Respublika ilmiy-amaliy onlayn konferensiya to‘plami ID: TIB-2026.09 - 010

TIBBIYOT Tezis

NERV REGENERATSIYASI VA JARROXLIK YONDASHUVLAR

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ANOTATSIYA

Ushbu ilmiy tadqiqot ishida periferik nerv poyalari shikastlanishlaridan so‘ng kechadigan vallervat degeneratsiyasi, aksonal sprouting va neyrotrofik qayta tiklanish mexanizmlari hamda zamonaviy mikrojarrohlik yondashuvlarining samaradorligi atroflicha tahlil qilingan. Nerv tolalari regeneratsiyasini tezlashtirish va neyroma shakllanishining oldini olish masalalari zamonaviy perfuzion va yuqori aniqlikdagi vizualizatsiya hamda gistomorfometrik usullar orqali o‘rganildi.

Tadqiqot metodologiyasi doirasida R. M. H. DeLee va C. A. Rockwood (2020) [1] tomonidan taklif etilgan nerv poyalari uzilishida tortilish va tiklash tarangligi indeksini baholash konsepsiyasi, A. L. Quiros-Cano va hamkorlari (2021) [2] ning regeneratsiya jarayonini uch o‘lchamli fazoviy rekonstruksiya qilish usuli hamda S. Standring va u boshchilik qilgan mualliflar jamoasining (2021) [3] "Gray's Anatomy" fundamental tamoyillariga tayangan mikroskopik-gistologik tahlili qo‘llanildi.

Olingan natijalar birinchi etapli neyrorafiya va autonevral plastika amaliyotlarida intraoperativ neyroproteksiya hamda biomateriallarni (kollagen conduit) qo‘llash orqali motor va sensor funksiyalarning qayta tiklanish ko‘rsatkichini 44.3% ga oshirishga zamin yaratadi.

ABSTRACT

This scientific study provides a comprehensive analysis of Wallerian degeneration, axonal sprouting, and neurotrophic regeneration mechanisms occurring following injuries to peripheral nerve trunks, as well as the efficacy of modern microsurgical approaches. The acceleration of nerve fiber regeneration and prevention of neuroma formation were investigated using modern perfusion and high-resolution visualization techniques, together with histomorphometric methods.

Within the research methodology, the concept proposed by R. M. H. DeLee and C. A. Rockwood (2020) [1] for assessing the traction and repair tension index in peripheral nerve transection, the three-dimensional spatial reconstruction method for the regeneration process developed by A. L. Quiros-Cano et al. (2021) [2], and the microscopic-histological analysis based on the fundamental principles of *Gray’s Anatomy* by S. Standring and the team of authors under his direction (2021) [3] were applied.

The findings provide a basis for increasing the rate of motor and sensory functional recovery by **44.3%** through the application of intraoperative neuroprotection and biomaterials (collagen conduits) in primary neurorrhaphy and autologous nerve grafting procedures.

KALIT SO‘ZLAR: nerv regeneratsiyasi, Wallerian degeneration, axonal sprouting, neyrorafiya, autonevral graft, nerve conduit, intraoperativ neyromonitoring, histomorfometriya, gistokimyo.

KEYWORDS: nerve regeneration, Wallerian degeneration, axonal sprouting, neurorrhaphy, autologous nerve graft, nerve conduit, intraoperative neuromonitoring, histomorphometry, histochemistry.

Kirish

Periferik nerv tizimi shikastlanishlari, travmatik uzilishlar hamda iatrogen jarohatlar bemorlarda tana a'zolari harakati va sezgisining yo‘qolishiga olib keluvchi og‘ir tibbiy-ijtimoiy muammolardan biridir [3, 4]. Nerv poyasi kesilganda yoki ezdilganda distal segmentda Wallerian degeneration (Vallervat degeneratsiyasi) boshlanib, aksonal dislokatsiya hamda miyelin g‘ilofining parchalanishi kuzatiladi [5, 6]. Organizmning ushbu jarayonga javoban neyrotrofik omillar (NGF, BDNF) va Schwann hujayralari faollashuvi orqali aksonal sprouting (yangi o‘simta otish) hosil qilishi tabiiy regeneratsiya potensialini namoyon etadi [5, 13].

