Microdialysis of paraspinal muscle in healthy volunteers and patients underwent posterior lumbar fusion surgery

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Abstract Paraspinal muscle damage is inevitable during conventional posterior lumbar fusion surgery. Minimal invasive surgery is postulated to result in less muscle damage and better outcome. The aim of this study was to monitor metabolic changes of the paraspinal muscle and to evaluate paraspinal muscle damage during surgery using microdialysis (MD). The basic interstitial metabolisms of the paraspinal muscle and the deltoid muscle were monitored using the MD technique in eight patients, who underwent posterior lumbar fusion surgery (six male and two female, median age 57.7 years, range 37–74) and eight healthy individuals for different positions (five male and three female, age 24.1 ± 0.8 years). Concentrations of glucose, glycerol, and lactate pyruvate ratio (L/P) in both tissues were compared. In the healthy group, the glucose and glycerol concentrations and L/P were unchanged in the paraspinal muscle when the body position changed from prone to supine. The glucose concentration and L/P were stable in the paraspinal muscle during the surgery. Glycerol concentrations increased significantly to 243.0 ± 144.1 μM in the paraspinal muscle and 118.9 ± 79.8 μM in the deltoid muscle in the surgery group. Mean glycerol concentration difference (GCD) between the paraspinal muscle and the deltoid tissue was 124.1 μM ($P = 0.003$, with 95% confidence interval 83.4–164.9 μM). The key metabolism of paraspinal muscle can be monitored by MD during the conventional posterior lumbar fusion surgery. The glycerol concentration in the paraspinal muscle is markedly increased compared with the deltoid muscle during the surgery. It is proposed that GCD can be used to evaluate surgery related paraspinal muscle damage. Changing body position did not affect the paraspinal muscle metabolism in the healthy subjects.

Keywords Glucose · Lactate pyruvate ratio · Glycerol · Paraspinal muscle · Microdialysis

Introduction

Posterior approach is a common and important surgical procedure for various lumbar diseases. Owing to the anatomy, the damage of paraspinal muscle is inevitable during conventional posterior lumbar fusion surgery. Degeneration and malfunction of the paraspinal muscle might associate with pain and inferior postoperative clinical outcome [19].

One argument for introducing minimally invasive spine surgery techniques is that these techniques minimise the paraspinal muscle damage during surgery. However, this relation has not been established. Various methods have been used to evaluate the paraspinal muscle damage during posterior lumbar surgery. These methods include muscle biopsy and histological evaluation [1, 6, 7], muscle performance studies [2, 10, 15], intramuscular pressure studies [6, 9, 21], imaging studies [1, 2, 15], and systemic biochemical parameter studies [7, 8, 11, 13] Previous studies have not documented direct evidence for a link between posterior lumbar surgery and paraspinal muscle injury.

Microdialysis (MD) is a valuable minimally invasive technique to monitor the metabolism at tissue level in vivo. MD can provide metabolic information specific to the tissue of interest. When physical and biochemical injury factors act on the paraspinal muscle during spinal surgery, the local metabolism level is changed. MD could be one

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method to explore the changes in the metabolism of the paraspinal muscle tissue. The aim of the present study was to evaluate the metabolism changes of the paraspinal muscle during posterior lumbar surgery using MD. At the same time, we also explored the effect of changing position on the metabolism of the paraspinal muscle in the healthy subjects.

Materials and methods

The study was approved by the local ethics committee (VN2005/43), and informed consent was obtained from all the subjects.

Healthy group

Eight healthy volunteers [five male and three female, age 24.1 ± 0.8 years, body mass index (BMI) 23.8 ± 1.3 kg/m^2] without chronic metabolic disease or low back pain were enrolled in this group. All the participants were non-smokers and non-medicated. There were no spinal deformities in the volunteers or local tenderness on the back by inspection and palpation. All the participants were asked to avoid excess physical activities 24 h before the experiment day.

After having a normal lunch, the experiment started at 4.00 p.m. in the outpatient operation theatre with a room temperature of 23°C. No food or water intake was allowed during the whole procedure. The experiment protocol is shown in Fig. 1.

