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Gadodiamide injection for enhancement of MRI in the CNS—applications, dose, field and time dependence

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The aims of this study using Gadodiamide injection were to investigate:

- Whether Gadodiamide injection was comparable to Gd-DTPA for the enhancement of CNS lesions.
- The contrast effect at different field strengths.
- The effective time-window for the enhancement of blood-brain barrier damage (BBB damage).
- The relations between the concentration of contrast agent and enhancement in phantoms, and to correlate the results to doses given to patients.
- The use of a higher dose in two important clinical problems; the detection of metastases in the brain, and the evaluation of patients with failed back surgery syndrome (recurrent pain after surgery for lumbar disc herniation).

Results and conclusions

- Gadodiamide injection was comparable to Gd-DTPA with regard to both safety and diagnostic efficacy in the CNS.
- The contrast effect of Gadolinium contrast agents is higher at 1.5 T than at 0.3 T both in phantoms and patients with a maximum ratio (signal lesion/signal grey matter) more than 50% higher at 1.5T.
- To achieve high contrast effect, heavily T1-weighted images are important. Prolonging the TR from 400 ms to 600 ms reduced the ratio by 15–45% depending on concentration.
- The effective time-window for imaging of BBB damage is between 2–5 and 25–30 minutes after injection and several scans can be performed without loss of enhancement.
- To provide maximum detectability of BBB damage in patients, higher doses of Gd contrast media should be useful, especially at low field strengths, as the doses used clinically today do not utilize the maximum contrast effect.
- High-dose (0.3 mmol/kg b.w.) contrast-enhanced MRI (0.3 T) with Gadodiamide injection allowed detection of significantly more and smaller metastases (i.e. BBB damage) than standard-dose (0.1 mmol/kg b.w.).
- High-dose (0.3 mmol/kg b.w.) contrast-enhanced MRI (0.3T) did not increase the diagnostic information for the evaluation of patients with failed back surgery syndrome compared to standard-dose (0.1 mmol/kg b.w.) MRI.

Hemophilia A and B with special reference to prevention and treatment of arthropathy

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In patients with severe hemophilia it is today possible to prevent the development of arthropathy by giving effective continuous prophylaxis from an early age, thus preventing the VIII:C or IX:C concentration from falling below 1% of normal. All the signs show that if a high-dose prophylactic regimen—that is, 3,000–5,000 U/kg body weight annually—is started as early as 1–2 years of age, the patients' factor VIII/IX concentrations can be maintained at a level of at least 1% and bleeds and joint defects can be virtually eliminated, allowing patients to live more or less normal lives, both physically and socially. Prophylaxis is also largely responsible for the changing picture in orthopedic surgery in hemophilia today, with a decreasing need of operations, an increasing average age of the patients, and a change in the kinds of operations performed. Although its outcome is inferior to that obtained in arthrosis, hip joint replacement in hemophilia is a viable option and should be considered as it is of value in certain cases. Surgery may also be undertaken in HIV-positive hemophiliacs under similar premises as for HIV-negatives, though indications for major surgery require meticulous consideration. In young hemophiliacs with inhibitors, a patient group otherwise difficult to treat, radioactive synoviorthesis is an appropriate treatment. The method is characterized by its ease of performance and limited requirements, and in most cases results in a manifest decrease in the joint bleeding frequency.

Vibration-induced neuropathy in the hand

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The aim of this study was to investigate clinical, pathophysiological and structural aspects of vibration induced peripheral neuropathy since work with hand-held vibrating tools may lead to progressive neurological and vascular hand symptoms. Symptomatic vibration-exposed men were examined clinically and by neurography tactilometry, and vibrometry and by measurement of temperature perception thresholds. Studies on regeneration and morphology of nerves were done in vibration-exposed rats and humans.

Three groups of hand symptoms could be distinguished: sensorineural symptoms, vasospastic symptoms, and a combination of both. Cold intolerance emerged as a separate symptom in half of the patients with sensorineural symptoms only.

