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Metabolism in the hand tissues and functional microcirculation resourses in patients with sequelae of cold injury treated with the Ilizarov method

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Objective To explore metabolism and microcirculation of the hand in patients with remote effects of severe cold injury treated with the Ilizarov method using functional tests. **Material and methods** Metabolism and microcirculation of the hand were studied in 19 patients with remote effects of severe cold injury treated with the Ilizarov method. The patients' age ranged from 24 to 46 years (32.8 ± 2.9 years). Control group consisted of 14 normal peers. Depending on finger stump length, presence of contractures in adjacent joints and postlengthening basal syndactyly techniques employed for treatment included finger stump lengthening (4 observations of less than 30 mm stumps and 10 observations of more than 30 mm stumps); finger stump lengthening followed by plasty of web space in 3 patients; finger stump lengthening and repair of adduction contracture in 2 cases. Laser Doppler Flowmetry (LDF) BLF21 (Transonic Systems Inc., U.S.A.) was used to assess microcirculatory function. Local vascular occlusion test was applied, blood flow recorded at rest and after 3 minute ischemia, and Peak Capillary Blood Flow Index calculated (PBFI, % = CBFpeak/CBFrest × 100 %), Δ t, sec – period from occlusion relief to maximal runup of capillary blood flow. A Doppler ultrasound (DUS) using diagnostic Minimaxdoppler K device (St.Petersburg) was used to assess peripheral hemodynamics of finger and stump arteries. **Results** DUS showed signs of vasoconstriction of digital arteries. Period of CBF semi-recovery and length of reactive hyperemia were sharply decreased. Transcutaneous polarography showed prevailing anaerobic metabolism with two-fold decrease in pO_2 half-life and two-fold increase in pO_2 semi-recovery, and oxygen exhaust was recorded within 2 minutes. **Conclusion** It was concluded that evaluation of capillary blood flow using laser Doppler flowmetry with a 3-minute vascular occlusion test was the method of choice for examination of patients with sequelae of severe cold injury of limb segments. The method allowed for assessing preclinical extent of ischemia, disorders in vascular reactivity of pre-capillary portion. A tailored approach to distraction rate under control of objective and subjective findings and microhemodynamics is essential for patients treated with transosseous distraction osteosynthesis using Ilizarov external fixator. Medications targeting the relief of vasoconstriction prescribed for patients with sequelae of cold injury treated with Ilizarov traction demonstrated hardly noticeable effect due microcirculation recourses had been largely consumed by the method of transosseous osteosynthesis. We suggest that preventive angiogenic and neurotrophic therapies can be efficient at pre-distraction stage.

Keywords: Ilizarov method, hand, cold injury, microcirculation, ischemia, angiogenic and neurotrophic therapy, transcutaneous polarography

There have been new concepts of treatment developed to prevent cold injury related necrosis and improve clinical results. Introduction of transosseous compression-distraction osteosynthesis and Ilizarov mini-fixator into clinical practice has discovered new possibilities for reconstructive hand surgery using local tissues [4] in lengthening of posttraumatic finger stumps. Operative treatment entails a risk of vascular disorders in the segment being transformed with compensatory response of tissues to metabolic and oxygen demands. The study of biological condition of soft tissues of the hand and adaptive resources of microcirculation system in patients with late sequelae of cold injury plays a prognostic role to allow for planning treatment tactics.

Disturbed microcirculation developing in pre-responsive period is the most sensitive part in pathogenesis of severe cold injuries of limbs accompanied by irreversible changes in progressive blood flow decrease to biological nil and necrosis in 100 % of the cases [6]. Post-cold neuropathy is a dominating symptom of late sequelae of cold injuries. The patients develop steady cold intolerance with abnormal threshold of thermal and vibration sensitivity at short- and long-terms of cold injury [12].

Dysfunction of vascular endothelium is one of mechanisms contributing to pathological processes with endotheliocytes damaged due to accumulation of different biologically active agents (cytokines) at the site of injury [7].

Objective The purpose of the study was to explore metabolism and microcirculation of the hand in patients with remote effects of severe cold injury treated with the Ilizarov method using functional tests.

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MATERIAL AND METHODS

The study included 19 patients aged from 24 to 46 years (32.8 ± 2.9 years). Cold injury was 2 to 3 years old. Control group consisted of 14 normal peers.