Following the local skin anaesthesia with 1% lidocaine 1–2 ml, two MD catheters were placed in the right paraspinal muscle (at L4 spinous process level, 3 cm away from midline) and the righ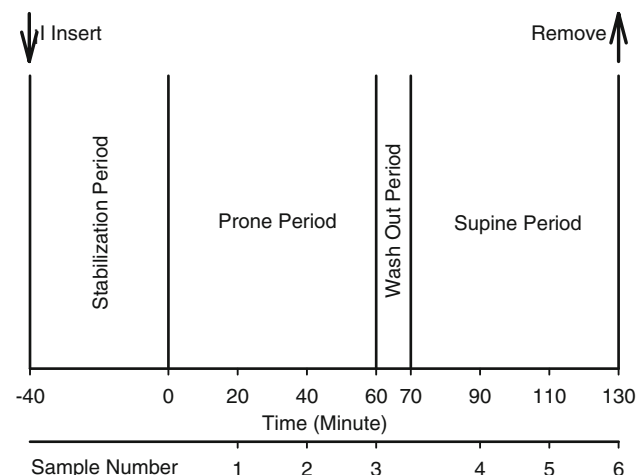t deltoid muscle (lateral part) in a prone position. After the stabilisation period of 40 min, the subjects were asked to lie in the prone position for 1 h and in a supine position for another hour. There was a 10-min wash-out period between the two periods. MD samples (dialysates) were collected every 20 min.

Surgery group

Eight patients (six male and two female, median age 57.7 (37–74) years, mean BMI 28.1 ± 2.2 kg/m^2) who underwent conventional instrumented posterolateral lumbar fusion were included. Patients' diagnosis was degenerative spondylolisthesis with/without spinal stenosis. Exclusion criteria included: previous fusion, chronic metabolic disease, tumour or metastasis, and surgical complications during and postoperation. Fusion level and operative time is shown in Fig. 2. All the operations were performed by one of the authors (Sten Rasmussen).

Following the standard general anaesthesia, two MD catheters were placed in the paraspinal muscle at the level of midpoint of incision bilaterally (in case of catheter breakage during surgery), 3 cm away from midline. A reference catheter was placed in the deltoid muscle as above. Dialysates were collected every 20 min during whole operation period after 40-min stabilisation period.

Microdialysis

CMA 60 (CMA/Microdialysis AB, Sweden) MD catheters, with a polyarylethersulphone membrane length of 30 mm, outer diameter 0.6 mm, and a molecular weight cut off of 20,000 Da, were used in the study. All the catheters were inserted parallel to the muscle fibres with the tip proximal.

Fig. 1 Study protocol for eight healthy subjects. Three dialysates were collected in either period for one catheter
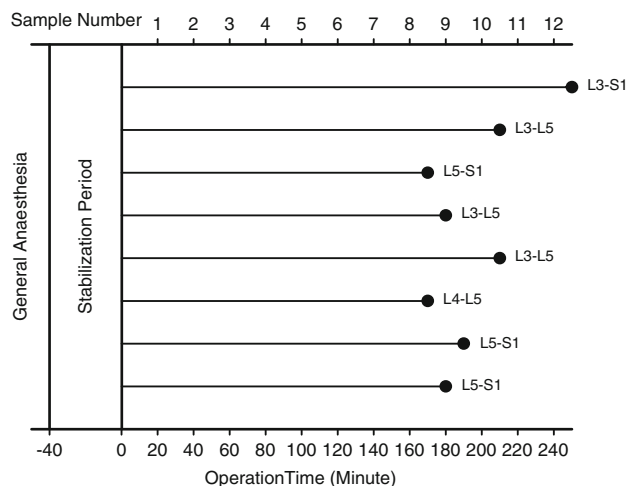

Fig. 2 Study protocol for eight patients who underwent posterior lumbar fusion surgery. Operation level and operation time were showed

CMA 106 (CMA/Microdialysis AB, Sweden) MD pump pumped the catheters with perfusion fluid T1 (CMA/Microdialysis AB, Sweden, Na^+ 147 mM, K^+ 4 mM, Ca^{2+} 2.3 mM, Cl^- 156 mM) at a rate of 0.3 μl/min. The dialysate was analysed using the ISCUS (CMA/Microdialysis AB, Sweden) clinical MD analyser with kinetic enzymatic method immediately after dialysate collection. The concentrations of key metabolites, such as glucose, glycerol, and lactate pyruvate ratio (L/P) were measured. Quality control was carried out with control samples at the beginning of the measurement.

