.
ASIA score at the end of HBO-treatment was motor: 54 and sensible: 100.

The total number of HBO-treatments was 27.

Patient 3

Trauma mechanism, history and on-site findings

A 63-year-old male patient fell from 1,8m height onto a concrete floor. He was first admitted to a peripheral hospital but given the seriousness of his injuries, he was transferred to LKH Graz.

In-hospital neurological / clinical findings

The patient was intubated and sedated upon arrival at the University hospital and was immediately referred to surgery. On first examination, he had incomplete tetraplegia symptoms. ASIA score was motor: 96 and sensory: 106; impairment calculation: C

Radiological findings

He had on open tibial fracture on the left side and a C5/C6 luxation fracture with compression of the spinal cord to 50% of normal.

Surgery

The C5/C6 luxation fracture was surgically repositioned and stabilised with plates. The tibial fracture was also stabilised with plates.

Postsurgical course

The procedure went perfectly, but the patient had to stay in the ICU first given the nature of his injuries.

He was extubated the day after the procedure being hemodynamically stable, alert and oriented at that time.
He was transferred from ICU to the normal surgical ward after his first HBO treatment.

Interval between trauma and first HBO
Hemodynamic stability allowed for HBO the day after the accident.

Neurological findings before HBO therapy
There was a weakness when stretching the fingers on both sides (ASIA grade 4) and difficulties when forming a fist on the right side (ASIA grade 4), the degree of paraesthesia was unchanged. (ASIA motor score: 97, sensory score: 106).

Neurological findings during and after HBO therapy
The patient had 5 weeks of HBO therapy (29 single therapy session) and reported major improvements day by day. On the VAS-score motor function plunged to 1-2. At the end of HBO-treatment ASIA scoring yielded motor: 100; sensory: 112.

Final outcome
The patient was subsequently referred to a rehabilitation centre. At a follow- up 5 months after the accident he reported only minor pain in the neck and had no sensomotoric deficits anymore. The tibial fracture was healing well.

The total number of HBO treatments was 29.

Patient 4

Trauma mechanism, history and on-site findings
A 53 years old, otherwise healthy patient fell from a height of 3 metres onto solid ground. He had emergency treatment at a peripheral hospital (findings not available) and was immediately transferred to the University hospital.

In-hospital neurological / clinical findings
On first assessment a plexus paresis on the left upper extremity was suspected.

He also complained of hypaesthesia at C2 to C7. The patient was able to move his other arm and his legs without any difficulties. ASIA score was 82 motor and 95 sensory, impairment calculation: C

Radiological findings
There was a C2 fracture without dislocation with significant oedema of the spinal cord as well fractured processi spinosi of C 4, 5 and 7.

Surgery
There was neither indication for surgical intervention on the C2-fracture nor on the fractured processi spinosi. A neck brace was applied.

Neurological findings before HBO therapy
ASIA score was 82 motor and 95 sensory

Interval between trauma and first HBO
Since both the motor and sensory deficits remained unchanged in spite of antiphlogistic therapy, HBO was begun 12 days after the accident.

Neurological findings during and after HBO therapy
There was objective and subjective improvement of the neuro-motoric function. On the VAS-score both sensory and motor function improved to 9 by week 2 and kept going down by 1 each following week to 5 at the end of the sixth week. He reported a major pain reduction. There was still some paraesthesia in the left and right upper limb and some sensibility issues in his right arm. After discharge from the hospital he continued his HBO treatment as an outpatient.

Final outcome
Upon finishing the HBO sessions, the motor function of the arm had markedly improved. Paraesthesia had almost resolved (ASIA motor: 97; sensory: 110)

The total number of HBO treatments was 30.

Patient 5

Trauma mechanism, history and on-site findings

A 65-year-old male patient fell down a flight of who fell down a flight of 22 stairs. At the site of the accident he was immediately unable to move his legs. He had emergency helicopter transport to the University hospital.

In-hospital neurological / clinical findings

The patient was awake and oriented on arrival. The motor function in both arms was intact (ASIA grade 5), although he still had no motoric function in either lower limb (ASIA grade 0). Sensory deficits were present from TH9 downwards on the right side and downwards from TH8 on the left. He was able to feel the insertion of the urinary catheter and had sensibility left down to the level of the toes on both sides.
ASIA score was 85 sensory and 52 motor, impairment calculation: B

Radiological findings

The CT showed a multi-fragment fracture of TH 4 with significant compression of the spinal cord.

Surgery

The patient underwent a primary laminectomy at TH IV and dorsal stabilisation at TH II-VI.

Postsurgical course

The patient had no complications post-surgery, his pain was manageable, and he was otherwise stable.

Neurological findings before HBO therapy

The patient was able to move his left foot (ASIA grade 2) one day postoperatively. ASIA score was 85 sensory and 56 motor.

Interval between trauma and first HBO

The hyperbaric treatment started the day after surgery, two days after the accident.

Neurological findings during and after HBO therapy

On the VAS-score he was still at 10 after the first week of treatments but then improved rapidly to an 8 by week 2, 7 the week thereafter, a 5 on week 4 and a 3 after his last week of treatment sessions, with significant improvement of paraesthesia in his legs. (ASIA sensory: 100, motor: 77)

Final outcome

Upon the patient´s discharge there was major improvement in the left leg with a proximal motor strength grade 5; (4 for dorsal flexion and 5 for plantar flexion); He was able to wriggle his toes on the right side (ASIA grade 1). Total score: ASIA sensory: 100, motor: 77.

The total number of HBO treatments was 30

Patient 6

Trauma mechanism, history and on-site findings

A 23-year-old, male patient was admitted following a high-velocity motorcycle accident.

In-hospital neurological / clinical findings

On arrival the patient had a GCS 14 (verbal -1). There was crepitation when moving his right elbow and right underarm, the pelvis was stable by physical evaluation. There were multiple bruises on his face, but no noticeable injuries on the lower extremities.

The patient stated decreased sensibility on the left upper arm, the motor function was markedly reduced at the left upper extremity. ASIA score was 102 sensory and 76 motor, impairment calculation: D

Radiological findings

There was oedema of the spinal cord at the cervical level, hairline fractures on TH 5 and TH 6, compression fractures at L1 and L3, bilateral pneumothorax with lung contusions, a liver laceration in segment VI, subcapsular kidney haematomas on both sides, distal

radius fractures on both arms as well as a processus coronoideus fracture and a radius head fracture on the left side. Additional trauma to the arm plexus was found on MRI.

Surgery

The arm fractures were treated conservatively by applying casts, the compression fractures were stable and did not require surgery either. The visceral injuries were also treated conservatively.

Postsurgical course

His ICU stay was without any complications. The patient was cardiopulmonary stable, kidney function was within normal parameters.

Interval between trauma and first HBO

The hyperbaric oxygen treatment commenced 6 days after the accident.

Neurological findings before HBO therapy

When starting HBOT the patient was able to breathe on his own. The neurological findings were unchanged (ASIA: 102 sensory and 76 motor).

Neurological findings during and after HBO therapy

The patient did not report neurological improvement throughout the first 2 weeks of therapy. However, in week 3 both motor and sensible VAS-scoring improved to 6 and to 5 in week 5. ASIA scoring at the end of HBO treatment was motor: 87; sensory: 105.

