

Research Article

Patients' Satisfaction and Complications after Muscle Biopsy for Malignant Hyperthermia Diagnostics

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Abstract

Introduction: The gold-standard to diagnose malignant hyperthermia (MH) susceptibility is the in-vitro-contraction test (IVCT) requiring an open muscle biopsy. The aim of the presented investigation was to evaluate intra- and postoperative patients' satisfaction and the incidence of serious complications following muscle biopsy for MH diagnostics.

Subjects and methods: In a retrospective study anonymous standardized questionnaires were sent out to 149 patients who underwent muscle biopsy and IVCT according to the diagnostic guidelines of the European MH-Group at the department of Anesthesia and Critical Care of the University of Wuerzburg between 2006 and 2012. Questions concerning general conditions and postoperative recovery were included.

Results: 96 patients returned the questionnaires. 29 individuals were classified MH susceptible and 67 MH non-susceptible. Patients felt well informed about the procedure, were content with the anesthetic procedure and appreciated the friendliness of the staff. Complications of wound healing were uncommon. However, postoperative pain and dysesthesia of the scar appeared more problematic. The duration of pain varied between 0 and 35 days. After the test 81% of the patients indicated feeling safer for future operative procedures.

Conclusions: Muscle biopsy for IVCT is generally well accepted by the patients and serious complications are rare. However, main problems still consist in postoperative pain and in some cases long lasting physical restrictions.

INTRODUCTION

Malignant hyperthermia (MH) is a rare but potentially lethal pharmacokinetic disorder characterized by a disturbance of the skeletal muscle calcium homeostasis. In susceptible patients, triggering agents such as inhalation anesthetics and/or the depolarizing muscle relaxant succinylcholine may induce a hypermetabolic muscular syndrome based on an uncontrolled sarcoplasmic calcium release via functional altered ryanodine receptors subtype 1 or dihydropyridine receptors leading to hypoxemia, hypercapnia, tachycardia, muscular rigidity, acidosis, hyperkalemia and hyperthermia [1]. Even if aberrations in these two receptors are responsible for the functional changes seen in calcium regulation in MH, genetic evidence of a causative mutation for MH is found in less than 50% of susceptible individuals. Hence, at time the invasive in-vitro-contraction test (IVCT) with halothane and caffeine according to standardized test protocols

of the European and the North American MH Groups represent the only reliable procedures to diagnose MH susceptibility [2,3]. However, due to its requirement of open muscle biopsy, testing might be associated with relevant risks to the patients, such as wound infections, postoperative bleedings or sensory deficits.

Therefore, the aim of our study was to evaluate intra- and postoperative patients' satisfaction and the incidence of serious complications following muscle biopsy for MH diagnostics at the MH lab of the University of Wuerzburg.

SUBJECTS AND METHODS

In a retrospective study an anonymous standardized questionnaire was sent out to 149 patients, who underwent open muscle biopsy and IVCT according to the diagnostic guidelines of the European MH-Group [2] at the MH lab of the University of Wuerzburg between 2006 and 2012.

The muscle biopsy was performed according to a standardized internal clinical investigation protocol. In brief, the patient was positioned in supine position on the operating table and received an intravenous pre-medication with midazolam 0.03-0.05 mg/kg (Roche Pharma AG, Germany). Afterwards, the femoral nerve was blocked by ultrasound-guided application of mepivacaine 6 mg/kg (AstraZeneca GmbH, Germany). Following locating of the lateral vastus muscle, the skin was disinfected and draped in a standard fashion. A 4-cm longitudinal incision was performed followed by sharp atraumatic dissection of the muscular fascia and en bloc excision of 2-4 g muscular tissue. Prior to closure, haemostasis was ensured and the wound was sutured in layers. Finally, a compressive bandage was applied to avoid postsecondary bleeding. Three hours after the biopsy patients received 75 mg diclofenac per os to achieve postoperative analgesia.

For IVCT, muscle bundles weighing 200-250mg were kept in a tissue bath filled with carboxygenated (95% oxygen, 5% carbon dioxide) Krebs-Ringer's solution. After equilibration, incremental concentrations of either caffeine (0.5, 1, 1.5, 2, 3, 4, and 32 mM) or halothane (0.11, 0.22, 0.44, and 0.66 mM) were added at 3 minutes intervals. Contractures \geq 2 mN developed at concentrations up to 2 mM caffeine or 0.44 mM halothane confirmed MH susceptibility, while the absence of significant contractures excluded MH [2].

Eight weeks after the biopsy a standardized questionnaire was sent out to the investigated patient. Questions concerning general conditions (information about the procedure, friendliness of the staff, anesthetic procedure and expertise of the staff) and postoperative recovery e.g. wound healing, postoperative pain, period of physical limitations and disability, wound infection, hematoma, wound dehiscence, excessive scarring as well as dysesthesia were included. Answers were graded from 1 (very good) to 6 (poor) or given as time intervals.

STATISTICS

Data are displayed as medians and interquartile ranges. Student's t-test was applied for differences between MH susceptible (MHS) and MH non-susceptible (MHN) patients. A value of $p < 0.05$ was considered statistically significant.