Depending on finger stump length, presence of contractures in adjacent joints and postlengthening basal syndactyly techniques employed for treatment included:

1. Finger stump lengthening (stumps measuring less than 30 mm (n = 4), stumps measuring more than 30 mm (n = 10));
2. Finger stump lengthening followed by web space plasty (n = 3);
3. Finger stump lengthening and repair of adduction contracture (n = 2).

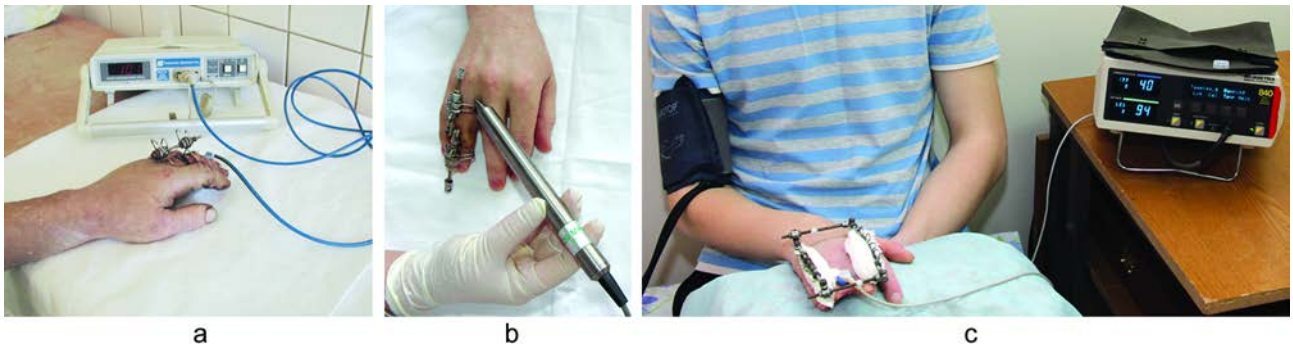
Noninvasive functional tests appear to be informative in detection of latent disorders of microhemodynamics and adaptive resources of microcirculation systems [3].

Laser Doppler Flowmetry (LDF) BLF21 (Transonic Systems Inc., U.S.A.) was used to assess microcirculatory function (**Fig. 1a**). Local vascular occlusion test was applied to explore mechanisms of blood flow regulation with occlusion cuff placed on the forearm. Capillary blood flow was recorded at rest (CBFrest, PF) and after 3-minute ischemia (CBFpeak, PF), and we calculated Peak Capillary Blood Flow Index (PBFI, % = CBFpeak/CBFrest × 100 %) as an increase in capillary blood flow after 3-minute occlusion, Δ t, sec – a period between occlusion relief and maximal runup of capillary blood flow; semi-recovery of capillary blood flow ($T_{1/2}$, sec) and the length of reactive hyperemia (T, sec) as an interval between maximal capillary blood flow and return to baseline values.

A Doppler ultrasound (DUS) using diagnostic *Minimaxdoppler K* device (St.Petersburg) and 20 MHz probe were applied to assess peripheral hemodynamics of finger and stump arteries (**Fig. 1b**). Standard measurements of Doppler ultrasonography included peak systolic flow velocity under the mean velocity curve (Vs, cm/sec), mean velocity under the mean velocity curve (Vm, cm/sec), end-diastolic velocity under the mean velocity curve (Vad, cm/sec) to calculate pulsatility index (PI) using the equation PI = (Vs - Vd) / Vm).

Transcutaneous monitoring of oxygen and carbon dioxide with Model 840 (VFD, U.S.A.), thermal transducer (t = 44º) with modified Clark electrode for continuous measures of pO_2 and pCO_2 were employed to determine gas embolism in the tissues (**Fig. 1c**). Transcutaneous oxygen and carbon dioxide tension was recorded at rest, at three-minute ischemia (every other minute) and 10 minutes of post-ischemic reactive hyperemia taken at an interval of 30 seconds. Measurements included pO_2 and pCO_2 at baseline, oxygen elimination half-life ($T_{1/2life}$ pO_2, sec), oxygen half-recovery ($T_{1/2recovery}$ pO_2, sec), maximum carbon dioxide content (t pCO_2, sec) and carbon dioxide tension increase (Δ pCO_2, %). Flow charts of pO_2 were used to measure balanced oxygen deficiency (BOD, conventional units) as an area limited by pO_2 below oxygen elimination half-life and pO_2 semi-recovery values. The simplified formula can be used to measure triangle area with a base (T) being the time (sec) from $T_{1/2\ life}$ pO_2 point to $T_{1/2\ recovery}$ pO_2 point, an altitude (P) being the difference between pO_2 values at $T_{1/2\ life}$ pO_2 point and minimal pO_2 values during ischemia. So, balanced oxygen deficiency can be calculated using the equation, BOD = T × P/2.