Final outcome

The patient was discharged to a peripheral hospital after the last HBO-treatment. There were no further follow-up data.

The total number of HBO treatments was 30.

Patient 7

Trauma mechanism, history and on-site findings

A 69-year old female patient fell after tripping over a carpet. Following the accident, she noticed some weakness in her fingers.

In-hospital neurological / clinical findings

She did not present to a peripheral hospital until 2 days after the incident when both motor and sensory functions had deteriorated with impairment at C6 to Th1. She had initial treatment for bruise of the shoulder. An injury to the brachial plexus was suspected and left for outpatient radiological assessment. Yet the patient was re-admitted the day after because of further worsening of symptoms. Since a fracture of the cervical spine was suspected on CT scan, she was transferred to the University hospital. She was alert and oriented. There was incomplete paraplegia from C7 downwards. ASIA score was 106 sensory and 78 motor, impairment calculation: D

Radiological findings

MRI showed a C5 fracture and pronounced oedema of the spinal cord from C4-C6.

Surgery

Given the stable nature of the fracture, it was decided to treat the patients conservatively with a soft neck brace.

Postsurgical course

The patient had physiotherapy and ergotherapy.

Neurological findings before HBO

Upon examination the patient was hardly able forming a fist at both sides (ASIA grade 1-2) as well as troubles in bending and stretching her arms (strength grade 4 on both sides). There was sensory impairment on the upper extremities at C6 to C8 (ASIA: motor 78; sensory 106).

Interval between trauma and first HBO

The first HBO-session was initiated 6 days post-trauma.

Neurological findings during and after HBO therapy

The patient noted some improvements in sensitivity in both her hands and her 10-grade scale evaluation changed to an 8. ASIA-scoring after treatment yielded motor: 90, sensory: 110.

Final outcome

During rehabilitation therapy further improvement was documented.

The total number of HBO treatments was 15.

Patient 8:

Trauma mechanism, history and on-site findings

A 45-year old male patient had emergency transfer to the University hospital after having crashed into a fence with his motorcycle. Immediately after the injury he was tetraplegic and could neither feel his arms nor his legs.

In-hospital neurological / clinical findings

On arrival a Fast-sono didn't show any free fluid in the abdominal region at stable arterial blood pressure, normal heart rate and peripheral oxygen saturation. The pupillary reflex was slowed on both sides. ASIA score was 6 sensory and 1 motor, impairment calculation: A

Radiological findings

CT-imaging showed a TH 5 and a TH 9 fracture which did not compromise the spinal cord. There was severe osteochondrosis at C6/C7. In his history, the patient had a dorsal C4/C5 fusion with spinal cord stimulation.
The MR in the later course (see below) yielded a C3/C4 disc prolapse with accompanying oedema.

Surgery

The fractures of the thoracic spine were stable and therefore treated conservatively.

Because the spinal cord stimulator was still implanted, it was not possible to do an MRI on the day of admission. The stimulator probes were removed on the 10th day after the injury.
Following MRI diagnosis, the patient had C3/C4 decompression and ventral spondylodesis on day 55 after admission.

Postsurgical course
The course both following removal of the spinal probe and following cervical spinal fusion was uneventful.

Interval between trauma and first HBO
The hyperbaric treatments were started 4 days after the accident.

Neurological findings before HBO therapy
At the time HBOT was commenced, he still had incomplete tetraplegia (ASIA score: motor: 1, sensory: 6) distal to C6 with the right side being more severely affected

Neurological findings during and after HBO therapy
Both motor function and sensibility improved steadily over the next 3 weeks with a remarkable increase of motor functions in the hands noted during the third week.

Final outcome
In the 4th, final week of HBO treatment the VAS-score indicated grade 5 for sensible and grade 7 for motoric function. ASIA score yielded motor: 78 and sensory: 93)

The total number of treatments was 21.

Patient 9

Trauma mechanism, history and on-site findings
The 50-year-old male fell on a furniture edge. He collapsed and fainted during the night. It took him hours to call help after he had regained consciousness.

In-hospital neurological / clinical findings

Upon arrival at the University hospital the patient was stable, fully awake and oriented. The clinical evaluation showed paraplegia of both lower extremities, with deficiencies in sensibility starting at L2. ASIA score was 50 motor and 68 sensory, impairment calculation: B

Radiological findings

The emergency CT confirmed a dislocated fracture in the upper L2 area. The subsequent MRI additionally showed a widespread epidural haematoma from TH10 to L3 with subtotal compression and obliteration of the spinal cord.

Surgery

The patient underwent emergency decompression and dorsal spondylodesis from TH11-L4.

Postsurgical course

He was transferred to the ICU after the procedure, where he was successfully weaned from the respirator overnight.

Interval between trauma and first HBO

Hyperbaric treatments proceeded 5 days after the incident consisting of 27 sessions over 4 weeks.

Neurological findings before HBO treatment

The neurological findings had remained unchanged after surgery (ASIA motor: 50; sensory: 68).

Neurological findings during and after HBO therapy

Improvement was slow but occurred at a steady rate. On the VAS-score there was improvement of both sensibility and motor function to 8 by week four.

Final outcome

The patient was transferred to a rehabilitation facility with an ASIA score of 76 motor and 88 sensory.

The total number of HBO treatments was 22.

Patient 10

Trauma mechanism, history and on-site findings

A 64- year old farmer fell 2 meters from a ladder while working in a forest. Immediately after the accident he showed signs of incomplete tetraplegia and had helicopter transport to the University hospital.

In-hospital neurological / clinical findings

Due to bad weather conditions the helicopter transport proved to be difficult, taking over 6 hours. Upon arrival the patient was alert with a GCS of 15, being able to recall the accident. He did not need any respiratory support and was in relatively stable condition give the circumstances.

He showed symptoms of an incomplete quadriplegia being neither able to move either arms or legs and complaining of decreased sensitivity at all four extremities and at the trunk. Bladder function was impaired, there was no residual anal tonus. ASIA score was 31 motor and 32 sensory, impairment calculation: B

Radiological findings

The MRI showed a decompensated C3/C4 spinal canal stenosis with 7mm residual width, a 2,5cm long myelon oedema and minor myelocompression.

Surgery

After conservative treatment no change of the neurological impairment occurred. On day 5 after admission the patient had discectomy C3/C4 and ventral spondylodesis.

Postsurgical course

The patient was transferred from ICU to the surgical ward 9 days post-surgery. He still had to be catheterized and had a urinary tract infection.

Interval between trauma and first HBO

The hyperbaric treatments started 6 days after the injury.

Neurological findings before first HBO treatment
The neurological symptoms were unchanged, ASIA score still ranging at 31 motor and 32 sensory. Bladder function and anal tonus had not improved.

Neurological findings during and after HBO therapy
The patient showed continuous improvement, noting definite changes in sensibility in all extremities after 14 sessions, improving from 9 after week one to 8 after week two and 7 in week 3 on the 10-degree VAS scale.

Final outcome
During the last neurological assessment after the HBO sessions, an overall – if minor - improvement of the symptoms was noted as well, especially in the legs.
(ASIA motor 55, sensory: 48)

The total number of HBO treatments was 27.