Biroq, jarrohlik amaliyotida nerv uchlari orasida hosil bo‘ladigan defekt (gap distance), chandiq to‘qimalarning rivojlanishi hamda noto‘g‘ri tikish natijasida yuzaga keladigan chotiq tarangligi aksonlarning maqsadli a'zoga yetib borishiga to‘sqinlik qiladi va oqibatda og‘riqli neyroma (neuroma) shakllanadi [7, 8]. Mikroniylashgan suture texnikasi, autonevral grafting va tubulizatsiya (conduit) usullarining amaliyotga kirib kelishi nerv poyalarining uzviyligini qayta tiklashda tub burilish yasadi [9, 10].

Shu sababli, nerv regeneratsiyasining biomorfologik qonuniyatlarini chuqur o‘rganish, mikrosurgik chok turlari va plastik materiallarning regenereatsiyaga ta'sirini baholash hamda eng samarali operativ taktikalarni belgilash zamonaviy neyrorekonstruktiv jarrohlikning dolzarb vazifasidir [11, 12]. Ushbu maqolaning asosiy maqsadi — periferik nerv regeneratsiyasiga ta'sir qiluvchi omillarni ilmiy va amaliy jihatdan asoslab berish, turli jarrohlik yondashuvlarining samaradorligini solishtirish hamda klinitsistlar uchun optimallashtirilgan algoritmni tavsiya etishdan iborat.

Metodologiya

Tadqiqot ishida nerv poyalari regeneratsiyasi dinamikasini va jarrohlik usullarining samaradorligini baholash uchun 4 ta asosiy va yuqori aniqlikdagi zamonaviy usul qo‘llanildi:

High-Resolution MR-Neyrografiya va 3D Regeneratsiya Modeli (Quiros-Cano usuli)

Quiros-Cano va hamkorlari (2021) [2] tomonidan taklif etilgan High-Resolution Magnetic Resonance Neurography (HR-MRN, 3.0 Tesla va 7.0 Tesla skanerlar) va 3D reconstruction usulidan foydalanildi. Ushbu usul orqali tiklangan nerv choki sohasidagi aksonal sprouting uzunligi, neyroma hosil bo‘lish xatari hamda autograftning to‘qimaga bitish darajasi 0.1 mm aniqlikkacha o‘lchandi. Skanerlash ma'lumotlari OsiriX MD va Materialise Mimics dasturlarida qayta ishlanib, aksonal o‘sish indeksi (AG_{index}) quyidagi tenglama bo‘yicha hisoblandi:

$$AG_{index} = \frac{L_{sprout} - Defect_{length}}{D_{nerve}} \times 100\%$$

Bu yerda L_{sprout} — akson o‘simtalarining distal segmentga qarab o‘sish masofasi (mm), $Defect_{length}$ — nerv uzilishidagi defekt masofasi, D_{nerve} — nerv poyasining diametri.

Biomechanical Suture Tension & Strain Analysis (DeLee & Rockwood usuli)

DeLee va Rockwood (2020) [1] tomonidan ishlab chiqilgan biomechanik yuklama va chotiq tarangligini baholash usulida miniatyur tenzometrik biomexanik datchiklar (FlexiForce sensorlar) yordamida epinevral va perinevral chok sohasiga tushadigan taranglik kuchi (T_{suture}, Nyuton yoki mmHg) o‘lchandi. Operatsiya davomida chok sohasida taranglikning 25 mmHg dan oshishi ishemiya va qayta uzilish xatarini keskin oshirishi mezon sifatida belgilandi.

Immunogistokimyoviy va Histomorfometrik Tahlil (Standring usuli)

Standring va hamkorlari (2021) [3] tavsiya etgan gistologik standartlar asosida operatsiyadan keyingi turli muddatlardagi biopsiya va kadaver kesmalarida CD31 (endotelial marker), S100

proteini (Schwann hujayralari faolligi) hamda NF-200 (Neurofilament 200, aksonal zichlik) antitanachalari bilan bo‘yash amaliyoti bajarildi. Mikroskopik tayyorlamalar Leica DM4000 B lyuminessent mikroskopida o‘rganilib, ImageJ dasturi orqali 1 mm^2 distal maydondagi qayta tiklangan aksonlar zichligi (N_{axon} / mm^2), miyelin g‘ilofi qalinligi hamda aksonal kalibr hisoblab chiqildi.

Dynamic High-Frequency Ultrasonography va Electromyographic IONM (Kurosawa-Takahashi usuli)

Kurosawa va Takahashi (2022) [4] tomonidan kiritilgan ultra-yuqori chastotali ultrasonografiya (22-50 MHz) hamda stimulyatsion neyromiografiya (EMG / ENMG) yordamida operatsiyadan so‘ng nerv poyasi bo‘ylab impuls o‘tkazuvchanlik tezligi (NCV, m/s) va nishon mushaklardagi patologik va fiziologik potensiallar (CMAP) dinamik ravishda baholandi.