Microsoft was used to complete statistical analysis. Sample mean (M), standard error of the mean (m) and Student's test were estimated with normal sample distribution to determine statistically significant differences.



a b c

Fig. 1 Photographs showing procedure performance: (a) Laser Doppler Flowmetry; (b) Doppler ultrasonography of finger arteries; (c) recording measurements of tissue metabolism with transcutaneous polarography

RESULTS

The findings indicated to vasoconstriction of digital arteries in sequelae of cold injury of the hand (**Table 1**) with the mean flow velocity (Vm, cm/sec) being less than 50 % of Vs, средняя скорость кровотока (Vm, см/сек) составляет менее 50 % Vs, negative values of end-diastolic velocity (Vad, cm/sec), increased PI re-

flecting visco-elastic arterial properties.

CBFrest and CBFpeak measurements showed no significant differences with normal values indicating to blood flow recourses maintained but half-recovery of capillary blood flow and reactive hyperemia were very low at 3-minute ischemia (**Table 1**).

Transcutaneous polarography showed prevailing anaerobic metabolism with a 2-fold decrease in elimination half-life of pO_2, a 2-fold increase in semi-recovery of pO_2, 2-minute complete oxygen depletion with $pO_2 = 0$ and aggravating hypercarbia, and balanced oxygen deficiency increase of 2.8 times [1] (**Table 1**).

Special attention should be given to skin condition at the stump butt throughout the distraction due to maximal tension in the scars to prevent perforation. Patients with sequelae of cold injury of the hand developed clinical ischemic manifestations of expressed pains, changed skin colour in 30 % of the cases (n = 6) after 7-to-10-day longitudinal traction of phalangeal stump lengthening and it required correction of treatment tactics. Ischemia of tissues entailed prevailing anaerobic metabolism and measurements as follows,

– oxygen deficiency pO_2 up to 30 mmHg;

– a 4-fold decrease in elimination half-life of pO_2;

– a 3-fold increase in semi-recovery of pO_2;

– continuous complete oxygen depletion (up to 4 minutes) and aggravating hypercarbia (50 % increase in pCO_2);

– increase in balanced oxygen deficiency up to 3800 conventional units.

Clinical instance. A 42-year-old male patient was diagnosed with sequelae of cold injury of both hands, posttraumatic amputation stumps of the 1st, 2nd, and 5th fingers at the capital level of metacarpal bones and of the 3rd and 4th fingers at the level of the base of proximal phalanges.

Two years ago the patients sustained frostbite of both hands grade 4 that resulted in necrosis of fingers on both sides. Debridement, plasty of stumps with local tissues, bilateral stump formation were performed at a local hospital. He was referred to hand department of the Russian Ilizarov Scientific Centre "Restorative Traumatology and Orthopaedics" and presented with failed activities of daily living due to severely limited function of both hands. Double osteotomy of the Ist metacarpal bone on the left side and osteosynthesis of the Ist metacarpal with the Ilizarov apparatus were produced to lengthen the Ist metacarpal bone and create the first web space. Fixators were also applied to the IInd and IIIrd metacarpals to provide additional traction forces.

Initial distraction rate was 0.5 mm/day performed at 4 increments. The patient developed expressed pains and pale skin at the butt of the Ist metacarpal after 7-day distraction and was diagnosed with ischemia of tissue due to longitudinal distraction.