Patient 11

Trauma mechanism, history and on-site findings
The 19-year-old male patient was transferred from a peripheral hospital for surgery after falling from 4 metres onto tarmac.

In-hospital neurological / clinical findings
There were motoric/strength deficits in the left upper extremity (ASIA grade 3 overall) and minor sensible deficits in the lower right extremity, no other deficits were present. ASIA score was 90 motor and 90 sensory, impairment calculation: D

Since he could not recall the accident, the patient he underwent a thorough neurological examination, excluding a first-time seizure event.

Radiological findings

There was a C6 comminute fracture with accompanying myelon oedema from C5-C7. lung contusion on the left side was an additional finding.

Surgery

C6 corporectomy and ventral fusion from C5 to C7 was done.

Postsurgical course

No further complications were noted after the procedure and the patient was cleared for hyperbaric oxygen therapy after having recovered from surgery.

Interval between trauma and first HBO

The patient started HBO sessions on day 4 after the trauma.

Neurological findings before start of HBO therapy

There had been only little change of his neurological symptoms (ASIA score: 92 motor and 91 sensory).

Neurological findings during and after HBO therapy

The patient reported no improvement during in the first week of treatment, but in treatment week 2 and 3 an improvement from 10 to 8 and then 6 on the 10-grade scale was noted. (ASIA sensory: 106, motor: 100)

Final outcome

After finishing the hyperbaric therapy, rehabilitation treatment was begun, the neurological status still showing ASIA sensory: 106, motor: 100.

The total number of HBO treatments was 14.

Patient 12

Trauma mechanism, history and on-site findings

The chest of a 59-year-old male lumberjack was crushed between 2 trees during work. On arrival of the emergency doctor the patient had a GCS of 15 and was able to move his arms. Yet he quickly deteriorated and had helicopter transport to the University hospital. During the transport he had to be intubated, bilateral chest tubes had to be inserted due to traumatic haemo-pneumothorax.

In-hospital neurological / clinical findings

ASIA score before intubation had been 30 motor and 51 sensory, impairment calculation: A. After stabilization of the cardiorespiratory function the patient went to radiological diagnosis and emergency surgery.

Radiological findings

There were TH 5/TH6 comminute corpus fractures and fractures of the processus spinosi of TH3 to 6. In addition, the patient had sustained a type B aortic dissection, dislocated serial rib fractures on both sides, sternal fracture and fracture of the left clavicle.

Surgery

The patient had transfemoral aortic an aortic stenting and a dorsal spondylodesis from TH 4 to TH 7. The left clavicle required osteosynthesis in the later course. The haemo-pneumothoraces and the serial rib fractures required thoracotomy on the left side.

Postsurgical course

There was initial concern about the perfusion of the left arm, which however normalized within a few days. The motor function of the upper extremities were intact, however, it was nil for the lower extremities. There were distinct sensory deficiencies in the left arm.

Interval between trauma and first HBO

HBO treatment was begun on day 22 when the sensory deficits in the left arm still had not improved. Due to the comminute fracture and the severe trauma to the thoracic spinal cord complete destruction of the latter at this level was anticipated.

Neurological findings before beginning of HBO

ASIA was 50 motor and 51 sensory

Neurological findings during and after HBO therapy

After a no-change course during the first week of treatment, he improved to 9, 8 and 7 on the VAS-scale from week 2 to 4.

Though the patient never had any problems during the HBO-treatment, he developed complications during his hospital stay: He had nosocomial pneumonia, rhabdomyolysis due to Cupimicin and bilateral central pulmonary artery embolism.

Final outcome

The sensory function of the left arm normalized whereas – as anticipated - both motor and sensory function of the lower extremities remained absent (ASIA sensory: 60, motor: 50). The patient was transferred to a rehabilitation unit.

The total number of HBO treatment sessions was 30.

Results:

VAS-scores

Both, motor function and sensibility as well as paraesthesia assessed by the VAS-score showed a constant improvement.
Of note, deficits of all three qualities motor function, sensibility and paraesthesia were not present in each patient.

Spearman's rank-order correlation analysis of the 10-grade subjective score showed a very high 92% (-,9220) negative correlation between treatment week and severity of motoric deficits with the symptoms declining over the treatment course. There was also a high correlation between treatment time and sensory deficits – 81% (-0,8194) and between HBO treatment time and paraesthesia symptoms – 74% (-,7489). P was 0,000 for all parameters.

Motor function changes

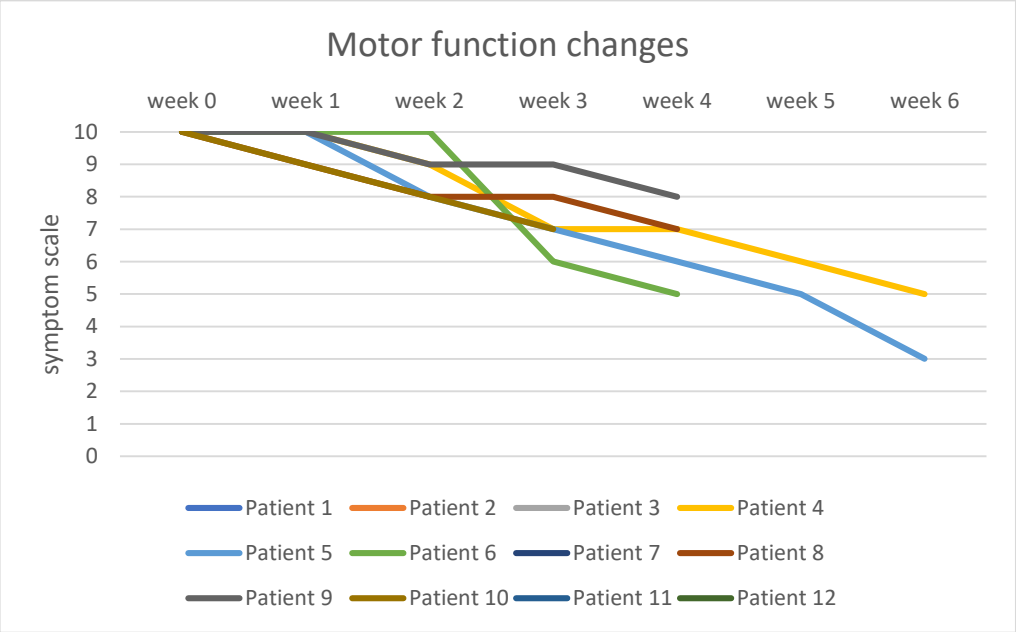

Chart 1: Motor function changes on the VAS-scale

Patient	week 0	week 1	week 2	week 3	week 4	week 5	week 6
Pat 1	no data						
Pat 2	no data						
Pat 3	10	no data	no data	no data	no data	1,5	
Pat 4	10	10	9	7	7	6	5
Pat 5	10	10	8	7	6	5	3
Pat 6	10	10	10	6	5		
Pat 7	no data						
Pat 8	10	9	8	8	7		
Pat 9	10	10	9	9	8		
Pat 10	10	9	8	7			
Pat 11	no data						
Pat 12	no data						

