tanja zatvorenog tipa ispitana je učestalost (nikad = 1, rijetko = 2, često = 3 i uvijek = 4) pojedinih postupaka izvananalitičke faze laboratorijske dijagnostike uz prekodiranje negativnih pitanja. Odgovori na pitanja izražavaju se prosječnom ocjenom 1,0-4,0. Pitanja su podijeljena u tri skupine: kriteriji prihvatljivosti uzorka (6 pitanja), postupci vađenja krvi (6 pitanja), izvještavanje nalaza (7 pitanja) i izdvojeno je pitanje o bilježenju nesukladnosti u radu. Na upitnik je odgovorilo 144 ispitanika (27% aktivnih članova HKMB) prosječne dobi medijan (interkvartilni raspon) = 47 (26-65) godina, 93% žena. Ispitanici su 57% diplomirani inženjeri medicinske biokemije, 40% specijalisti i 3% docenti i profesori. Farmaceutsko-biokemijski fakultet je završilo 96% ispitanika, 62% je dobre informatičke pismenosti. U laboratorijima primarne zdravstvene zaštite (PZZ) radi 40% ispitanika, 15% u laboratorijima općih bolnica, 13% u specijalističkim bolnicama, 12% u kliničkim bolnicama, 13% u kliničkim bolničkim centrima te 7% u privatnim laboratorijima.

Rezultati: Prosječna ocjena odgovora na sva pitanja u svih ispitanika iznosi X ± SD = 3,1 ± 0,4. Nema statistički značajne razlike s obzirom na vrstu ustanove, stupanj usavršavanja i informatičku pismenost, dok razlika s obzirom na spol i završen fakultet nije ispitana zbog izrazite nejednolikosti raspodjele. Nema povezanosti prosječne ocjene i dobi ispitanika. Postoji statistički značajna razlika između prosječne ocjene sve tri skupine pitanja, prihvatljivosti uzorka 3,3 ± 0,5 vs. postupci vađenja krvi 2,8 ± 0,5 vs. izvještavanje nalaza 3,2 ± 0,5 (P < 0,001). Nesukladnosti u radu nikad i rijetko bilježi 21%, a često i uvijek 79% ispitanika.

Zaključci: Iako bi se prosječna ocjena 3,1 mogla bi se smatrati visokom, najniža ocjena faze vađenja krvi pokazuje potrebu za dodatnom izobrazbom i kontrolom kako ovog segmenta tako i cijele izvananalitičke faze.

e-pošta: lhonovic@obpula.hr

ng anonymous questionnaire with 20 Likert scale questions to testing frequency (never = 1, rarely = 2, often = 3, always = 4) of representative procedures of pre-analytical phase with recoding of negative questions. Answers were expressed as average grade 1.0-4.0. There were three groups of questions: criteria of acceptance of sample (6), procedures of phlebotomy (6), reporting of results (7) and one separate question about recording of non-conformity in work. The questionnaire was completed by 144 subject (rate response 27%) with median age 47 ranged from 26 to 65 years, 93% women. Subjects were 57% clinical chemist, 40% specialists and 3% professors; 96% of subjects graduated from Faculty of Pharmacy and Biochemistry; 62% had good computer skills; 40% of subjects work in primary care laboratories, 15% in laboratories of general hospitals, 13% in special hospitals, 12% in clinical hospitals, 13% in university hospital centers and 7% in private laboratories.

Results: Average grade of all answers in whole subject group was X ± SD = 3.1 ± 0.4. There was no difference regarding type of laboratory and institution, professional degree or computer skills. There was no correlation between average grade and age. There is statistically significant difference between average grade of three groups of questions: criteria of acceptance of sample 3.3 ± 0.5 vs. procedures of phlebotomy 2.8 ± 0.5 vs. reporting of results 3.2 ± 0.5 (P < 0.001). 21% of subject never or rarely record nonconformities in work while 79% often or always.

