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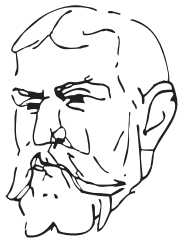

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SPIS TREŚCI

PERIPHERAL ARTERIOVENOUS FISTULA AS VASCULAR ACCESS FOR LONG-TERM CHEMOTHERAPY

ПЕРИФЕРИЧЕСКАЯ АРТЕРИО-ВЕНОЗНАЯ ФИСТУЛА КАК СОСУДИСТЫЙ ДОСТУП ДЛЯ ДЛИТЕЛЬНОЙ ХИМИОТЕРАПИИ

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ABSTRACT

Introduction: To provide long-term vascular access in clinical oncology peripheral forearm veins (up to 95% of patients in Ukraine), central venous access and "complete implanted vascular systems" are used most often. Many oncology patients have contraindications to catheterization of superior vena cava. Besides, exploitation of central veins is associated with potential technical and infectious complications.

The aim - to study short-term and long-term results of arteriovenous fistula exploitation as vascular access for continuous anticancer therapy.

Materials and methods: Peripheral venous bed status in 41 oncology patients taking long-term chemotherapy treatment is analyzed in the article. Doppler sonography, morphologic and immune histochemical analyses were used in the study.

Results: Doppler sonography found qualitative and quantitative changes in forearm veins at different time periods after initiation of chemotherapy in the majority of patients. The major morphologic manifestations of venous wall damage were chemical phlebitis, local or extended hardening of venous wall, venous thrombosis and extravasations with necrosis and subsequent paravasal tissue sclerosis. Alternative vascular access created in 12 patients completely met the adequacy criteria (safety, multiple use, longevity, realization of the designed therapy program).

The conclusion was made about inapplicability of forearm veins for long-term administration of cytostatic agents. If it is impossible to use central veins, arteriovenous fistula can become an alternative vascular access.

KEY WORDS: central venous access, peripheral venous access, arteriovenous fistula, chemotherapy.

РЕЗЮМЕ

Вступление: Для обеспечения длительного сосулистого доступа в клинической онкологии наиболее часто используют периферические вены предплечья (в Украине – до 95% больных), центральный венозный доступ и «полностью имплантируемые сосудистые системы». У многих онкологических пациентов имеются противопоказания к катетеризации верхней полой вены, к тому же при эксплуатации центральных вен возможны потенциальные технические и инфекционные осложнения.

Цель исследования - изучить ближайшие и отдаленные результаты эксплуатации артерио-венозной фистулы в качестве сосудистого доступа для длительной противоопухолевой терапии.

Материалы и методы: В статье проведен анализ состояния периферического венозного русла у 41 онкологического больного, получающих длительное лечение химиотерапией. Использованы методы допплерографии, морфологические и иммуногистохимические исследования.

Результаты: Качественные и количественные допплерографические изменения в венах предплечья в различные сроки после начала химиотерапии были обнаружены у большинства пациентов.

Основными морфологическими проявлениями повреждения венозной стенки были химические флебиты, локальное или продолженное склерозирование стенки вены, венозные тромбозы и экстравазации с некрозом и последующим склерозом паравазальных тканей.

У 12 больных сформированный альтернативный сосудистый доступ полностью отвечал критериям адекватности (безопасность, многократное использование, долгосрочность, реализация запланированной лечебной программы).

Выводы: Сделан вывод о непригодности периферических вен предплечья для длительного введения цитостатиков. При отсутствии возможности эксплуатации центральных вен, альтернативным сосудистым доступом может быть артерио-венозная фистула.

КЛЮЧЕВЫЕ СЛОВА: центральный венозный доступ, периферический венозный доступ, артерио-венозная фистула, химиотерапия.

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INTRODUCTION

Creation of long-functioning vascular access is the mandatory component of antitumor chemotherapy. At present peripheral venous catheters or "complete implanted vascular systems" can be used for this purpose [1,].

Multiple puncture of peripheral veins during polychemotherapy inevitably leads to mechanic damage of venous wall and luminal obliteration. High peak concentrations of cytostatic agents during chemotherapy as well as chronic chemically induced activation of venous

endothelium result in its sclerosis. These factors increase the risk of chemotherapeutic agent extravasation and make impractical long-term use of upper extremity veins for administration of cytostatic agents [2].

Complications after continuous use of synthetic external or completely dip venous catheters are neutropenias, thrombocytopenias, coagulopathies, chronic or acute active infections [3,4].

Elaboration of modern vascular access complying requirements of easy application, safety and reliability is an urgent problem nowadays.

Subcutanous arteriovenous fistula is considered to be an alternative vascular access for chemotherapy delivery. It was suggested by James Cimino and Michael Brescia in 1965 for treatment of patients with end-stage renal disease by means of chronic hemodialysis method. This method had no use in oncology practice till present time.