Table 1: Motor function changes on the VAS-scale

Sensible changes

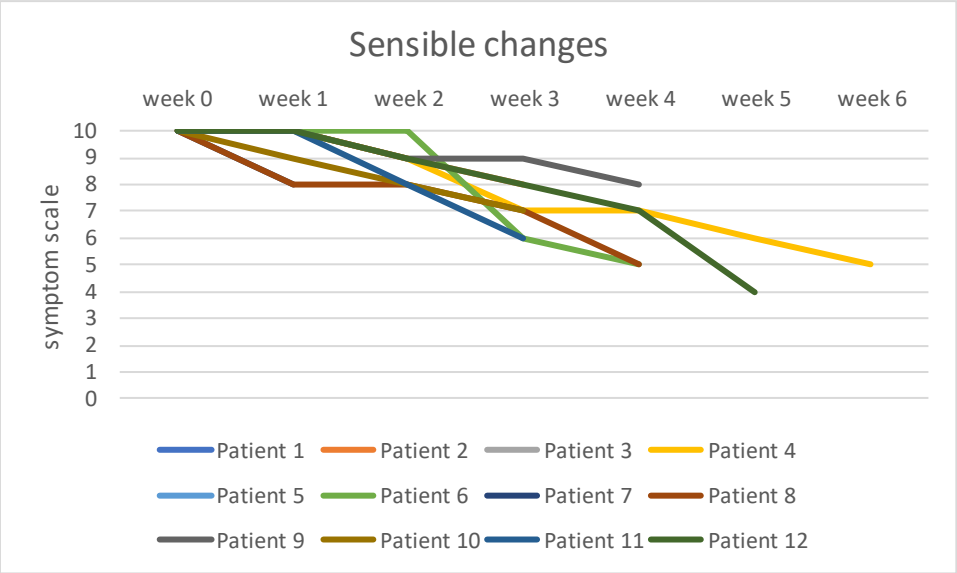

Chart 2: Sensible changes on the VAS scale

Patient	week 0	week 1	week 2	week 3	week 4	week 5	week 6
Pat 1	no data	no data	no data	no data			
Pat 2	10	10	9	8			
Pat 3	no data						
Pat 4	10	10	9	7	7	6	5
Pat 5	no data						
Pat 6	10	10	10	6	5		
Pat 7	10	8					
Pat 8	10	8	8	7	5		
Pat 9	10	10	9	9	8		
Pat 10	10	9	8	7			
Pat 11	10	10	8	6			
Pat 12	10	10	9	8	7	4	

Table 2: Sensible changes on the VAS-scale

Paraesthesia changes

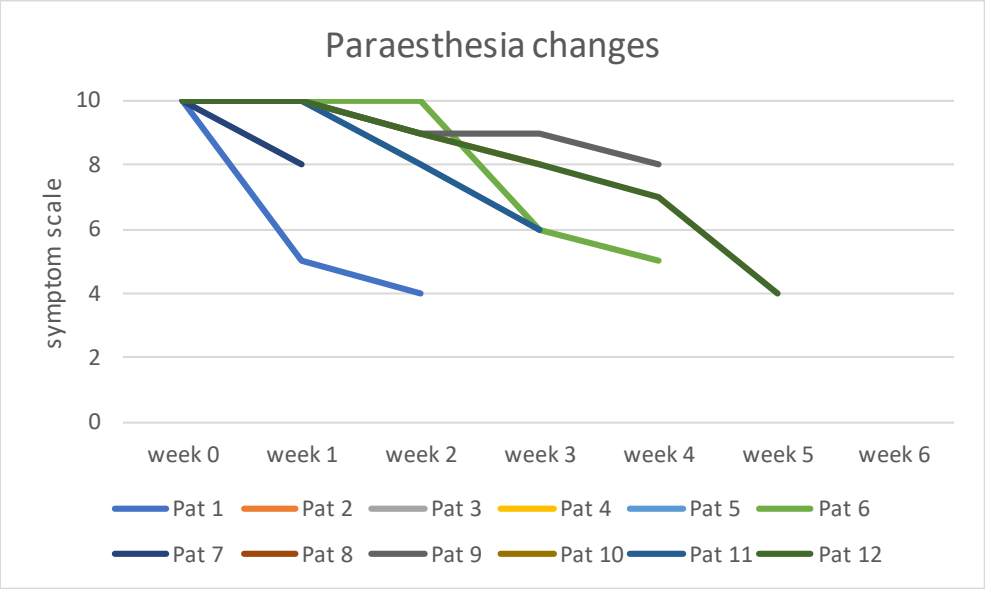

Chart 3: Paraesthesia changes on the VAS scale

Patient	week 0	week 1	week 2	week 3	week 4	week 5	week 6
Pat 1	10	5	4				
Pat 2	10	10	9	8			
Pat 3	no data						
Pat 4	no data						
Pat 5	no data						
Pat 6	10	10	10	6	5		
Pat 7	10	8					
Pat 8	no data						
Pat 9	10	10	9	9	8		
Pat 10	no data						
Pat 11	10	10	8	6			
Pat 12	10	10	9	8	7	4	

Table 3: Paraesthesia changes on the VAS -scale

ASIA Score

Sensory and motoric ASIA score was assessed before and after HBO therapy (Table 4).

ASIA score (sensory and motor) before and after HBO therapy.

	before HBO	after HBO	p (Wilcoxon test)
sensory	78.9+-9.5	92.2+-7.3	**p = 0.0031**
motoric	61.9+-8.9	78.1+-5.9	**p = 0.0031**

Table 4 ASIA score (sensory and motor) before and after HBO therapy.

There was a significant increase of both the sensory and motoric score (Wilcoxon matched pairs signed rank test: p = 0.0031). Eleven patients showed an improvement in both scores, one patient was improved in the sensory score and unchanged in the motoric score. In none of the patients a decrease of either score was found after HBO therapy.

ASIA sensory			ASIA motoric		
	before HBO	after HBO		before HBO	after HBO
Pat 1	100	112	**Pat 1**	100	100
Pat 2	96	100	**Pat 2**	52	54
Pat 3	106	112	**Pat 3**	97	100
Pat 4	95	110	**Pat 4**	82	97
Pat 5	85	100	**Pat 5**	56	77
Pat 6	102	105	**Pat 6**	76	87
Pat 7	106	110	**Pat 7**	78	90
Pat 8	6	93	**Pat 8**	1	78
Pat 9	68	88	**Pat 9**	50	76
Pat 10	32	48	**Pat 10**	31	55
Pat 11	90	106	**Pat 11**	90	100
Pat 12	51	60	**Pat 12**	50	50

Table 5 ASIA scores for each individual patient

Discussion:

The aim of this retrospective study was to evaluate the effects of intention-to-treat hyperbaric oxygenation therapy during the sub-acute and chronic stages of traumatic spinal injuries. Though the intricate mechanisms of HBO therapy for central nervous damage have been extensively documented in experimental studies (4 – 14) the clinical use for this indication is still sparse.

The reason for this is the fact, that most hyperbaric chambers are focused on treating diving accidents, thus being localized on shores rather than in hospitals specialized in treatment of central nervous injuries.