Conclusion: Although average grade of 3.1 may seems high, the lowest grade of phlobotomy phase reveals the neediness for additional education on primary sample collection and control of all non-analytical phases.

e-mail: lhonovic@obpula.hr

S07 – Transplantacija

S07-1

Krv pupkovine kao izvor matičnih stanica

Golubić-Čepulić B

Zavod za kliničku transfuziologiju, Klinički bolnički centar Zagreb, Zagreb

Autor nije poslao sažetak.

S07 – Transplantation

S07-1

Cord blood as a source of stem cells

Golubić-Čepulić B

Department of Clinical Transfusiology, Zagreb University Hospital Center, Zagreb, Croatia

The author did not provide an abstract.

S07-2

Transplantacija krvotvornih matičnih stanica u djece s primarnim imunodeficijencijama

Kelečić J

Klinika za pedijatriju, Klinički bolnički centar Zagreb, Zagreb

Primarne imunodeficijencije nasljedni su poremećaji imunosti, obično s lošom prognozom. Transplantacija krvotvornih matičnih stanica (TKMS) liječenje je izbora u mnogih bolesnika s primarnim imunodeficijencijama (PID), npr. bolesnika s teškom stanično humoralnom imudeficijencijom (SCID), Wiskott-Aldrich sindromom (WAS), spolno vezanim hiper IgM sindromom, kroničnom granulomatoznom bolesti, Chediak-Higashi sindromom, spolno vezanim limfoproliferativnim sindromom, hemofagocitnim sindromima. Prve TKMS srodnog podudarnog darivatelja u bolesnika s primarnim imunodeficijencijama učinjene su 1968. godine u tri bolesnika (dva s teškom stanično humoralnom ID/SCID, i jednog bolesnika s Wiskott-Aldrich sindromom/WAS). Od tada postignut je velik napredak u liječenju bolesnika s primarnim imunodeficijencijama transplantacijom krvotvornih matičnih stanica. Nekoliko čimbenika utjecalo je na poboljšanje ishoda TKMS: 1) poboljšanje tehnika tipizacije tkiva, 2) mogućnost određivanja subpopulacija i broja hematopoetskih stanica, 3) dostupnost transplantata HLA-podudarnih nesrodnih darivatelja (koštana srž, periferne matične stanice, umbilikalna krv), 4) manje agresivni protokoli u pripremi bolesnika za transplantaciju s posljedično manjim brojem komplikacija u posttransplantacijskom razdoblju. Važni čimbenici koji utječu na rezultat liječenja su dob bolesnika i njegovo zdravstveno stanje. Niža životna dob i odsutnost teških infekcija, posebice virusnih (herpes virusi, enterovirusi) smanjuju rizik od komplikacija u posttransplantacijskom razdoblju. Najpovoljniji ishod za bolesnike s PID postiže se transplantacijom krvotvornih matičnih stanica srodnog podudarnog darivatelja, koja je usješna u oko 90% bolesnika s teškom stanično humotralnom imunodeficijencijom (SCID), spolno vezanim hiper IgM sindrom, Wiskott-. Aldrich sindromom i drugim spolno vezanim imunodeficijencijama. Mogućnost liječenja transplantacijom krvotvornih matičnih stanica podudarnog srodnog darivatelja je ograničena. Tansplantacija krvotvornih matičnih stanica djelomično podudarnog srodnog darivatelja u bolesnika sa SCID-om povezana je sa značajno odgođenim i nekompletnim oporavkom imunološkog sustava. Zbog dostupnosti krvotvornih matičnih stanica nesrodnih darivatelja TKMS optimalan je izbor za liječenje mnogih bolesnika s primarnim imunodeficijencijama. Izbor odgovarujećeg darivatelja, liječenje i kontrola infekcija, priprema