To ensure the position of the catheter in the muscle tissue different techniques were applied in the two groups. In the healthy group, smaller BMI and thinner thickness of subcutaneous tissue on the back were found in the subjects. Therefore, "fascial click" and "muscle spasm" were noted when the MD catheters were inserted into the paraspinal muscle [12, 20]. In the surgery group, magnetic resonance imaging was performed. The thickness of the subcutaneous tissue on the back in the axial plane T2 sequence image was measured. Only patients with subcutaneous tissue thickness <20 mm (CMA 60 catheter shaft length) were included.

Statistical procedure

Normal distributed data were presented as mean ± standard deviation (SD), otherwise median and range were used. SPSS statistical software 15 for Windows was used for statistical analyses. The level of significant was set to $\alpha = 0.05$ (2-tailed testing). Two-way repeated measures analysis of variance was used to test for differences between two tissues (paraspina muscle and deltoid muscle) over time or different position periods. Multiple comparisons were done by followed Bonferroni post hoc analysis, if necessary. Student's t test was used to compare the differences between the results from the eight healthy subjects and the eight patients. Mann–Whitney test was performed if the assumptions for the t test were not fulfilled.

Results

All the subjects in the two groups completed the study. No complication (bleeding, infection, pain, etc.) was observed related to the MD catheter. The MD results are shown in Table 1 and Fig. 3a–f.

Healthy group

The glucose concentration was unchanged when the body position changed from prone to supine ($P = 0.778$), in both muscle tissues ($P = 0.176$), with 4.9 ± 0.7 mM in the paraspinal muscle and 4.8 ± 0.4 mM in the deltoid muscle. There was no difference in glucose level between the two tissues ($P = 0.696$).

In both tissues ($P = 0.767$), L/P decreased when the position changed from prone to supine, but not significant ($P = 0.077$). There was no difference between the average levels of the two tissues ($P = 0.286$), with 29.5 ± 8.8 in the paraspinal muscle and 26.1 ± 8.2 in the deltoid muscle.

The glycerol concentration was stable ($P = 0.135$), in both tissues ($P = 0.344$), with 54.4 ± 20.1 μM in the paraspinal muscle and 48.9 ± 17.0 μM in the deltoid muscle. There was no difference in the glycerol level between the two tissues ($P = 0.498$).

Surgery group

In the surgery group, the operative time varied from 170 to 250 min (Fig. 2). To ensure that every sampling time point included all the eight patients, only data collected before 160 min (eight samples for each catheter) were analysed. If the MD catheter on the right side was intact until removal (in six patients), data collected from this catheter were used. Otherwise data from the left side catheter (in two patients) were analysed.

The glucose concentrations were stable over time ($P = 0.916$) in both muscle tissues ($P = 0.575$). There was no difference between the two tissues ($P = 0.366$), averaging 5.2 ± 1.7 mM in the paraspinal muscle and 5.6 ± 1.4 mM in the deltoid muscle. The glucose levels in both tissues were higher compared with the glucose levels of healthy subjects, but not significant ($P = 0.294$ and 0.081, respectively).

