

A New Concept for Evaluation of Long-Term Medication Effects on Gait Parameters

Schmid Oskar A., Than Peter

Abstract— To have no side effects of medication is essential for the acceptance by the patient. Therefore the evaluation of possible side-effects of medication is an important part in drug development or after launch evaluations. But also on the primary effect, especially in pain killers, must be focused.

Most of the methods are invasive or painful, like the CO₂-Inflation into to nose to measure the cortex activity after pain killer application.

A common side effect of drugs, especially pain killers, is the negative alteration of the gait in patients due to inconstancy or even falls due to side effects. Therefore the evaluation of the effects of drugs on gait parameters is of importance.

Different drug application, e.g. neuropathic pain killers, opioids or Cox-2-inhibitors, may have different effects on the gait parameters.

The new concept consists of noninvasive parameters which could be accomplished in different environments and with low side costs. The gait of the person to be evaluated is monitored by the system. The gait analysis consists of a walkway or treadmill in order to measure the velocity of gait. The other parameters are conducted by EMG of different leg muscles and a pressure distribution measurement.

The present pilot study evaluates for the first time the long-term effect of a Cox-2 Inhibitor (Celecoxib 200mg, once a day) on the gait parameters during 4 weeks of application. The patients suffered from pain during walking or standing in one hip unilaterally. The gait velocity increased by 0.66km/h (SD 0,52) or 25.4% from baseline to the 4 weeks measurement. Effects on the EMG patters and the pressure distribution were seen in the pilot study, but numbers of patients were too few for a real statistically relevant effect. The new concept shows that the less cost effective parameter of gait velocity is a good parameter to show effects on gait. But the further parameters of pressure distribution and EMG may show in larger numbers of investigated patients more difficile effects of brain affecting drugs.

Index Terms— Drug, drug development, gait, gait velocity, gait analysis; EMG, pressure distribution, cox-2-inhibitor.

I. INTRODUCTION

In the arthritis of the hip biomechanical und structural alteration are present. Painkillers like nonsteroidal anti-inflammatory drugs (NSAID) reduce the pain and the inflammation caused by the joint alteration based on different causes.

There are some models to measure pain reduction objectively with the drawback of invasiveness. E.g. painful inflation of

CO₂ into the nose is used to elicit cortical activity. The more reduction in activity the more powerful was valued the medication [1], [2].

Non-invasive methods were mostly based on scores like the Harris-Hip-Score or WOMAC Score. These questionnaires have a very high amount of subjective parameters. Therefore they are suggestible.

In arthritis obvious gait disturbances are seen by human eye. But they could be measured by instrumented gait analysis. Only a few parameters are known to be altered by patients with arthritis, especially in hip osteoarthritis: gait velocity and stride length [3]. No reliable data is available for the symmetry of gait [4].

So far no information is known about the *long-term* effect on gait parameters using NSAID or Cox-2-Inhibitors in hip osteoarthritis.

The present pilot study should evolve objectively and non-invasively the effect of the Cox-2 Inhibitor celecoxib during a four week therapy on gait parameters in patients with hip arthritis without any other side therapies.

II. METHODS

A. Gait parameters

The parameter gait velocity was selected for the primary outcome parameter, because it is known to be altered in arthritis also in the hip joint arthritis [3], [4].

A walk way or a treadmill could be used to measure gait velocity. In this pilot study we used a treadmill, which alters the treadmill speed according to the patient naturally speed by using an ultrasound sensor. The measured treadmill speed was therefore the natural speed of the patient.

Another parameter using EMG with on- and offset of muscle activity was used to get more information about to symmetry aspects of gait. The EMG System from biovision, Wehrheim, Germany was used. Timing parameters of EMG ware used to measure the on- and off- profiles of the different muscles during the gait cycle [5]. EMG measurement were performed on following muscles: M. vastus medialis, M. vastus lateralis, M. rectus femoris, M biceps femoris and M tibialis anterior. Ground reaction parameters and pressure distribution were gathered using the Tekscan F-scan foot system.

B. Patients and Medication

Five patients (one female, four males) with different stages in unilateral hip osteoarthritis and limitations in function were measured in the pilot study. No other locations of osteoarthritis, varus- or valgus-malalignments or pain areas in the lower limbs were reported by the patients.

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The average in age was 52.2 years (29 to 74 years). Four patients suffered from pain during walking or standing with a pain free walking distance of a maximum of 200m. One patient mentioned no pain free walking distance and pain also during the night and at rest.

The patients did not receive any further therapy, e.g. physiotherapy, before and during the pilot study.

Before the measurements started no pain medication was used by the patients for the period of two weeks.

The first gait analysis was performed before starting the medication with celecoxib 200 mg every morning one dosage for 4 weeks. Rescue medication was given to the patients with paracetamol 500mg up to 3 times a day.