S07-2

Haematopoetic stem cell transplantation in primary immunodeficiencies

Kelečić J

Department of Pediatrics, Zagreb University Hospital Center, Zagreb, Croatia

Primary immunodeficiencies (PIDs) are complex congenital disorders characterised by impairment of innate or adaptive immunity, and usually a poor prognosis. Hematopoietic stem cell transplantation (HSCT) represents a curative approach in many of these disorders, including severe combined immunodeficiencies (SCIDs), Wiskott-Aldrich syndrome, phagocyte disorders such as chronic granulomatous disease and leucocyte adhesion deficiency, Chediak-Higashi syndrome, hemophagocytic syndromes, X-linked hyper IgM syndrome, X-linked lymphoproliferative syndrome. The first hematopoetic stem cell transplantation with durable success in humans were reported in 1968 in three patients with primary immunodeficiencies who received grafts from HLA-matched siblings (two with severe combined immunodeficiency, and one with Wiskott-Aldrich syndrome).Since then significant progress has been made with HSCT for PIDs. There are several factors that influence the outcome of HSCT in PIDs patients: 1) high resolution tissue typing, 2) ability to phenotype and quantitate hematopoetic stem cells, 3) availability of closely matched unrelated donor bone marrow, peripheral blood stem cells and cord blood, 4) the aplication of reduced intensity conditioning regimens pre-transplant associated with significantly reduced early post-transplant mortality. The most important factors are the age at transplant and general health of the patient. Young age is associated with fewer comorbidities and less frequent pre-transplant exposure to herpes family and enteric viruses, thus lowering the risks of related post-transplant complications. The optimal results of HSCT in primary immunodeficiencies have long been obtained with related HLA-identical donors. HSCT using HLA-identical healthy sibling donors can provide correction of PIDs such as SCID, Wiskott-Aldrich syndrome (WAS) and other X-linked immunodeficiencies in approximately 90% of the cases. This option is limited to a minority of patients. Transplantation from mismatched related donors has been used with good results mainly in infants with severe combined immunodeficiency, but has been associated with significantly delayed or incomplete immune reconstitution. Recent data indicate that transplantation from matched unrelated donors and cord blood tranplantation represent valid alternatives, which can be used in all forms of severe primary immunodeficien-

bolesnika prije transplantacije znatno utječu na povoljan ishod transplantacije krvotvornih matičnih stanica u bolesnika s primarnim imunodefcijencijama.

e-pošta: jadranka.kelecic@zg.t-com.hr

cies. Optimal donor choise, monitoring of infection and preemptive treatment has resulted in a significant improvement for severe form of primary immunodeficiencies.

e-mail: jadranka.kelecic@zg.t-com.hr

S07-3

Hepatitis C i ortotopna transplantacija jetre

Čolić-Cvrlje V

Klinika za unutarnje bolesti, Klinička bolnica Merkur, Zagreb

HCV infekcija najčešća je indikacija za transplantaciju jetre u Europi: 40-60%. Ishod ortotopne transplantacije jetre (OTJ) zbog HCV infekcije je univerzalna virusna reinfekcija i recidiv hepatitisa s progresijom u cirozu jetre. Učestalost progresije bolesti i teških oblika HCV kroničnog hepatitisa postOTJ u porastu su posljednjih godina.
Indikacije za OTJ su: jetrena dekompenzacija CTP > 7, refraktorni ascites, encefalopatija, preboljeli spontani bakterijalni peritonitis, krvarenje iz varikoziteta jednjaka unatoč liječenju. HCV i HCC na listi su bez jetrene dekompenzacije, uz Milanske kriterije: 1 tumor manji od 5 cm, 3 tumora manja od 3 cm, bez invazije u veće krvne žile, bez ekstrahepatalnih metastaza. Bolesnici imaju prioritet s dodatnim MELD bodovima 20-24 koji se povisuju svaka 3 mjeseca. Posttransplantacijski dolazi do HCV reinfekcije i HCV RNA je pozitivna u serumu. 75% bolesnika razvije akutni hepatitis kroz 6 mjeseci postOTJ, 80% kronični hepatitis kroz 1-2 g, 30% cirozu kroz 5 godina, < 10% FCH. Čimbenici povezani s težinom, progresijom bolesti i preživljavanjem postOTJ povezani su sa domaćinom, virusom, okolinom, donorom. Pre i postOTJ vrijednosti HCV RNA su prediktor težine oboljenja jetre postOTJ. Donorski faktori povezani s teškim recidivom HCV: dob > 50, steatoza - lošiji ishod, prolongirano vrijeme ishemije, CMV koinfekcija. Kortikosteroidi povećavaju HCV viremiju, a bolusi su štetni za primaoca. Nema razlike u težini HCV recidiva u odnosu na terapiju takrolimusom ili ciklosporinom. MMF nema utjecaja na razinu HCV RNA. Pretransplantacijska antivirusna terapija daje se kod visokih vrijednosti HCV RNA prije OTJ. Antivirusna terapija kod Child B i Child C ciroze se teško provodi i rezultira sa SVR 13% kod genotipa 1. Antivirusna terapija ograničena je za Child A cirozu. Preemptivna terapija 4-6 tjedana postOTJ je profilaksa, ali je slaba antivirusna efikasnost i loša podnošljivost. Terapija za kronični recidivirajući HCV hepatitis je kom-