RESULTS

96 (= 64%) out of 149 patients returned the questionnaire. 29 of the individuals were classified MHS and 67 MHN by IVCT using muscle bundles of the vastus lateralis muscle.

High satisfaction concerning the general conditions of the hospital stay was reported by the patients. They felt well informed about the procedure, were content with the anesthesia and appreciated the friendliness of the staff (Table 1). Fortunately, complications of wound healing were uncommon. However, postoperative pain and dysesthesia of the scar appeared more problematic (Table 2). The duration of pain varied between 0 and 35 days. Furthermore, the period of disability and the duration of physical limitations are remarkable (Table 3).

After the test 81% of the patients indicated feeling safer for future operative procedures. Interestingly, the results were not significantly different between MHS and MHN patients.

Table 1: Patients' satisfaction concerning general procedures after muscle biopsy for malignant hyperthermia diagnostic. Answers graded from 1 (very good) to 6 (poor); Data as median and interquartile range. MHS = malignant hyperthermia susceptible; MHN = malignant hyperthermia non-susceptible.

Diagnosis	MHS (n=29)	MHN (n=67)
General conditions	2 [1-2]	2 [1-2]
Information about the procedure	1 [1-2]	1 [1-2]
Friendliness of the staff	1 [1-2]	1 [1-1]
Anesthetic procedure	1 [1-2]	1 [1-2]
Expertise of the staff	1 [1-2]	1 [1-2]

Table 2: Patients' satisfaction concerning convalescence after muscle biopsy for malignant hyperthermia diagnostic. Answers graded from 1 (very good) to 6 (poor); Data as median and interquartile range. MHS = malignant hyperthermia susceptible; MHN = malignant hyperthermia non-susceptible.

Diagnosis	MHS (n=29)	MHN (n=67)
Wound healing	2 [1-2]	2 [1-2]
Postoperative pain	2 [2-3]	3 [2-3]
Signs of inflammation	2 [2-3]	2 [2-3]
Hematoma	1 [1-2]	1 [1-2]
Wound dehiscence	1 [1-2]	1 [1-2]
Excessive scarring	1 [1-3]	2 [1-3]
Dysaesthesia	2 [1-3]	2 [1-3]
Mobility impairments	1 [1-1]	1 [1-3]

Table 3: Patients' satisfaction concerning convalescence after muscle biopsy for malignant hyperthermia diagnostic. Answers are given as time intervals. Data as median and interquartile range. MHS = malignant hyperthermia susceptible; MHN = malignant hyperthermia non-susceptible.

Diagnosis	MHS (n=29)	MHN (n=67)
Duration of pain	7 [4-21] days	10 [4-21] days
Period of physical limitations	14 [8-19] days	14 [7-27] days
Period of disability	7 [3-14] days	0 [0-14] days

After regression of the femoral blockade, all patients were discarded from the hospital without serious delay at the day of admission.

DISCUSSION

Biopsy of muscle tissue is frequently performed to aid a diagnosis in patients suspected to suffer from neuromuscular diseases such as muscular dystrophy, myopathies, inflammatory myositis or MH. In case of MH, indication of muscle biopsy is of extreme importance to confirm or refute MH susceptibility in affected patients, due to the inheritance of this life threatening disease, especially after genetic counseling failed. Nevertheless, a muscle biopsy represents an invasive surgical procedure, which might be associated with noteworthy adverse effects, e.g. wound infections, postoperative bleeding or sensory deficits. In the current literature, the rate of serious side effects following muscle biopsy is highly variable. In part, this might be caused by the retrospective nature of the performed studies and the limited reporting accuracy of the interviewed patients [4]. According to recent surveys persistent postoperative pain varies between 29% and 33%, while wound infections after biopsies occurred

in 14% and 20% respectively of the investigated patients [5,6]. Generally, surgical site infections accounted for about 15% of nosocomial infections. However, the occurrence mainly depends on the operative procedure and might be reduced to less than 5%, if patients undergo clean extra-abdominal surgery [7].

The overall low rate of serious surgical side effects reported by the investigated patients in the presented study, might be a result of the standardized performance of the muscle biopsy and the fact, that only three physicians performed the biopsies during the analyzed time period. The procedure was performed according to the standardized guidelines of the European MH Group [2] and a senior colleague supervised the performing surgeon for at least 25 muscle biopsies. However, besides an overall good acceptance, pain, motor impairment and physical limitations are the main problems affecting patients after muscle biopsy according to the present survey.

Noteworthy, 81% of the interviewed patients stated to feel safer for future operative procedure independently of their MH diagnosis. These finding clearly demonstrates that, even due to the invasive character of the IVCT the benefit for patients suspected to suffer from MH predominates and increases patients' safety.

Nevertheless, in selected patients, less invasive procedures to diagnose MH, e.g. genetic analysis as an established procedure [8] or a recently proposed metabolic test [9] as a promising alternative method, might avoid serious complications and increase patients' comfort.

CONCLUSION

Muscle biopsy for IVCT is generally well accepted by the patients and serious complications are rare. However, main problems still consist in postoperative pain and in some cases long lasting physical restrictions. To further enhance patient comfort, the future aim should be the search for less or minimal invasive diagnostic methods to diagnose MH susceptibility, since genetic analysis is only suitable for a limited number of patients.

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