Lactate pyruvate ratio levels responded differently in the two tissues during surgery ($P = 0.008$). In the paraspinal muscle, the L/P level was stable ($P = 0.431$) with average level of 27.8 ± 16.1. In the deltoid muscle, the L/P level decreased over time ($P = 0.008$) with value of

Table 1 Mean and standard deviation of glucose, lactate pyruvate ratio (L/P), and glycerol level in healthy subjects

	Glucose (mM)		L/P		Glycerol (μM)	
	Prone	Supine	Prone	Supine	Prone	Supine
Paraspinal muscle	4.9 ± 0.8	4.8 ± 0.7	32.9 ± 8.7	26.1 ± 8.0	57.5 ± 19.9	51.2 ± 21.3
Deltoid muscle	4.7 ± 0.5	4.8 ± 0.3	28.6 ± 10.4	23.7 ± 4.8	57.4 ± 15.7	40.3 ± 14.6

Fig. 3 Glucose, L/P ratio, and glycerol level in the eight healthy subjects (**a**, **c**, and **e**) and eight patients during surgery (**b**, **d**, and **f**). Significant glycerol concentration differences (*asterisk*) were found from 60 to 160 min during surgery between the paraspinal muscle and the deltoid muscle (**f**)
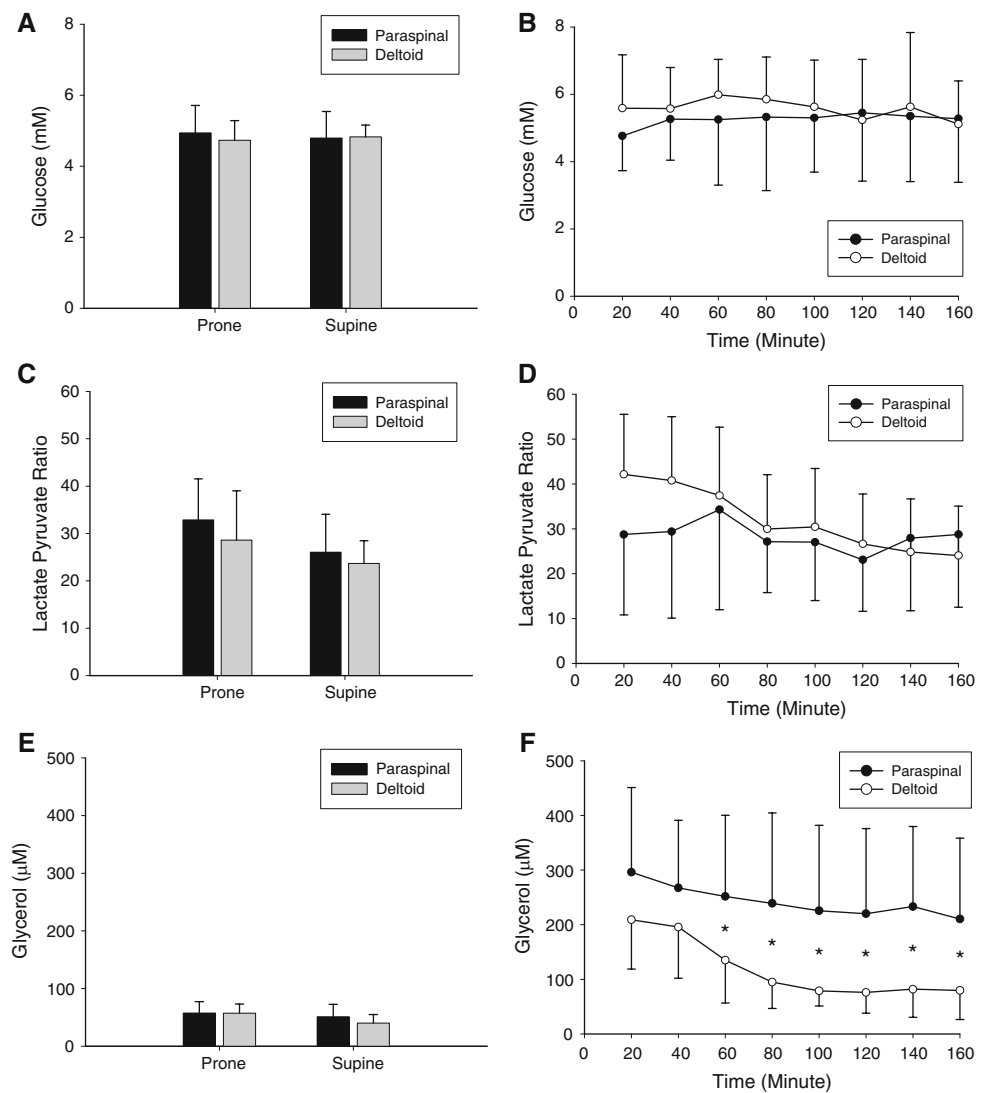
42.1 ± 13.4 at 20 min and decreased to 24.0 ± 11.0 at 160 min after surgery.