S07-3

Hepatitis C i orthotopic liver transplantation

Čolić-Cvrlje V

Department of Internal Medicine, Merkur University Hospital, Zagreb, Croatia

HCV infection in Europe and USA is the most common indication for liver transplantation 40–60%. Outcome of HCV related OLT is universal viral infection and recurrent hepatitis C with progression to cirrhosis. The frequency of disease progression and the risk for severe HCV hepatitis postOLT are increasing in recent years.
Indication for OLT are liver decompensation CTP > 7, refractory ascites, encephalopathy, history of spontaneous bacterial peritonitis, varicel bleeding unresponsive to treatment, hepatocellular carcinoma. HCV + HCC coexistence are listed in the absence of hepatic decompensation according the Milan criteria: 1 nodule less than 5 cm, 3 nodules less than 3 cm, abscence of vascular invasion, absence of extrahepatic metastases. Pts are given added priority with minimum MELD score 22 that increases every three months.
Posttransplant HCV recurrent infection is evident by reappearence of HCV in serum, decrease of HCV RNA in anhepatic phase. HCV RNA level increases rapidly 2 weeks postOLT and is 10-20 fold higher 1 year after OLT. 75% patients develop acute hepatitis in 6 months post OLT, 80% chronic hepatitis in 1-2 years, 30% cirrhosis in 5 years and < 10% accelerated FCH. Factors influencing disease severity, progression and survival postOLT are related to host, virus, enviroment, donor. PreLT and early postLT viral loads are predictors of severe liver disease. Higher preLT viral load – lower is postLT survival.
Donor factors are: age > 50, steatosis - worse outcome, prolonged ischemic time, CMV coinfection. Corticosteroids increase levels of hepatitis C viremia in nontranspant HCV infected pts and postOLT boluses are harmful to HCV recipients. They increase HCV levels. Corticosteroide treatment for rejection have increased risk of death. Greater immunosupression leads to more sever postOLT HCV hepatitis. There is no difference among patients re-

binacija PEG IFN + RBV. Doza IFN ista kao u netransplantiranih, ribavirin prema klirensu kreatinina. Trajanje terapije najmanje 6 mjeseci nakon negativiziranja HCV RNA. Vrijeme uvođenja terapije: akutni hepatitis, kronični HCV hepatitis, kolestatski fibrozantni hepatitis. Multidisciplinarni pristup zbog optimiziranja pune doze. Upotreba filgastrima (Neupogen) zbog sprječavanja redukcije doze ili prekida terapije. Terapija održavanja za FCH do SVR. Rani virusni odgovor prediktor je SVR. Veća efikasnost kod non-1-genotipova. Retransplantacija se vrši rutinski. Prediktori lošijeg ishoda su: dob > 50, bilirubinemija, renalna insuficijencija, FCH, rani recidiv sa zatajenjem grafta unutar 1 godine. U Kliničkoj bolnici „Merkur" izvršeno je 300 OTJ različitih indikacija. Zbog HCV ciroze 41 bolesnik. 9 je umrlo nakon OTJ, 32 bolesnika živi 3 mjeseca do 6 godina, u dijelu bolesnika provodi se terapija pegiliranim interferonom i ribavirinom. Kod 2 bolesnika izvršena je retranplantacija zbog recidiva HCV ciroze.
Loš ishod HCV transplantiranih bolesnika posljednjih godina povezan je sa svim pre i posttransplantacijskim faktorima: domaćinom, donorom, virusom, okolinom, imunosupresijom, terapijom kortikosteroidima, uspješnosti pre i postOTJ antivirusne terapije, retransplantacijom. Bolesnike s recidivom oboljenja potrebno je liječiti antivirusnom terapijom pegiliranim interferonom i ribavirinom.