THE AIM

Objective - to study short-term and long-term results of arteriovenous fistula exploitation as vascular access for continuous anticancer chemotherapy.

MATERIALS AND METHODS

The article presents the analysis of examination, treatment and observation data of 41 patients (23 males and 18 females) with histologically confirmed diagnosis of malignant tumor, undergoing anticancer chemotherapy at Vinnytsia and Zaporizhzhya regional oncology hospitals during 2012-2016.

27 patients receiving chemotherapeutic agents in peripheral forearm veins by puncture method or temporary catheterization with butterfly catheter made the control group. The main group consisted of 14 patients with breast, gastric and colon carcinoma (5 males and 9 females aged 35-58) assigned to long-term adjuvant and palliative chemotherapy using arteriovenous forearm fistula as vascular access.

Depending on fistula formation level there were distal (radiocarpal) arteriovenous fistula (anatomic snuffbox region – in 3 patients, and lower third of the forearm – in 4 patients) and proximal arteriovenous fistula (the middle third of the forearm or the cubital fossa – in 7 patients). In all cases arteriovenous end-to-side anastomosis was used.

In 5 patients arteriovenous fistula was formed before the initiation of therapy while in 9 – in various periods (4-6 months) after its beginning.

The combination of cytostatic agents was used for anticancer chemotherapy according to conventional national standards (CMF, AC, TAC, FOLFOX4, FOLFIRI). By the mechanism of their action on soft tissues and venous endothelium, cytostatic agents belonged to abscessing and irritative chemotherapeutic preparations.

Planning the formation of arteriovenous fistula, anatomic suitability and functional reserve of forearm veins were evaluated. For this purpose duplex Doppler sonography of neck and upper extremity veins as well as X-ray contrast angiography were performed.

Doppler sonography was done on Lgi PVR/APL device (USA) using 7.2 mHz transducer. Duplex scanning of forearm veins and arteriovenous fistula was done on Acuson x 300 device (Siemens). Qualitative indices (dopplerographic curve pattern, anacrotic and dacrotic waves) and quantitative indices (cross-section area, linear and volumetric blood flow velocity) were studied.

Morphologic analyses were carried out to assess the damaging effect of cytostatic agents of various mechanisms of action on the venous wall status. Biopsy sampling with subsequent morphologic and immune histochemical analyses of forearm veins was performed during placing arteriovenous fistula.

Biopsy material was embedded in paraffin after its fixation in 10% solution of neutral formaline and preparation in ethanol solutions of increasing concentrations. In histologic study specimen staining with haematoxylin-eosin and picrofuscin by van- Gieson was performed. In histochemical analysis Mallory's staining and PAS-reaction were done; CD-34 expression was determined (proliferating epithelium marker). During morphological examination immune morphological, morphometric and statistical methods were used.

Short-term and long-term results of arteriovenous fistula exploitation were assessed as good, satisfactory, and unsatisfactory. For this purpose standard questionnaire EFC11784/XRP6258 adjusted for vascular access evaluation was used.

RESULTS AND DISCUSSION

Qualitative and quantitative dopplerographic changes in forearm veins in various time periods after chemotherapy initiation were found in the majority of patients.

In the course of exploitation, often after 3-4 courses of chemotherapy, thickening of forearm vein wall was observed not only in the site of the puncture but also on rather extended area in the direction of cephalic vein. At the same time decreased vein wall elasticity and decreased diameter of its lumen were registered. There was uneven and tuberous inner contour of the veins. Valvular apparatus of the veins was partially destructed. Calcified hematomas were formed at the puncture sites and in paravasal soft tissues.

Quantitative changes in forearm veins after their exploitation detected by Doppler sonography are given in Table I.

The severity of morphologic damages of venous walls was influenced by the number of chemotherapy courses and their duration, combination of cytostatic agents as well as technical complications during vein exploitation.

The major morphologic manifestations of venous wall damage were chemical phlebitis, local or extended hardening of venous wall, venous thrombosis, extravasations with necrosis and subsequent paravasal tissue sclerosis.

Within the period of 2-4 months after chemotherapy initiation the changes by myoelastosis type were detected

Table I. Quantitative indices of Doppler sonography and Duplex scanning in exploitation of peripheral forearm veins for chemotherapy treatment (n=12)

Blood flow indices	Baseline data	Indices after 6 months
Vascular cross-section area, mm	3.1±0.4	1.9±0.9
TAmx1, cm/c	6.4±2.4	0
FV1, l/min	0.053±0.012	0

in venous wall intima – solution of vascular wall continuity leading to defect formation and disorganized structural alignment of endotheliocytes on the basal membrane. Masson's staining demonstrated that cellular component began to disappear in the vein intima with predominance of collagen bands. Endothelial cell destruction as well as massive foci of damaged endothelium was observed in some patients. The changes described are presented on Fig.1.

Microscopic and immune histochemical changes in muscular membrane of venous wall after 6 months of its exploitation for cytostatic agent infusion are presented on Fig.2.