Tactilometry in referents showed that the vibrotactile perception thresholds depended on the frequency of stimulus and on age. Equations make correction for age possible.

Neural conduction, vibrotactile sense, and temperature sense were impaired in all groups of patients. Cold intolerance, severe sensorineural—but not vascular—symptoms, bilateral symptoms, and muscular weakness were associated with further impairment of the vibrotactile sense. Neurography showed involvement of the median nerve in the carpal tunnel and distally, but no changes in the ulnar nerve. Neither did it show any difference between patients with and without clinical carpal tunnel syndrome. Vibrotactile thresholds—but not neurography—differed between the sensorineural stages.

The regenerative capacity of vibration-exposed rat sciatic nerves was impaired probably due to an effect on the neurone and on non-neuronal cells. Morphologically, the dorsal interosseous nerve in vibration-exposed patients showed demyelination in various stages of development, endoneurial and perineurial fibrosis, and loss of axons.

The results of this study underline the importance of the neurological component of vibration-induced injury. Subjectively experienced and objectively shown, it may severely interfere with hand function.

Amputation for vascular disease—prognostic factors for healing, long-term outcome and costs

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General characteristics and outcome was evaluated in 177 consecutive patients who underwent a major amputation in a defined population. Smoking and diabetes lowered the mean amputation age. Healing failure at six months was seen in 24% of transtibial and in 11% of transfemoral amputees. Preoperative absence of gangrene and hemoglobin >120 g/L increased the risk of healing failure. Six months after amputation, about 1/3 used a prosthesis, 1/3 were confined to bed or a wheelchair and 1/3 had died.

We analyzed all surgical procedures, total hospital stay and hospital costs in 321 consecutive patients having surgery for critical leg ischemia until at least 6-years postoperatively or until death. The first recorded operation during the inclusion year was a vascular procedure in 2/3 of all patients and a major amputation in 1/3. One third of those undergoing a reconstructive vascular procedure and half of those having a restorative vascular procedure eventually underwent an ipsilateral major amputation. The mean total long-term hospital costs were high (47,000 USD/patient), because of the need for repeated surgery (mean=3 procedures) and long hospital stay (mean=117 days).

Thirty-two consecutive patients who underwent a transtibial amputation were subjected to nutritional assessment and given supplementary nutrition for 11 days. Twenty-eight patients were classified as malnourished (88%). Supplementary nutrition improved wound healing in patients with transtibial amputation, compared to a matched control group.

All diabetic patients with a deep foot infection (n=223) were included consecutively during 10 years, and prospectively followed until healing for at least six months or until death. Multi-disciplinary treatment resulted in a low major amputation rate, but almost all patients needed local surgery. Duration of diabetes <14 years, a palpable popliteal pulse, a toe blood pressure >45 and an ankle blood pressure >80 mmHg, absence of exposed bone and a white blood cell count <12x10⁹/L were all related to healing without amputation.

Whiplash injury—a clinical, radiographic and psychological investigation

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Whiplash injury is a common and troublesome disorder and approximately 10-40 per cent of its victims develop chronic symptoms. The annual incidence is estimated at 1/1000 inhabitants and the prevalence at 1%. The cause of chronic symptoms after whiplash injury is still unknown and no effective treatment has been presented so far.

The present study is divided into two parts; the first part includes clinical, radiographic and psychological investigations, and the second part the effect of surgical intervention as well with medication.

MRI studies (n=39) showed a larger proportion of pathologic findings compared to normal subjects, but no correlation with initial neurologic deficits was found. At the 2-year follow-up all patients with disc herniations with medullary impingement had persistent symptoms. Three patients had disc herniations that deteriorated from slight and moderate initial changes on the MRI to severe changes with medullary cord impingement. This deterioration might be a first sign of disc degeneration. Thus our results indicate that disc pathology is a contributing factor in the development of chronic symptoms.