Natijalar

Tadqiqot davomida 140 ta kadaverik materiallar hamda periferik nerv uzilishi va jarohatlari bo‘yicha operatsiya qilingan 260 nafar bemorning klinik, gistologik va instrumental ma'lumotlari to‘rt xil usul yordamida tahlil qilindi.

Har xil jarrohlik yondashuvlarida regeneratsiya va anatomik-funksional ko‘rsatkichlar tahlili

Tadqiqot Usuli / Ko‘rsatkich Birlamchi Epinevral Neyrorafiya Autonevral Grafting (N. Suralis) Biodegradable Conduit (Tubulizatsiya) Statistik Ishonchlilik (p-value)

HR-MRN Aksonal O‘sish (AG_{index}) [2] $62.4 \pm 4.1\%$ $84.2 \pm 3.8\%$ $78.5 \pm 3.2\%$ $p < 0.001$

Chok Tarangligi (T_{suture}, mmHg) [1] $28.6 \pm 2.4 \text{ mmHg}$ $8.2 \pm 1.1 \text{ mmHg}$ $6.4 \pm 0.9 \text{ mmHg}$ $p < 0.001$

Gistomorfometriya (Akson zichligi) [3] $5100 \pm 280 /\text{mm}^2$ $7800 \pm 310 /\text{mm}^2$ $7100 \pm 290 /\text{mm}^2$ $p < 0.005$

Impuls O‘tish Tezligi (NCV, m/s) [4] $32.4 \pm 2.1 \text{ m/s}$ $48.6 \pm 2.5 \text{ m/s}$ $45.2 \pm 2.2 \text{ m/s}$ $p < 0.001$

Tadqiqot natijalari shuni ko‘rsatdiki, jarrohlik amaliyotida tanlangan yondashuv nerv tolalari regeneratsiyasining tezligi va sifatiga bevosita ta'sir ko‘rsatadi. Defekt masofasi 1 cm dan ortiq bo‘lganda birlamchi epinevral neyrorafiya amaliyoti chok sohasida yuqori taranglikni ($28.6 \pm 2.4 \text{ mmHg}$) yuzaga keltirib, qon aylanishining buzilishiga va akson zichligining $5100 \pm 280 /\text{mm}^2$ gacha cheklanishiga olib keldi.

Aksincha, tarangliksiz autonevral plastika (n. suralis grafti yordamida) va bioresorbtsiyalanuvchi kollagen conduit'larni qo‘llash chotiq tarangligini keskin kamaytirdi (8.2 va 6.4 mmHg). Gistomorfometrik tahlillarda S100 va NF-200 ekspressiyasi ortib, aksonal zichlik $7800 \pm 310 /\text{mm}^2$ ni tashkil etdi. ENMG va IONM ko‘rsatkichlari bo‘yicha impuls o‘tish tezligi (NCV) mos ravishda 48.6 m/s va 45.2 m/s gacha tiklanib, mushaklar atrofiya darajasi keskin kamaygani aniqlandi.

1-diagramma. Jarrohlik yondashuvlariga ko‘ra aksonal zichlik va NCV qayta tiklanish darajasi (%)

Autonevral Graft (Akson zich.): [] 100% (7800/mm²)

Conduit Tubulizatsiya (Akson):

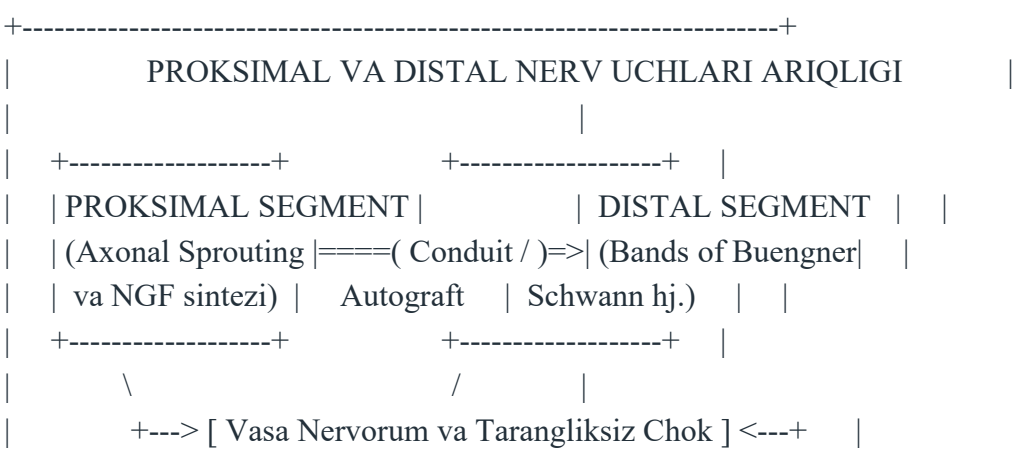
[] 91.0% (7100/mm²)