Table 1

Measurements of peripheral hemodynamics and transcutaneous polarography measured in patients with cold injury of hand (M ± m, (n), number of observations)

Description	Normal values (n = 14)	Involved limb (n = 19)	Description	Intact limb (n = 14)	Involved limb (n = 19)	Description	Intact limb (n = 14)	Involved limb (n = 19)
Laser Doppler Flowmetry			Transcutaneous polarography			Doppler ultrasonography of finger arteries		
CBF rest	5.54 ± 0.74	5.05 ± 0.85	pO_2, mmHg	56.4 ± 4.01	58.9 ± 5.19	Vs	22.14 ± 0.54	15.67 ± 0.89* decrease of 1.5 times
CBF peak	12.5 ± 0.89	14.1 ± 3.52	pCO_2, mmHg	55.7 ± 3.11	17.9 ± 5.09 decrease of 3 times	Vm	17.08 ± 0.61	5.11 ± 0.42 decrease of 3.3 times
PBFI	278.0 ± 17.89	270.0 ± 39.5	$T_{1/2\ life}$ pO_2, sec.	70.2 ± 5.05	45.7 ± 5.15* снижено в 2 раза	Vad	2.17 ± 0.29	-0.42 ± 0.12* values < 1.0
Δ t	15.0 ± 0.5	10.0 ± 0.5* decrease of 1.5 times	$T_{1/2\ recovery}$ pO_2, sec.	35.2 ± 3.91	50.0 ± 5.46* decrease of 2 times	PI	0.98 ± 0.27	2.18 ± 0.19* increase of 2 times
$T_{1/2}$	97.1 ± 0.52	15.0 ± 0.35* decrease of 6 times	t pCO_2, sec.	55.0 ± 5.55	20.4 ± 6.18* decrease of 2.5 times			
T	250.0 ± 0.38	45.0 ± 0.20* decrease of 5 times	Δ pCO_2, %	22.1 ± 3.16	10.5 ± 2.49* decrease of 2 times			
			BOD, conventional units	1050.0 ± 100.0	2997 ± 200.0* increase of 2.8 times			

Note: *– statistically significant differences with controls using Student's t-test, P ≤ 0.05; M – sample mean, m – standard error of the mean.

Distraction rate was reduced to 0.25 mm/day performed at 4 increments and therapy administered with with Sol. Euphyllini 2.4 % 5.0 intravenously № 5 to improve vasoconstriction. Doppler ultrasonography indicated to persisted vasoconstriction of finger arteries after the course of injections, slight increase in CBF semi-recovery and length of reactive hyperemia after 3-minute ischemia. Transcutaneous polarography showed no increase in pO_2 but 3-minute ischemia resulted in low-level increase in elimination half-life of pO_2 and decrease in semi-recovery of pO_2 due to considerably short period of complete oxygen depletion at 3-minute ischemia (**Fig. 2**). Similar microvascular medically induced responses of skeletal musculature aimed at vasodilation were reported in patients with age-related changes in vascular endothelium combined with neuropathy [10].

The patients persisted with pains and pale skin at the butt of the Ist metacarpal, and distraction was stopped for 3 to 5 days to improve tension of the soft tissues and relaxation to enable soft tissue adapt to the new length gained.

Distraction resumed with skin colour improved at the butt of the stump. Doppler US showed persisted vasoconstriction, and Laser Doppler Flowmetry indicated to positive dynamics in increased semi-recovery of CBF at 3-minute ischemia. Total distraction period was 48 days followed by 89-day fixation. A stock of skin was reserved for the first web space. The Limberg skin plasty technique was used for the web space. The bone was lengthened by 2.5 cm (**Fig. 3**).