e-pošta: vesnacoliccvrlje@yahoo.com

ceiving tacrolimus or cyclosporin. MMF treatment has no impact on HCV levels. With higher RNA levels preOLT there is 30% greater mortality. In cirrhosis Child B and C antiviral therapy is poor tolerated with serious AE. SVR is only 13% in genotype 1. Antiviral therapy is limited to Child A cirrhosis. Posttransplant antiviral therapy is preemptive therapy for prophylaxis is tolerable but not efficient. Therapy for established HCV recurrence is PEG IFN monotherapy or PEG IFN+RBV combination. Dose reduction of PEG IFN is 80% patients. Low initial doses of ribavirin are required with gradual dose escalation. Retransplantation for HCV is routine. Poor outcome predictors are: age > 50, high bilirubin, renal failure, FCH. Indications for ReTx is therefore without consensus. In hospital "Merkur" 300 OLT were performed for different indications. 41 pts for HCV cirrhosis. 9 pts died post OLT, 32 pts lives 3 months to 6 years. Some pts are treated with PEG IFN + RBV. 2 pts were retransplanted for HCV cirrhosis recidive.
In conclusion the worse outcome of HCV related patients in recent years is associated with the all pretransplant and posttransplant variables: host, donor, viral, enviroment, immunosupression, corticosteroid therapy, success of pre and postOLT antiviral therapy, retransplantation.

e-mail: vesnacoliccvrlje@yahoo.com

S07-4

Imunološki status u transplantaciji solidnih organa

Šiftar Z

Zavod za kliničku kemiju, Klinička bolnica Merkur, Zagreb

Uvod: Transplantacija je danas široko prihvaćena metoda izbora u liječenju pacijenata s terminalnim stadijem bolesti bubrega, jetre, pankreasa, koji mogu podnijeti transplantacijski zahvat i dugotrajno uzimanje imunosupresivne terapije, neophodne za preživljenje presadka i samog pacijenta.
Prosudba optimalnog doziranja kombinirane terapije, inicijalne i terapije održavanja, je još uvijek jedan od najvećih problema u transplantaciji bubrega. Akutno odbacivanje može dovesti do gubitka presadka i vrlo je važan rizični faktor za nastanak kroničnog odbacivanja, pri čemu T limfociti igraju važnu ulogu u patogenezi odbacivanja. U najmanju ruku, barem određene limfocitne skupine bi morale odražavati sliku aktiviranih stanica koje se nalaze

S07-4

Immune profile in solid organ transplantation

Šiftar Z

Institute of Clinical Chemistry, Merkur University Hospital, Zagreb, Croatia

Introduction: Transplantation is now widely accepted method of choice in the treatment of patients with terminal stage kidney, liver, pancreas disease etc who can resist transplantation procedure and long-term intake of immunosuppressive therapy, necessary for graft survival and the patient.
Assessment of the optimal dosage of combined therapy, the initial and maintenance therapy, is still one of the greatest problems in kidney transplantation. Acute rejection may lead to graft lost and it is an important risk factor for the emergence of chronic rejection, in which T cells play an important role in the pathogenesis of rejection. At least certain groups of lymphocyte in circulation should reflect the image of active cells that are found locally