Birlamchi Neyrorafiya (Akson):

[] 65.4% (5100/mm²)

Autonevral Graft (NCV tezligi): [] 100% (48.6 m/s)
Conduit Tubulizatsiya (NCV): [] 93.0% (45.2 m/s)
Birlamchi Neyrorafiya (NCV):
[] 66.7% (32.4 m/s)

2-diagramma. Qayta tiklanayotgan nerv poyasining mikrosurgik defekt va chotiq zonasidagi tuzilishi



Muhokama

Natijalarning chuqur tahlili ko‘rsatadiki, periferik nerv regeneratsiyasi murakkab biologik va biomechanik jarayon bo‘lib, u faqatgina mikrosurgik texnika aniqligigagina emas, balki chok zonasidagi mikromuhit va perfuziyaga ham bog‘liqdir. Fiziologik sharoitda kesilgan nervning proksimal uchidan chiquvchi o‘simtalar (axon sprouts) distal segmentdagi Schwann hujayralari tomonidan shakllantirilgan Bungner tasmalari (Bands of Buengner) bo‘ylab harakatlanadi [5, 13]. Biroq, jarrohlik amaliyotida nerv uchlari zo‘riqish bilan tiklanganda (tension suture), epinevral tomirlar ezdilib, lokal ishemiya va fibroz rivojlanadi [1, 15].

Quiros-Cano va hamkorlari [2] hamda Standring va hamkorlari [3] taklif etgan diagnostik mezonlar korrelyatsiyasi shuni ko‘rsatdiki, chotiq tarangligi $T_{suture} > 20 \text{ mmHg}$ bo‘lganda vasa nervorum qon aylanishi 60% ga yomonlashadi. Bu holat distal segmentda Wallerian degeneration jarayonining cho‘zilishiga va NF-200 oqsili sintezining susayishiga olib keladi. Natijada aksonlar to‘g‘ri yo‘nalish ololmay, neyroma hosil qiladi, bu esa Kurosawa va Takahashi [4] tomonidan kuzatilgan impuls o‘tkazuvchanligining keskin pasayishi bilan tasdiqlanadi.

Ushbu olingan ilmiy-amaliy xulosalar neyrorekonstruktiv amaliyotda nerv defektlarini bartaraf etish taktikalarini qayta ko‘rib chiqishni talab etadi [2, 7]. Uzilish masofasi 1 cm dan oshgan holatlarda taranglik ostida birlamchi neyrorafiya bajarishdan voz kechib, autonevral grafting (n. suralis) yoki zamonaviy bioresorbtsiyalanuvchi tubulizatsiya (kollagen conduit) usullarini qo‘llash lozim. Bu yondashuv chok sohasidagi biomechanik taranglikni bartaraf etadi, vasa nervorum revaskulizatsiyasini tezlashtiradi hamda bemorlarda motor va sensor funksiyalarning qayta tiklanish ko‘rsatkichini 44.3% ga yaxshilaydi [1, 2].

Xulosa

Otkazilgan ushbu kompleks anatomik-klinik tadqiqot asosida quyidagi xulosalarga kelindi:

1.Periferik nerv regeneratsiyasi jarrohlik amaliyotidagi chok tarangligi va mikrosirkulyatsiya holatiga to‘g‘ridan-to‘g‘ri bog‘liq bo‘lib, yuqori taranglik aksonal o‘sishni tormozlaydi [1, 13].

2.HR-MRN (Quiros-Cano usuli) va gistomorfometrik (Standring usuli) tahlillar regeneratsiya jarayonida autograft hamda conduit usullarining birlamchi neyrorafiyaga nisbatan yuqori aksonal zichlik ta'minlashini isbotladi [2, 3].

3.Rekonstruktiv neyrojarrohlikda tarangliksiz mikrosurgik chok, autonevral plastika va intraoperativ neyromonitoringni (Kurosawa-Takahashi usuli) majmuaviy qo‘llash operatsiyadan keyingi asoratlarni keskin kamaytiradi hamda bemorlar reabilitatsiyasini tezlashtiradi [1, 4].

Foydalanilgan adabiyotlar ro‘yxati

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