During surgery, the glycerol levels in the two tissues changed over time with the same pattern ($P = 0.672$). In both the tissues, the glycerol concentration decreased ($P = 0.002$). In the paraspinal muscle, the glycerol level was 296.0 ± 154.9 µM at 20 min and decreased to 210.5 ± 147.9 µM at 160 min. Although in the deltoid muscle, the glycerol level was 209.1 ± 90.3 and 79.6 ± 53.3 µM, respectively. The average glycerol level was significantly higher in the paraspinal muscle of 243.0 ± 144.1 µM than in the deltoid muscle of 118.9 ± 79.8 µM ($P = 0.003$, mean difference 124.1 µM, with 95% confidence interval 83.4–164.9 µM).

Multiple comparisons showed no difference in glycerol level between the two types of tissue in the first two sampling time point (20 and 40 min). However, the differences increased significantly from 60 to 160 min ($P < 0.05$).

Discussion

Microdialysis

Microdialysis was initially developed by Ungerstedt and Pycock [22] to monitor neurochemical changes in the brain tissue. The technique has been showed to be valuable in many tissues of human being, including skeletal muscles [17, 18], even in the clinical settings [12, 14, 16].

This minimally invasive technique can provide metabolic information specific to the tissue of interest. Based on the concept of diffusion, the concentrations in the dialysate are only a fraction of the real concentrations in the interstitial fluid. The ratio between the concentration of a particular substance in the dialysate and the interstitial concentration of the same substance is defined as "relative recovery." The recovery is influenced by several factors, molecular weight of substance, perfusion flow rate, area of

the MD membrane, tissue temperature, and so on. Previous studies suggested that with a longer MD membrane (3 cm) and a slower perfusion rate (0.33 μl/min), the recovery close to 100% [17]. In the present study, relative recovery was not evaluated. However, it was considered to be near to 100%. For this reason, the concentration ratio (L/P) and difference (glycerol concentration difference, GCD) were analysed to minimise the effect of relative recovery.

Changing position effect

In some lumbar cases, it is necessary to operate using both the posterior and the anterior approaches. The positions of the patients are changed during these surgeries and are kept in one position for a period of time. In the healthy group, we explored the effect of changing position on the paraspinal muscle metabolism. The concentrations of glucose and glycerol were unchanged. The L/P level decreased, but not significant.

The metabolism of paraspinal muscle might be varied from patients during surgery to the healthy subjects without anaesthesia. The present results were insufficient to predict the situation during the surgery. However, changing body position from prone to supine did not influence the MD results of the paraspinal muscle in healthy subjects.

Based on our data, the mean values of glucose, L/P, and glycerol in the paraspinal muscle were estimated, 4.9 ± 0.7 mM, 29.5 ± 8.8, and 54.4 ± 20.1 μM, respectively. With the same length of MD membrane catheter and perfusion speed, these values were comparable with the data from the following study.

Paraspinal muscle damage

The increase in the L/P is an accurate marker of cell ischaemia [4]. In the present study, L/P in the paraspinal muscle was stable at 27.8 ± 16.1 which was compatible with the result from the healthy group during surgery. No paraspinal muscle tissue ischaemia was observed.

It is important to point out that in the deltoid muscle, L/P was at higher level at the beginning of the surgery and decreased afterwards. The MD results of the deltoid muscle, which severs as the control tissue, represent the systemic reaction. Higher L/P value was also expected in the paraspinal muscle. However in the study, the L/P level was stable in the paraspinal muscle. The increase was suppressed in the paraspinal muscle by the surgical procedure and kept at a lower level. L/P is inadequate to be a marker of paraspinal muscle damage.