lokalno unutar presadka. Trenutačno ne postoji pojedinačni biljeg koji bi sigurno predvidio odbacivanje izuzev PHD analize bubrežne biopsije i kontinuirano praćenje raspodjele limfocitnih populacija može imati klinički značaj. Za direktno mjerenje efektivnog učinka imunosupresivne terapije na staničnoj razini otprije su korišteni broj T limfocita i broj CD4+ T limfocita, omjer CD4/CD8, dvostruko pozitivna (CD3+CD4+CD8+) i dvostruko negativna (CD3+CD4-CD8-) populacija T limfocita, te broj aktiviranih T limfocita (CD25+).

Materijal i metode: Tijekom 2007. i 2008. godine 72 transplantirana pacijenta u Kliničkoj bolnici „Merkur", (54 bubreg, 13 bubreg/pankreas /SPKT/ i 5 bubreg/jetra /LKT/), 42 muških i 30 žena, prosječne dobi od 44 godina (raspon 16-68), je primilo kombiniranu, inicijalnu, prije transplantacije: kortikosteroid, kalcineurinski inhibitor, anti-CD25 ili anti timocitni globulin i terapiju održavanja, poslije transplantacije: kortikosteroid, kalcineurinski inhibitor, anti-CD25 ili anti timocitni globulin, mikofenolat mofetil. Histološki nalaz indicirane biopsije bubrega tijekom prve godine je potvrdio akutno odbacivanje u 27 pacijenta (21 bugreg,4 SPKT, 2 LKT). Provedeno je višestruko određivanje brojnosti limfocitnih populacija u venskoj krvi: T limfocita, B limfocita, NK stanica, CD4+ i CD8+ T limfocita, aktiviranih T limfocita: CD25+, CD69+, CD127+, aktiviranih (CD25+) CD4 i CD8 T limfocita, i specifične populacije T limfocita, CD3+CD4+CD25high+ metodom protočne citometrije. Kvantifikacija limfocitnih populacija je urađena na protočnom citometru EPICS XL, Coulter, prema "liziraj/ne peri" standardnom postupku s FlowCount kalibracijskim česticama, uz uvjete čitanja na citomeru prema protokolu CD45/postranično raspršenje (SSC). Obilježavanje stanica je urađeno sa direktno obilježenim protutijelima za protočnu citometriju firme Beckman-Coulter i Dako. Rezultati mjerenja su bili u suglasju i unutar ciljnih vrijednosti unutarnje i vanjske kontrole kvaliete UKNEQAS Immune Monitoring.

Rezultati: Nakon indukcijske faze, očekivano se javlja smanjenje brojnosti svih skupina limfocitne populacije, pri čemu je pad drastičniji kada se primjenjuje antitimocitni globulin umjesto anti-CD25. Tijekom terapije održavanja postupno se javlja oporavak istih, do normalizacije unutar 3 mjeseca, pri čemu nije uočena različitost ponašanja između 2 skupina pacijenata. Broj aktiviranih CD25+ T limfocita tijekom 1 mjeseca raste i uglavnom se nalazi u populaciji CD4+ T limfocita. Populacija CD3+CD4+CD25high+ je dio CD25 aktiviranihCD4+ T limfocita, a literaturno ima pozitivan efekat na stabilnost presadka, za razliku od CD69+ aktiviranih T limfocita. Pozitivnost biljega CD25+ na CD8+ se javlja usporedo sa izražajem na CD4+ T limfocitima i tada govori u prilog upalnim komplikacijama, tipa infekcija. Rezultati mjerenja na EPICS XL su ponovljivi i provjereni u praksi na drugom citometru, FC500, Beckman-Coulter.

within graft. So far, there is no single marker that would safely predict rejection except PHD analysis of renal biopsy, and continuous monitoring of lymphocyte population distribution may have clinical significance. To directly measure the effective impact of immunosuppressive therapy at the cellular level previously were used T cell number and the number of CD4+T lymphocytes, CD4/CD8 ratio, double positive (CD3+CD4+CD8+) and double negative (CD3+CD4-CD8-) populations of T lymphocytes, as the number of active T lymphocytes (CD25+).