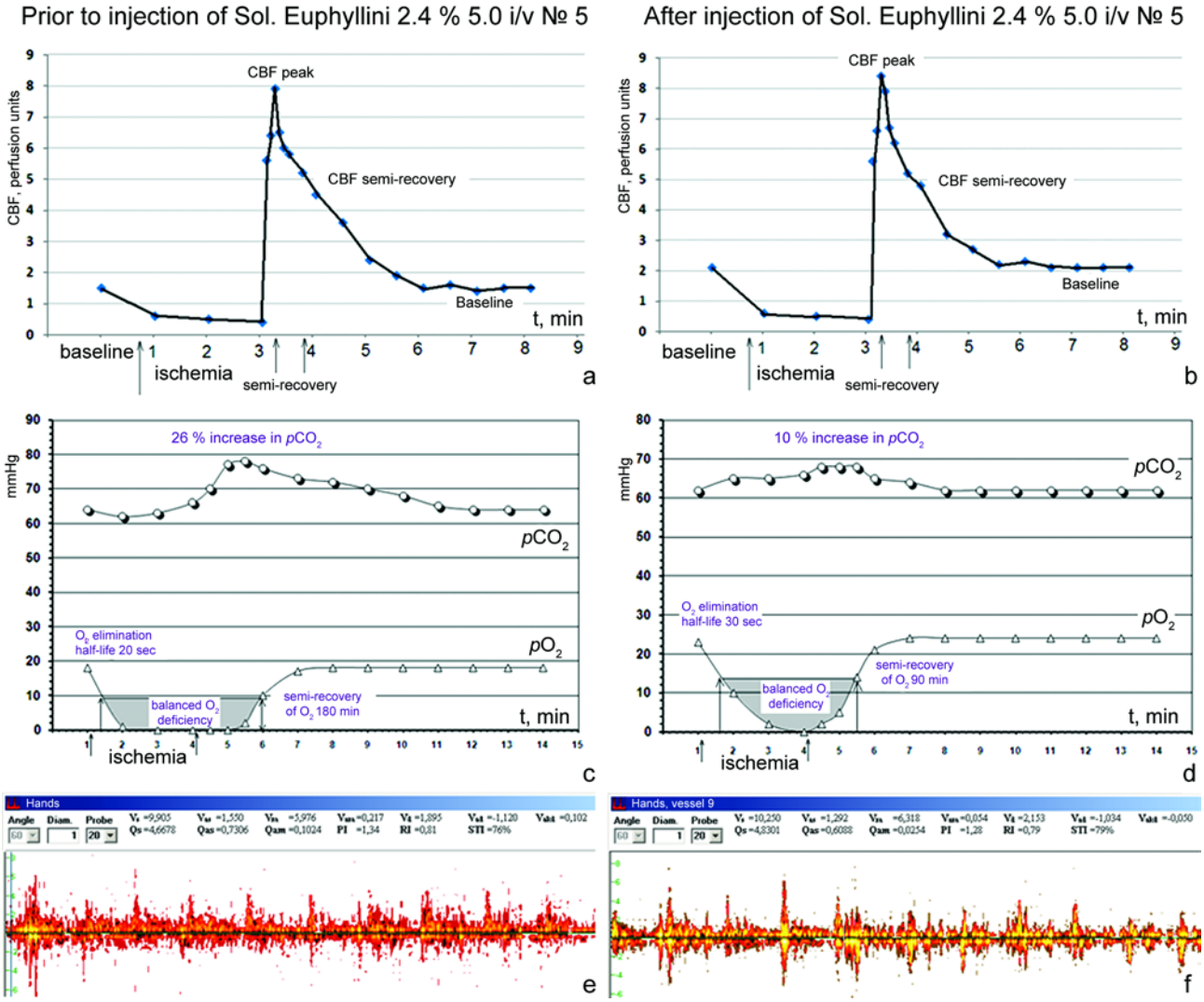


Fig. 2 Measurements of capillary blood flow (a, b), partial tension of skin gases at the site of traction (b, c) during ischemia and Doppler ultrasonography (e, f) of finger arteries