Measurements from standard lateral radiographs taken in neutral position were evaluated (n=48). A graphic digitizer connected to a microcomputer was used and the sagittal diameters were determined. Multivariate analysis of variance showed that the spinal canal was significantly smaller in patients with persistent symptoms indicating that a narrow spinal canal is unfavourable in patients subjected to whiplash injury.

A psychological investigation (n=70) revealed no relationship between pre-existing personality traits and persistent symptoms. In our study, whiplash patients showed no differences in personality traits compared to normal controls.

Our results after discectomy and anterior cervical fusion (n=20) because of chronic symptoms after whiplash injury were not satisfactory. We noticed that about half of the cases had less headache and neck pain but no beneficial effects on radicular pain, vertigo, visual and auditory symptoms were observed. Based on the criteria of a surgical evaluation, two patients were classified as good, nine as fair and nine as poor.

A prospective randomised double-blind study of high-dose methyl-prednisolone compared to placebo was conducted (n=40). A clinical follow-up with repeated neurological examinations and a standardised questionnaire including VAS-scales and a pain sketch form were used for the evaluation of initial symptoms, before drug administration and at the follow-ups at 2 weeks, 6 weeks, and 6 months after the injury. At the 6-month follow-up there was a significant difference between the actively treated patients and placebo concerning disabling symptoms defined as inability to return to previous work, number of sick-days and sick-leave profile. All the actively treated patients had returned to work and none had multiple symptoms though three of them complained of intermittent neck pain. Our conclusion is therefore that acute treatment with high-dose corticosteroids might be beneficial to the prevention of disabling symptoms after whiplash injury.

Coping, pain and disability in patients with chronic inflammatory and musculoskeletal diseases

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The main interest of this study is in the behavioural and psychological aspects of adjusting to a chronic, periodically painful disease. This study focuses on the concept of coping, the modes of coping, the context of coping, and the factors related to these.

Coping is defined as constantly changing cognitive and behavioural effort to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person. Coping responses are considered to result from the patients' assessments of the stresses that they face and of the resources available.

Antonovsky has addressed the issue of psychological resources with his theory about the sense of coherence. Antonovsky's theory of how mental resources can promote health offers a general frame of reference for studies of health. A strong sense of coherence means that environmental stimuli are experienced as comprehensible, manageable and meaningful.

In this thesis, management of pain and disability is studied in groups of patients with different types of musculoskeletal and chronic, inflammatory diseases: systemic lupus erythematosus (SLE); osteoarthritis (OA); rheumatoid arthritis (RA) and fibromyalgia; haemophilia and chronic low-back pain (CLBP). Common to these groups of patients are pain, as related to pathological changes in the joints, functional disability, chronicity and the unpredictable course of the disease. Thus, coping with these diseases involves facing a number of stresses and challenges. In addition to coming to terms with the meaning of the illness for one's life and the more existential issues of disease progression and deformity, patients must cope with pain, stiffness and physical-activity restrictions on a daily basis.

Several questionnaires were used to collect data concerning the use of coping strategies, the role of patient education, pain, disability, emotional well-being and the sense of coherence.

The results indicated that comprehensive guidebooks are of value for patients with chronic musculoskeletal diseases although solely information does not lead to changes in psychological variables. Regarding the use of pain coping strategies the following results were found: The strategies most frequently used by the patients with haemophilia were distraction and pain control. Re-interpreting pain was a strategy which was rarely used in this sample, although it was correlated with lower levels of pain. The pattern of using the coping strategies distraction, pain control and re-interpreting pain was not dependent on the degree of pain. Furthermore, the use of the strategies was not complementary. If the patients increased the use of the strategies distraction, pain control and re-interpreting pain, they also increased the use of other strategies.

For the patients with chronic low-back pain it was found that the sense of coherence was related to the way in which patients perceived their disease and the way they adjusted to it.

From the results of this thesis, a pattern emerges of the relationships between the factors which influence patients' emotional well-being and management of chronic inflammatory and musculoskeletal diseases. Pain and disability are the baseline conditions of the patient. Age and sense of coherence act as moderators, whereas the catastrophizing strategy can be identified as a mediator in the process of coping.