Nevertheless, HBO has been successfully used to reduce oedema in traumatic cranial injuries and first small case series have shown positive effects also in acute spinal cord injury (SCI) cases where HBO therapy was initiated within less than 24 for hours after the accident (11) Experimental research in animals – mainly rats - suggests that hyperbaric oxygen treatment can still have a significant impact even when the therapy is started after that “24h-window” has passed. In most animal studies severe degrees of spinal trauma were induced by either clipping the spinal cord over a defined time interval or by dropping a weight onto the exposed spinal cord (10)

Based upon these experimental findings HBO had been used in SCI at the Division of Thoracic and Hyperbaric surgery in cooperation with the trauma surgeons. Since there were only casuistic reports in the literature, HBO was applied with “intention – to – treat” the indication being limited to selected cases.

This study analysed 12 cases where HBO was begun after more than a day after the trauma to the spinal cord. The treatment was well tolerated by all patients, though some of them had multiple, severe injuries or required major surgery. There were also no side-effects of HBO.

Though the collective of patients was very small both the level and the type of the spinal cord injuries varied considerably. There were fractures of the cervical, the thoracic and the lumbar spine, the impact of the trauma had been delivered from different sides. Some patients were quadriplegic or paraplegic after the accident while others the neurological changes were confined to one limb.

In addition to the classic assessment according to the ASIA score (1) and the daily routine documentation of the hyperbaric sessions, each patient had a weekly questionnaire where improvements of their main complaints were subjectively assessed on a 10- grade VAS-score. 10 described the severity of the symptoms before HBO was started (“week 0”) and 0 was categorised as a complete resolution of symptoms. The VAS-based questionnaire differentiated between a) motor deficits, b) sensible deficits and c) paraesthesia. This method had been established because ASIA scoring does not always reflect minor subjective changes.

We found, that the overall subjective sensation as reflected in the VAS-scores showed a more optimistic assessment as the one given by ASIA-scoring. This may be due to an overrating of perceived changes fuelled by hope, but in some cases the subjective improvement correlated well with a favourable further course.

Yet all 12 patients reported improvement over the course of their HBO sessions. The statistical evaluation of both the established ASIA scoring and our VAS-scoring-system showed significant improvement values for both motor and sensory parameters.

Since there was no control group, it is not possible to state, whether the patients would have equally improved without HBO within the same time interval. Of note, however, is the fact that in most cases there had been no clinical improvement until HBO was started.

There is definitive need for randomized studies including large collectives of patients to further elucidate the effectiveness of HBO in spinal cord injury.

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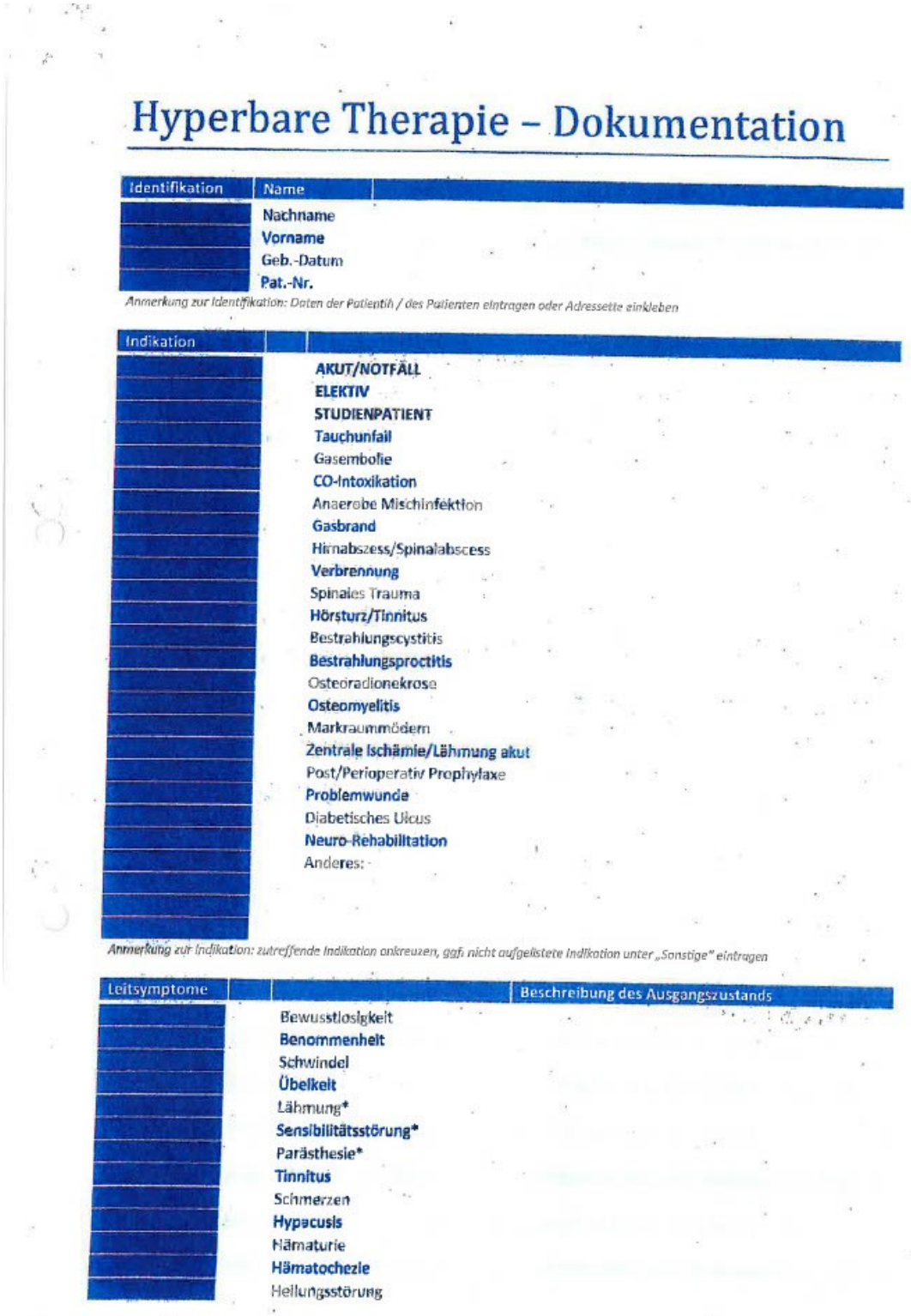
Appendix:
Questionnaire



Hyperbare Therapie – Dokumentation

Identifikation	Name
	Nachname
	Vorname
	Geb.-Datum
	Pat.-Nr.