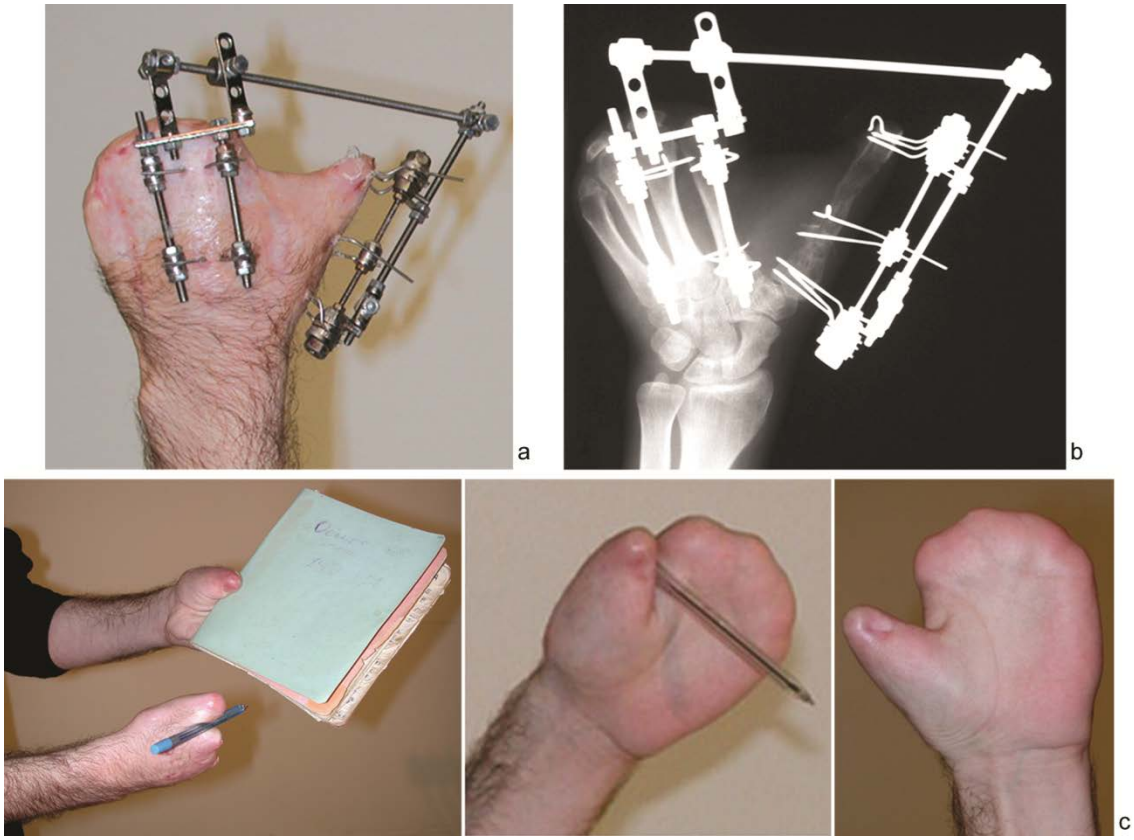


Fig. 3 A 42-year-old patient: (a) photograph of the hand during treatment, (b) radiograph of the hand during treatment; (c) functional capabilities with the left hand straight after frame removal (planar grip function developed)

DISCUSSION

Metabolism remains relatively low for a long time and is not likely to improve during distraction in the group of patients with finger stumps at long term sequelae of cold injury. Induction of cold receptors stimulates ergotropic activity of sympathetic nervous system [2], and vasoconstriction persists continuously following cold injury.

Evaluation of capillary blood flow and gas regime of tissues using ischemic test is helpful in detecting preclinical extent of ischemia at cold injury. Relationship between metabolism and microcirculation can be also observed in vascular endothelium dysfunction after severe cold injury when resting and peak capillary blood flow is no difference with the norm but there is decrease in CBF semi-recovery, elimination half-life of pO_2, length of reactive hyperemia, increase in semi-recovery of pO_2, complete oxygen depletion and aggravating hypercarbia and increase in balanced oxygen deficiency that are in line with reported findings [5, 13]. Ischemia-induced measurements were practical in grading severity of the condition.

According to literature, distractional forces applied to experimental animals are accompanied by greater expression of growth factors involved in angiogenesis of muscles [11]. Cold injury of distal limb segments (hand) results in microangiopathy at long term with spasms of precapillary vessels, largely impaired capillaries on the skin and greater microvascular permeability [9]. These changes in angiogenesis can appear to be pathomorphologic basis of clinical ischemic manifestations and pains during distraction.

A tailored choice of distractional rate and control of objective and subjective parameters of tissue condition and microhemodynamics are essential for postoperative care of the patients treated with transosseous distraction osteosynthesis with the Ilizarov apparatus. Clinical observations showed that medications administered to improve vasoconstriction of vessels in patients with sequelae of cold injury during Ilizarov traction provide inexpressive effect due to microcirculation recourses being completely exhausted with the usage of transosseous osteosynthesis (“Ilizarov effect”). Preventive angiogenic and neurotrophic therapy can be practical during predistractional period, and functional assessment of capillary blood flow should be considered when choosing individual tactics of treatment.

Capillary blood flow measurements are most labile being consistent with clinical manifestations of changes in skin colour. Dynamics in measurements of capillary blood flow after 3-minute ischemia is the major diagnostic criterion.

CONCLUSION

1. Evaluation of capillary blood flow at 3-minute ischemic test using laser Doppler flowmetry is the method of choice for patients with sequelae of severe cold injury of limb segments.

2. Ischemic test appeared to be practical for detecting preclinical ischemia as an impaired precapillary reactivity in patients with cold injury at a long term.

3. A tailored choice of distractional rate and timely therapeutic adjustments based on microcirculation monitoring are essential for postoperative care of the cohort. Patients with cold injury treated with transosseous osteosynthesis using the Ilizarov apparatus can benefit from preventive angiogenic and neurotrophic drug treatment performed during predistractional period.

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