No other therapies were performed during at the average of four weeks period of medication with celecoxib 200 mg once per day.

The second measurement of gait parameters was performed on the last day of medication.

III. RESULTS

All five patients could be measured at the beginning and the end of the medication period. None of them had to take any rescue medication. Four patients reported about subjective improvement in gait and a significant reduction of pain during load of the limb with osteoarthritis of the hip.

The patient with the most severe alteration in radiological signs of arthritis and the most limitation in joint motion before had no subjective change.

A. Gait parameters

The gait velocity before medication was on average 2.84 km/h or 0.79 m/s (SD 1.62 km/h; 0.45 m/s).

After medication an increase of 0.66 km/h or 0.18 m/s to an average speed of 3.50 km/h or 0.97 m/s (SD 0.52 km/h; 0.14 m/s)

B. EMG parameters

The EMG parameters before and after medication revealed a shift to a normal pattern of gait [5]. Due to the small amount of hip osteoarthritis patients no significant change could be evaluated (Fig 1).

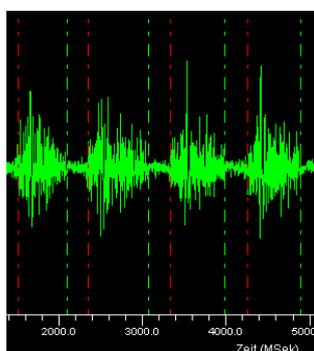


Fig.1: Phase activity of the EMG vastus medialis
Red: start of EMG activity
Green: end of EMG activity

C. Pressure distribution parameters

Also the Pressure distribution parameters before and after medication did not show a significant shift to a (complete) symmetry of gait (Fig 2).

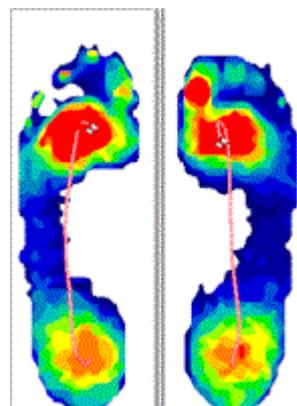


Fig.2: Pressure distribution comparison left-right in osteoarthritis of the hip

IV. DISCUSSION

The new concept for evaluation of long-term medication effects revealed the primary outcome parameter and the easiest to measure parameter – gait velocity – to be the most relevant in a small number of patients.

The concept could prove not only the subjective, but more relevant the objective positive long-term effect of the cox-2 inhibitor celecoxib after four weeks of therapy. Also the patient without subjective effect had a walking speed increase of 0.4 km/h or 0.11 m/s. All patients had in average an increase of 0.66 km/h or 0.18 m/s, which is an increase in speed of 25.4%.

Other studies about osteoarthritis of the hip deal with difference between healthy person and patients suffering from arthritis. The study by Eitzen et al. [6] revealed a walking speed of 5.51 km/h for osteoarthritis patients in contrast to healthy persons with 5.94 km/h. Both numbers are higher than the assumed normal walking speed of 5 km/h, which may be based on the set-up of the laboratory, which may force people to walk faster than normal.

Illyés and Kiss [3] revealed a walking speed of hip osteoarthritis patients in the range of 0.5 to 3.0 km/h with an average of 2.2 km/h measured on a treadmill.

In both studies no therapy effect was evaluated.

There is one study evaluating the NSAID etodolac on the gait parameters during 3 hours [7]. A significant change in walking speed was calculated within three hours after medication. No long-term efficacy measurement was taken.

Only the study presented here could demonstrate the long-term efficacy of a pain killer – we used here the Cox-inhibitor celecoxib with 200mg once per day for 4 weeks therapy without any other medication or therapy.

The primary effect of the walking speed increase could be demonstrated with only 5 patients in this study. Due to lack of greater numbers of patients the further parameters of EMG and pressure distribution did not show any significant alteration, but tendency to a normal activation or motion.

In further studies with higher numbers of patients the effect of a drug, e.g. NSAID or coxibs, on EMG and pressure distribution should be further evaluated in order to understand the positive effect of often used medication in osteoarthritis in more detail.

Nevertheless we could proof in this pilot study for the first time a long-term effect of a coxib by improving the gait parameter "walking velocity".

V. CONCLUSION

The simple parameter "walking velocity" is sufficient to demonstrate the (positive) effect of a drug, especially a painkiller or NSAID or coxib. Therefore we found a simple and cost effective parameter (gait velocity) to evaluate the efficacy of drugs which could be measured also in nearly all locations where patients are examined including developing countries.

Our primary endpoint in this pilot study "gait velocity" is an easy to measure und easy judged parameter for the improvement of locomotion of patients with hip-osteoarthritis.

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