Anmerkung zur Identifikation: Daten der Patientin / des Patienten eintragen oder Adressette einkleben

Indikation	
	AKUT/NOTFALL
	ELEKTIV
	STUDIENPATIENT
	Tauchunfall
	Gasembolie
	CO-Intoxikation
	Anaerobe Mischinfektion
	Gasbrand
	Hirnabszess/Spinalabscess
	Verbrennung
	Spinales Trauma
	Hörsturz/Tinnitus
	Bestrahlungscystitis
	Bestrahlungsproctitis
	Osteoradionekrose
	Osteomyelitis
	Markraumödem
	Zentrale Ischämie/Lähmung akut
	Post/Perioperativ Prophylaxe
	Problemwunde
	Diabetisches Ulcus
	Neuro-Rehabilitation
	Anderes:

Anmerkung zur Indikation: zutreffende Indikation ankreuzen, ggfs. nicht aufgelistete Indikation unter „Sonstige" eintragen

Leitsymptome		Beschreibung des Ausgangszustands
	Bewusstlosigkeit	
	Benommenheit	
	Schwindel	
	Übelkeit	
	Lähmung*	
	Sensibilitätsstörung*	
	Parästhesie*	
	Tinnitus	
	Schmerzen	
	Hypacusis	
	Hämaturie	
	Hämatochezie	
	Heilungsstörung	

	Anderes:
	Anderes:
	Anderes:

Anmerkung zu den Leitsymptomen: Bis zu drei Leitsymptome mit den Nummern 1 bis 3 versehen; klinische Beschreibung des Ausmaßes zu jedem der ein bis drei Leitsymptome eintragen

Nr.	Datum	bar	Verlauf	Nr.	Datum	bar	Verlauf	Nr.	Datum	bar	Verlauf
1.				11				21			
2.				12				22			
3.				13				23			
4.				14				24			
5.				15				25			
6.				16				26			
7.				17				27			
8.				18				28			
9.				19				29			
10.				20				30			

Anmerkung zu den Therapiesitzungen: jede Sitzung mit Datum, Druck und Dauer eintragen

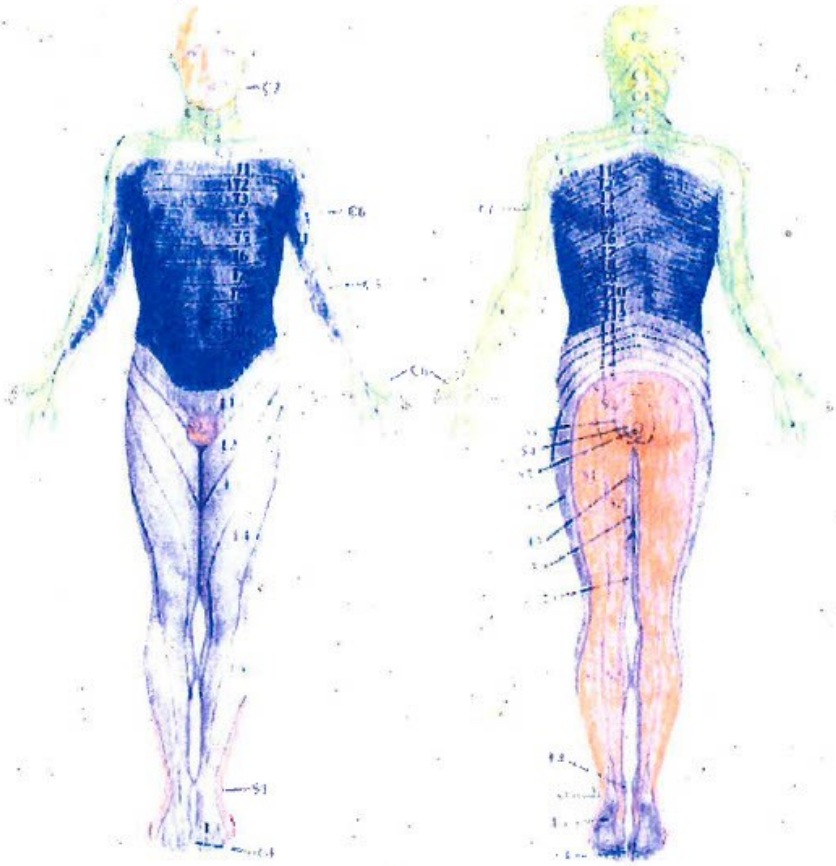
Evaluierung	vor Therapie	Woche 1	Woche 2	Woche 3	Woche 4	Woche 5
Datum						
1. Leitsymptom	10					
2. Leitsymptom	10					
3. Leitsymptom	10					

Anmerkung zur Evaluierung: Semiquantitative Beurteilung auf einer Skala von 0 bis 10; 10 entspricht dem Ausgangszustand laut Symptombeschreibung unter „Leitsymptome" (daher ist unter „vor Therapie" immer 10 eingetragen), 0 bedeutet vollständige Normalisierung.

Schema Sensibilitätsstörung/Parästhesie

Patient Name:

Datum:



Medical consent form HBO

Info **HBO**

Klinik/Praxis:

Sauerstoff-Überdruckbehandlung

(Hyperbare Sauerstofftherapie, HBO)

Bitte vor dem Aufklärungsgespräch lesen und den Fragebogen ausfüllen!

Sehr geehrte Patientin, sehr geehrter Patient, liebe Eltern,

die **Sauerstoff-Überdruckbehandlung (hyperbare Oxygenation**, abgekürzt **HBO**) wird bei unterschiedlichen Erkrankungen (z.B. Dekompressionskrankheit, Luft- oder Gasembolie, Funktionsstörungen des Innenohres, schlecht heilenden Wunden, Kohlenmonoxidvergiftung) sowie ergänzend zu anderen Behandlungsformen (z.B. zur Strahlentherapie) eingesetzt. Beim Einatmen von medizinisch reinem Sauerstoff in einer Überdruckkammer wird die Sauerstoffmenge, die in physikalisch gelöster Form im Blut und in den Geweben vorkommt, deutlich erhöht (etwa 20-fach). Damit lässt sich die Erkrankung oft günstig beeinflussen.

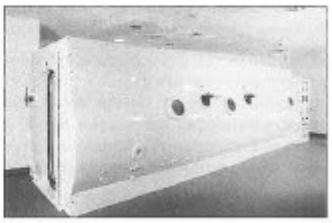


Abb. 1

In Ihrem Fall empfehlen wir/der die Grunderkrankung behandelnde Arzt die HBO zur Behandlung von:

_____

(bitte bezeichnen)

Über Behandlungsalternativen informieren wir Sie gerne im Aufklärungsgespräch.

Abb. 2

Durchführung der Behandlung (HBO)

Moderne Druckkammern (vgl. Abb. 1 und 2) verfügen über mehrere bequeme Sitzplätze, Sie sind also während der Behandlung nicht alleine.

Eine Behandlungssitzung gliedert sich in drei Abschnitte:

1. Zunächst wird der Luftdruck in der Kammer langsam (10 - 20 Minuten) über den normalen atmosphärischen Umgebungsdruck hinaus angehoben. Während der Druck erhöht wird, müssen Sie zum Ausgleich Nase und Mund verschließen und pressen; dieses „Valsalva-Manöver" werden wir vorher mit Ihnen üben. Hilfreich sind auch Bonbons und Getränke, die das Schlucken erleichtern.
2. Nach Erreichen des Behandlungsdruckes wird Ihnen reiner (100%iger) Sauerstoff zugeführt, meist über eine Atemmaske (vgl. Abb. 2), seltener über ein Kopfzelt. Dazwischen atmen Sie nach individueller Dosierung ohne Maske normale Raumluft (etwa 21% Sauerstoff).
3. In der letzten Phase wird der Kammerdruck wieder auf normalen Luftdruck gesenkt.

Abb. 3

Der Innenraum der Kammer wird zu Ihrer Sicherheit ständig über eine Videokamera eingesehen (vgl. Abb. 3).