Thus, the changes in venous intima are indicative of its myoelastosis; hypertrophy and sclerosis developed in the muscular layer while destructive changes and sclerosis – in its outer coat.

The changes indicated that already at early stages of exploitation of peripheral vascular access for cytotoxic chemotherapy, even with no technical complications during puncture and catheterization of the vein, inflammatory and sclerotic changes developed in all three venous coats, recognized as subclinical chemical phlebitis.

Clinical exploitation of peripheral forearm veins after 4 months of chemotherapy was labored in 21 patients (77.8%) and it was impractical in 24 patients (88.9%) after 6 months of chemotherapy.

Among the patients with alternative vascular access 12 had long-functioning fistulas (85.7%). In 2 patients (14.3%) vascular access was unfit for exploitation – one patient developed early thrombosis of the created fistula while the other had inadequate blood flow through the fistula (<5 ml/min) and arterialization of fistula venous segment failed. In those patients temporary vascular access through central vein was used thereafter.

In 12 patients created vascular access completely met the adequacy criteria (safety, multiple use, longevity, realization of designed therapy program). No complications during or after drug injections (extravasation, paravasal hematoma) were noted. Blood access was facilitated due to large diameter of arterialized vein and was achieved without further repeated punctures.

Time of exploitation of functioning arteriovenous fistula was over 12 months. In 6 patients chemotherapy treatment was discontinued because of completion of designed therapy program. Disconnection of arteriovenous fistula was not required. In 6 patients exploitation of arteriovenous fistula was continued until the completion of scheduled treatment protocol.

CONCLUSIONS

Thus, a wide range of complications - from asymptomatic to clinically significant chemical phlebitis, sclerosis and obliterations – leads to the conclusion that forearm veins should not be used for anticancer chemotherapy on the whole. Their exploitation is possible for hydration, administration of antibiotics and monitoring of blood chemistry.

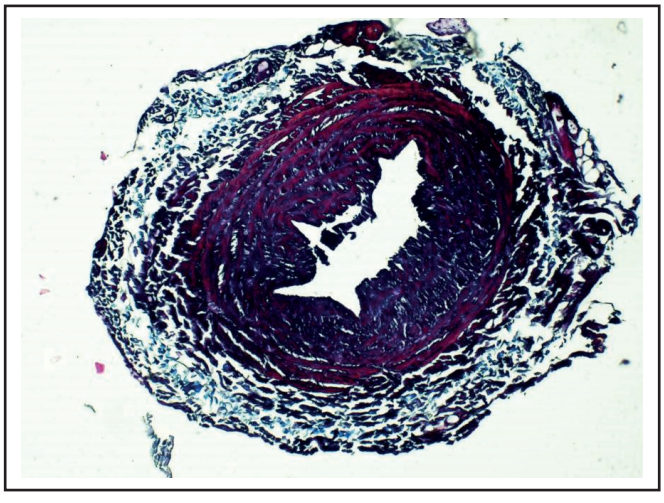

Fig.1. Photomicrograph of cubital vein cross section of oncology patient (The 56-year-old woman, diagnosis: breast cancer T4N1M1 after 4 months of palliative FAC chemotherapy). Masson's staining. Magnification x40. Vein lumen is considerably constricted and obliterated. Fragmentation of endothelial area is seen. There is hypertrophy of vein intima. The bands of collagen predominate instead of endotheliocytes (stained red). Massive foci of necrosis are present.

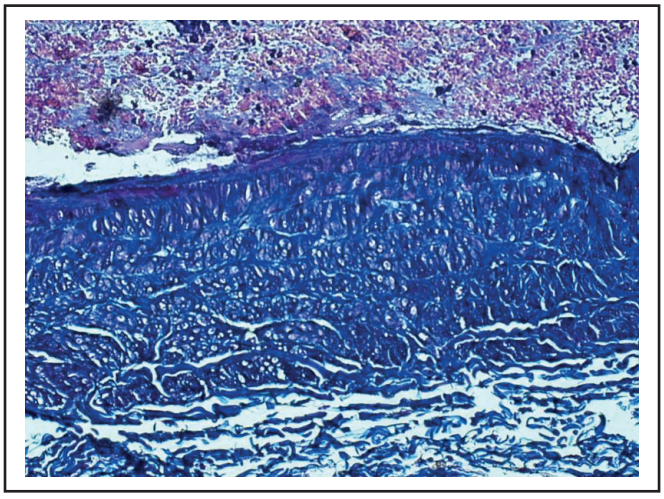

Fig.2. Photomicrograph of longitudinal section of forearm vein (6 months of CMF chemotherapy). Masson's staining. Magnification x100. Hypertrophy of muscular layer, separation of muscular fibers and massive proliferation are seen (stained pink).

In case of contraindications or inapplicability of "complete implanted vascular systems" arteriovenous fistula can be used as an alternative vascular access for long-term systemic chemotherapy in oncology patients.

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