Material and methods: During 2007 and 2008 there were 72 transplanted patients in "Merkur" University Hospital (54 kidney, 13 kidney/pancreas, /SPKT/ and 5 kidney/liver/LKT/), 42 male and 30 female, average age 44 years (range 16-68), who have received a combined, initial, prior transplantation: corticosteroids, calcineurin inhibitor, either anti-CD25 or polyclonal antythymocyte globulin (ATG) and maintenance therapy, after transplantation: corticosteroids, calcineurin inhibitor, either anti-CD25 or polyclonal antythymocyte globulin (ATG), mycophenolate mofetil. Histological findings of indicated renal biopsy during the first year has confirmed acute rejection in 27 patients (21 kidney, 4 SPKT, 2 LKT). The multiple determination of the number of lymphocyte populations in venous blood: T lymphocytes, B lymphocytes, NK cells, CD4+ and CD8+ T lymphocytes, active T lymphocytes: CD25+, CD69+, CD127+, activated (CD25+) CD4 and CD8 T lymphocytes, and specific population of T lymphocytes, CD3+CD4+CD25high+ was done using flow cytometry. Quantification of lymphocyte population is made on a flow cytometer Epics XL, Coulter, according to "lyse/no wash" standard procedure with FlowCount calibration particles, with the analyses conditions according to CD45/side scatter protocol (SSC). The staining has been done with antibodies for flow cytometry, directly conjugated, by Beckman-Coulter, and Dako. Measurement results were in accordance and within the target value of internal and external quality assurance programme UKNEQAS Immune Monitoring.

Results: After the induction phase, as expected, reducing the numbers occurs in all groups in lymphocyte compartment, with drastic decrease when ATG was applied instead of anti-CD25. During maintenance therapy, gradually recover of the same occurs, until normalization within 3 months, where diversity in behaviour is not observed between the 2 groups of patients. Number of activated CD25+ T lymphocytes grows during the 1 month and mainly is located in population of CD4+ T lymphocytes. Population of CD3+CD4+CD25high+ is a part of CD25+ activated CD4+ T lymphocytes, and according to literature has a positive effect on the graft stability unlike CD69+ activated T lymphocytes. Positivity of CD25 on CD8+ occurs in parallel with the expression on CD4+ T cells, and then speaks in favour of treating inflammation complications, like infection. The results of measuremen-

Zaključak: Longitudinalno praćenje broja imunosnih stanica u cirkulaciji je korisno u procjeni efikasnosti imunosupresivne terapije na staničnoj razini i oporavka pacijenta nakon kirurškog zahvata u transplantaciji bubrega, premda nedovoljno osjetljivo za predskazivanje odbacivanja presadka.

e-pošta: zoran.siftar@hdmb.hr

Conclusion: Longitudinal monitoring the number of immune cells in circulation is helpful in assessing the efficiency of immunosuppressive therapy at the cellular level and the recovery of patients after surgical procedures in kidney transplantation, although insufficiently sensitive for prediction of graft rejection.

e-mail: zoran.siftar@hdmb.hr

S07-5

Praćenje imunosupresivne terapije transplantiranih bolesnika

Ožvald I, Šurina B

Zavod za kliničku kemiju, Klinička bolnica Merkur, Zagreb

Praćenje uspješnosti transplanacije bolesnika spada u interdisciplinarni zadatak kliničara i medicinskih biokemičara. U Kliničkoj bolnici „Merkur" od 1998. g. učinjeno je 300 ortotopnih transplantacija jetre (OLT) i 100 transplantacija bubrega, te je razvoj transplantacijske medicine u našoj Bolnici zasigurno diprinio ulasku Hrvatske u članstvo Eurotransplanta od 5 mj. 2006. god.