Eine Gegensprechanlage ermöglicht es Ihnen, jederzeit und ohne Betätigen eines Schalters, mit dem betreuenden Arzt/Pflegepersonal in Verbindung zu treten. Falls erforderlich, kann der Arzt/das Pflegepersonal über eine Schleuse die Hauptkammer unverzüglich betreten. Sie können die Behandlung in Begleitung des Arztes/des Pflegepersonals jederzeit unterbrechen oder beenden.

Eine einzelne Behandlungssitzung dauert etwa 90 - 140 Minuten. Während dieser Zeit können Sie sich entspannen, lesen und/oder Musik hören. In aller Regel sind zur Behandlung mehrere Sitzungen erforderlich. Gesamtzahl und

Empfohlen von der Deutschen Gesundheitshilfe e.V.

DiOmed-Aufklärungssystem. Herausgeber: Prof. W. Weißauer, Prof. K. Ulsenheimer (Medizinrecht).
Autoren: Dr. F.-A. Buchner, Prof. W. Weißauer.

Bestell-Nr. 01/075

Dauer sind abhängig von der Grunderkrankung und dem Heilungsverlauf. Wir werden das vorgesehene Behandlungsschema vor und während der Behandlungen mit Ihnen abstimmen.

Welche Nebenwirkungen und Komplikationen können auftreten?

Die meisten der nachfolgend aufgeführten Nebenwirkungen und Komplikationen lassen sich vermeiden, wenn Sie die Fragen zur Anamnese sorgfältig beantworten und die Verhaltenshinweise gewissenhaft befolgen. Aufgrund von Voruntersuchungen schließen wir Patienten mit erhöhten Risiken von der Behandlung aus, es sei denn, sie ist lebensnotwendig (z.B. bei Gasbrand).

Manche Patienten empfinden die Behandlung als etwas anstrengend und fühlen sich nach der Behandlung **müde**. Sie sollten daher nach der Behandlung eine Ruhepause einplanen.

Gelingt der Druckausgleich ausnahmsweise nicht (z.B. wegen einer Erkältung), können geschlossene luftgefüllte Körperhohlräume sowie das umgebende Gewebe durch die Drucksteigerung geschädigt werden. So kann sich z.B. das Trommelfell bei der Druckänderung stark ausdehnen. Dies führt zunächst zu einem **belegten Gefühl** im Ohr, dann zu **stechenden Schmerzen**. Nimmt der Druckunterschied weiter zu, kann ein Trommelfellriss, ein **Erguss oder** eine **Entzündung im Mittelohr** die Folge sein. Ähnliche Komplikationen können auch im Bereich der **Nasennebenhöhlen** auftreten; eventuell vorhandene Zysten können platzen.

Maßnahmen zur Vorbeugung: Führen Sie die Ihnen gezeigten Maßnahmen zum Druckausgleich („Valsalva-Manöver") korrekt durch, wenden Sie ggf. Nasentropfen oder Nasenspray an und/oder lassen Sie sich, falls erforderlich, ausschleusen.

Für lungengesunde Patienten ist das Risiko eines **Lungenrisses** sehr gering. Die Luft kann dann aus der Lunge in den Brustkorb (Pneumothorax) oder in die Blutgefäße entweichen. Bei Patienten mit akuter oder chronischer Bronchitis, Asthma oder Lungenblähung (Emphysem) ist das Risiko deutlich erhöht.

Wird reiner Sauerstoff unter erhöhtem Umgebungsdruck über längere Zeit eingeatmet, kann eine **Sauerstoffvergiftung** auftreten; es kann dadurch zu einer **Schädigung der Lunge** (z.B. Lugenfibrose, verminderte Atemkapazität) **und/oder des Nervensystems** (z.B. Krampfanfall, der jedoch nichts mit einer Epilepsie zu tun hat, Röhrensehen, Gesichtsfeldeinschränkung, Angstgefühl) kommen. Die Behandlungsbedingungen werden so gewählt, dass solche Schädigungen nur sehr selten (1 : 10.000 bis 1 : 20.000) auftreten.

Nach zwanzig oder mehr Behandlungen kann sich, v.a. bei über 40-jährigen Patienten, das **Sehvermögen verschlechtern** (z.B. Kurzsichtigkeit); meist wird es etwa 6 Wochen nach Behandlungsende wieder besser. Bei Patienten mit **Grauem Star** (Katarakt) kann die Erkrankung fortschreiten. Eine vorhandene Weitsichtigkeit verbessert sich bei manchen Patienten während der Behandlung vorübergehend. Eine neue Brille sollten Sie sich daher frühestens 8 Wochen nach Ende der HBO verordnen lassen.

Auch ein möglicherweise auftretendes **Taubheitsgefühl in den Fingern** verschwindet in aller Regel etwa 6 - 8 Wochen nach Behandlungsende.

Durch **Flüssigkeitsansammlung im Ohr** kann ein Gefühl entstehen, als ob ein Kissen auf den Ohren läge. Dieses Gefühl verschwindet meist mit Verlassen der Überdruckkammer oder kann gegebenenfalls mit Nasentropfen behandelt werden.

Bitte unbedingt beachten! Sofern ärztlich nicht anders angeordnet!

- Vor der Behandlungssitzung

  Bitte **rechtzeitig** zu den vorgesehenen Terminen kommen, damit Patienten, die mit Ihnen an der Behandlung teilnehmen, nicht warten müssen.
  Folgende Gegenstände bitte nicht in die Überdruckkammer mitnehmen, da sie beschädigt werden können oder eine Gefahr darstellen:
  - **Herausnehmbare Implantate** (z.B. Kontaktlinsen, Glasaugen, Hörgerät). Patienten mit nichtherausnehmbaren Implantaten (z.B. Herzschrittmacher, Medikamentenpumpen, Brustprothesen) können in aller Regel nur nach vorheriger besonderer Überprüfung in der Überdruckkammer behandelt werden
  - **Schmuck** (z.B. Uhr, Ohrringe, Ketten, Ringe). Wertgegenstände möglichst nicht zur Behandlung mitbringen
  - **Luftgefüllte, geschlossene Gegenstände** (z.B. Kugelschreiber, Filzstifte, Dosen)
  - **Elektronische Geräte** (z.B.Walkman, Notebook, elektronischer Kfz-Schlüssel)
  - **Feuerzeug, Streichhölzer, Wärmegeräte, Wärmemittel**

– **synthetische Kleidung.**

Bitte nehmen Sie in die Kammer nur notwendige Utensilien (z.B. Taschentücher, Lektüre, Spiele) mit. Getränkedosen und Nasensprays sollten vorher geöffnet, Kosmetika und Haarsprays für den Aufenthalt in der Druckkammer auf ein Minimum reduziert werden. Nicht druckfeste Gegenstände, die versehentlich mitgenommen wurden, können während der Behandlung über eine Materialschleuse aus der Kammer entfernt werden. Alle Gegenstände, die Sie mit in die Druckkammer nehmen möchten, müssen vorher dem betreuenden Arzt/dem Pflegepersonal gezeigt werden. Sie dürfen nur mitgenommen werden, wenn das Pflegepersonal dies gestattet.
Bitte denken Sie daran, dass der Gang zur Toilette während der Behandlung nur durch den Abbruch der Behandlungssitzung möglich ist.
Während der Behandlung wechselt die Temperatur in der Kammer spürbar. Anfangs erwärmt sich die Kammeratmosphäre, gegen Ende kühlt sie sich ab. Bitte berücksichtigen Sie dies bei der Wahl Ihrer Kleidung.
Teilen Sie dem betreuenden Arzt/dem Pflegepersonal vor Antritt einer Behandlungssitzung alle **Änderungen Ihres Befindens** (z.B. akute Erkrankungen, Verschlechterung des Sehvermögens) mit und informieren Sie uns über neue oder geänderte ärztliche Behandlungen und Medikamente!