Glycerol is an important component of glycerophospholipid, which is the basic structure of the cell plasma membrane. When the integrity of cell membrane is destroyed, glycerol will be released to the interstitial fluid. Glycerol concentration is a marker of how severely the cells are affected by the ongoing pathology in the non-adipose tissues [5]. On the other hand, glycerol also originates from lipolysis which is regulated by the sympathetic tone [3].

During surgery, the glycerol level in the deltoid muscle was increased by 120% in the surgery group compared with the healthy group. The increased glycerol concentration implicated a systemic surgery related hyper-lipolysis and manifested in the deltoid tissue. As shown in Fig. 3f, the glycerol concentration was higher in the beginning of the surgery and decreased over time. In the paraspinal muscle, the glycerol concentration was increased by 350% in the surgery group compared with healthy subjects and increased by 100% compared with control tissue. The increase in glycerol concentration in the paraspinal muscle consisted of two parts, the increase due to hyper-lipolysis and the increase due to muscle damage. The GCD between the paraspinal muscle and the control muscle tissue represented the paraspinal muscle damage during posterior lumbar surgery (Fig. 4).

When the present study was designed, the deltoid muscle was selected as control tissue only because of accessibility during surgery. Based on our data, it is important and necessary to set muscle tissue as control tissue (most studies regarding MD used subcutaneous tissue as control tissue). No metabolic level difference was found in the healthy subjects without surgery between the two tissues. However during posterior lumbar surgery, the intervention of the surgical procedure which was the only difference between the two tissues made a significant increase in the glycerol concentration in the paraspinal muscle. Therefore, we conclude that GCD represents paraspinal muscle damage during posterior lumbar fusion surgery. To our knowledge, this is the first time that the
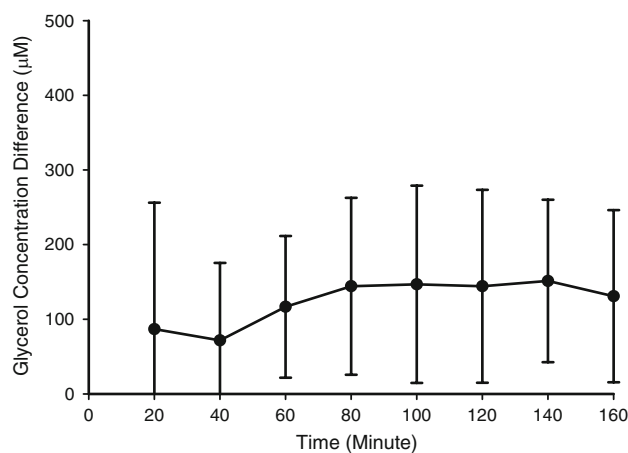

Fig. 4 Glycerol concentration difference (GCD) between the paraspinal muscle and the deltoid muscle during posterior lumbar surgery was showed. GCD increased with time and was stable at a relatively higher level after 100 min

paraspinal muscle damage has been quantified directly during posterior lumbar surgery.

Microdialysis results are specific to the local tissue of interest. This is an advantage of the technique compare to systemic biochemical parameters. For example, creatine phosphokinase MM (CPK-MM) was analysed as a systemic marker of the skeletal muscle injury after lumbar surgery [7, 8]. It is established that serum CPK-MM elevation is associated with skeletal muscle damage. Significant CPK-MM activity difference was found between posterior lumbar surgery and anterior surgery [8]. However, the CPK-MM activity is not specific to the paraspinal muscle. The elevation of CPK-MM activity can also due to the abdominal muscle damage during an anterior approach surgery. This is a limitation of the systemic biochemical parameter studies when we focus on the paraspinal muscle damage.

Conclusions

The study shows that MD is a feasible technique to monitor metabolic changes in the paraspinal muscle during conventional posterior lumbar fusion surgery. The glycerol level in the paraspinal muscle increased markedly compared with the deltoid muscle during surgery. The GCD between the two tissues represents the extent of surgery related paraspinal muscle damage. There was no effect of changing body position (from prone to supine) on the key metabolism of the paraspinal muscle in the healthy subjects.

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