- **Während der Behandlungssitzung**

Unterbrechen Sie die Sauerstoffatmung und sagen Sie unverzüglich laut und deutlich „Stopp", wenn sich Ihr Befinden ändert, z.B. bei

- Unwohlsein
- Kribbeln in den Fingerspitzen
- Zucken der Gesichtsmuskulatur
- stechenden Schmerzen im Bereich von Stirn oder Gesicht
- Sehstörungen (z.B. Doppelbilder, eingeschränktes Sehfeld, „Röhrensehen")
- zunehmendem Druck auf den Ohren, der sich auch mit den gezeigten Maßnahmen zum Druckausgleich nicht beheben lässt
- Zahnschmerzen
- Schmerzen beim Atmen oder Luftnot
- Husten, Brennen hinter dem Brustbein.

Die meisten Nebenwirkungen kündigen sich durch frühe Symptome an. Durch einen rechtzeitigen Abbruch der Behandlung lassen sich in aller Regel Schäden vermeiden.
Insbesondere in der Phase der Druckabsenkung am Ende einer Behandlung niemals die Luft anhalten, sondern stets durchatmen!

Rauchen und offene Flammen sind im gesamten Bereich der HBO-Einrichtung wegen der hohen Brandgefahr strengstens untersagt!

- **Nach der Behandlungssitzung**

sollten Sie sich noch etwa **30 Minuten** im Bereich der Klinik/Praxis aufhalten.

Kostenübernahme:

Bitte informieren Sie sich über die Übernahme/Erstattung der Kosten für die HBO bei der zuständigen Krankenkasse.

Unterschrift der Ärztin/des Arztes: _____

Ethikvotum:

Ethikkommission

Medizinische Universität Graz

Auenbruggerplatz 2, A-8036 Graz
ethikkommission@medunigraz.at
Tel.: +43 / 316 / 385-13928, Fax: -14348

VOTUM
gültig bis 03.05.2019

EK-Nummer:	30-124 ex 17/18
Studientitel:	Hyperbaric Oxygenation (HBO) as an additive measure in the late-course neurohabilitation of posttraumatic spinal cord injuries. Retrospective case-based analysis.
Prüfer:	Univ.-Prof. Dr. Freyja-Maria Smolle-Jüttner Abteilung für Thorax- und Hyperbare Chirurgie, Medizinische Universität Graz
Sponsor:	Med.Uni Graz, Univ. Klinik für Chirurgie
Ansprechpartner:	Univ.-Prof. Dr. Freyja-Maria Smolle-Jüttner, 8036 Graz, Auenbruggerplatz 29
CRO:	-
Antragsteller:	Abteilung für Thorax- und Hyperbare Chirurgie, Medizinische Universität Graz
Ansprechpartner:	Univ.-Prof. Dr. Freyja-Maria Smolle-Jüttner, 8036 Graz, Auenbruggerplatz 29

Die o.a. Studie wurde von der Ethikkommission erstmals im 'expedited Review' am 20.12.2017 behandelt. Die Ethikkommission ist zu folgendem Schluss gekommen:

Es besteht kein Einwand gegen die Durchführung der Studie in der vorliegenden Form.

Kommissionsmitglieder, die für diesen Tagesordnungspunkt als befangen anzusehen waren und daher gemäß Geschäftsordnung an der Entscheidungsfindung und Abstimmung nicht teilgenommen haben: keine

Zur Beurteilung vorliegende Dokumente:

Dokumente eingegangen am 05.12.2017, begutachtet im 'expedited Review' am 20.12.2017	
✓ Antragsformular ECS	05.12.2017
✓ Originalprotokoll KonzeptformularWissenschaftlicheArbeiten Zajac 01	28.11.2017
✓ CV CV_Smolle-Juettner englisch 20.10. 2017 01	20.10.2017
✓ CV CV Zajac 01	05.12.2017
✓ Sonstiges: Antrag auf Erlass des Bearbeitungsbeitrags 01	05.12.2017
Dokumente eingegangen am 26.04.2018 (in der nächsten Begutachtung mitbegutachtet)	
✓ Letter of Authorization	20.04.2018
Dokumente eingegangen am 02.05.2018, begutachtet im 'expedited Review' am 03.05.2018	
✓ Antragsformular ECS Unterschriftenseiten	26.04.2018

Die Ethikkommission geht - rechtlich unverbindlich - davon aus, dass es sich um keine klinische Prüfung nach AMG bzw. MPG handelt.

Es handelt sich um eine Studie im Rahmen einer Diplomarbeit.

Das Votum der Ethikkommission berührt in keiner Weise die alleinige Verantwortung der Prüferin / des Prüfers / der Prüfer für die ordnungsgemäße Durchführung der Studie unter Einhaltung aller einschlägiger gesetzlicher Bestimmungen und Richtlinien.

Weiters machen wir darauf aufmerksam, dass der Kommission unverzüglich zu melden sind:

- Abweichungen vom Protokoll aus Sicherheitsgründen oder Protokolländerungen

Medizinische Universität Graz, Auenbruggerplatz 2, A-8036 Graz. www.medunigraz.at
Rechtsform: Juristische Person öffentlichen Rechts gem. Universitätsgesetz 2002. Information: Mitteilungsblatt der Universität und www.medunigraz.at. DVR-Nr. 210 9494, UID: ATU 575 111 79. Bankverbindung: Bank Austria Creditanstalt BLZ 12000 Konto-Nr. 500 948 400 04, Raiffeisen Landesbank Steiermark BLZ 38000 Konto-Nr. 49510,

- Änderungen, die das Risiko der Teilnehmer/-innen erhöhen oder die Durchführung der Studie wesentlich beeinflussen

- Mutmaßliche unerwartete schwerwiegende Nebenwirkungen - SUSARs (AMG-Studien ab 1.5.2004) oder schwerwiegende unerwünschte Ereignisse - SAEs (andere Studien)

- Jegliche Information über sonstige Umstände, die die Sicherheit der Teilnehmer/-innen oder die Durchführung der Studie beeinträchtigen können

Dieses Votum gilt für ein Jahr ab dem Datum der Ausstellung. Bei längerer Studiendauer ist rechtzeitig vor Ablauf der Gültigkeit des Votums ein Zwischenbericht vorzulegen (Berichtsformular), um eine etwaige Verlängerung zu erlangen.

Graz, 03. Mai 2018

Univ.Prof.DI Dr.Josef Haas
Vorsitzender

i.V. Univ.Prof.Dr.Hermann Toplak
Stv. Vorsitzender

Achtung: Bitte bei allen das Projekt betreffende Schreiben oder telefonischen Anfragen die EK-Nummer angeben!