Laboratorijska medicina prati uspješnost i/ili odbacivanje presadka etabliranim „transplantacijskim follow-up protokolom", koji uključuje: KKS, PV, PV-INR, fibrinogen, AST, ALT, GGT, ALP, ChE, bilirubin ukupni i direktni, ukupni kolesterol, ukupni proteini, albumini, CRP, elektroliti u serumu (K, Na, Ca-ukupni i ionizirani, magnezij-ukupni i ionizirani), ureja, kreatinin, glukoza, pH i plinovi u krvi, koji je orjentiran na praćenje općeg statusa bolesnika, posebice na jetrenu i bubrežnu funkciju.

Osim navedenih laboratorijskih pretraga, vrlo je značajno praćenje uvedene imunosupresivne terapije, koja u ovih bolesnika predstavlja doživotnu terapiju. Za svakog bolesnika potrebno je titriranje i uvođenje optimalne i efikasne individualne terapijske doze primjenjivanih imunosupresiva sa svrhom da se postigne terapijski cilj bez izlaganja komplikacijama imunodeficijencije kao što su: infekcija, malignitet ili odbacivanje organa.

U tu svrhu u Zavodu za kliničku kemiju određujemo sljedeće imunosupresive: inhibitore kalcineurina (ciklosporin i takrolimus); selektivne imunosupresive - sirolimus (drugu generaciju imunosupresivnih lijekova koji djeluju na imunofiline i omogućavaju alternativu standardnoj imunosupresivnoj terapiji); kao i određivanje inhibitora sin-

S07-5

Monitoring of immunosuppressed therapy in transplated patients

Ožvald I, Šurina B

Institute of Clinical Chemistry, Merkur University Hospital, Zagreb, Croatia

Monitoring of successful transplantation is an interdisciplinary task of clinicians and medical biochemists. In Merkur University Hospital 300 orthotopic liver transplantations (OLT) and 100 kidney transplantations have been performed since 1998. Therefore, we strongly believe that the development of transplantation medicine in our hospital has contributed to the Croatian membership in Eurotransplant since May 2006.

Laboratory medicine monitors the success and/or rejection of transplant by established "transplantation follow-up protocol" which includes CBC, PT, PT-INR, fibrinogen, AST, ALT, GGT, ALP, ChE, total and direct bilirubin, total cholesterol, total proteins, albumins, CRP, serum electrolytes, (K, Na, total and ionized Ca, total and ionized Mg), urea, creatinin, glucose, pH and blood gasses, directed towards follow-up of general patient's state, especially towards liver and kidney function.

Beside these tests monitoring of immunosuppressed therapy is very important, which means lifelong therapy for these patients. Each patient needs titration and introduction of the optimal and efficient therapy dosage of appropriate immunosuppressive with purpose to achieve the therapeutic goal without exposing patient to immunodeficiency complications like infections, malignancy or organ rejection.

Therefore, in our Department of Clinical Chemistry we determine following immunosuppressives: calcineurin inhibitors (cyclosporin and tacrolimus), selective immunosuppressives – sirolimus (the second generation of immunosuppressive drugs which affect immunofilins and

teze nukleotida: mikofenolat, koji se primjenjuju u obliku monovalentne ili polivalentne kombinirane terapije.
Imunosupresivi selektivnim i specifičnim djelovanjem na stanice imunog sustava, posebice T limfocite, drže te stanice u stanju tolerancije prema presadku. Vrlo velika varijabilnost u bioraspoloživosti i distribuciji uvjetuje kontinuirano mjerenje koncentracije lijeka u cirkulaciji jer svaki imunosupresiv ima svoj terapijski raspon unutar uskih granica i doza se titrira prema izmjerenoj razini u cirkulaciji.
Gore navedene laboratorijske pretrage ne mogu razlikovati promjene nastale uslijed akutnog odbacivanja ili disfunkcije presadka druge etiologije, kao što ne mogu odrediti stupanj-težinu odbacivanja. S toga konačni odgovor daje histološki nalaz kao „zlatni standard", koji nije uvijek moguć, te je zato praćenje ishoda transplantiranog bolesnika interdisciplinarni zadatak.
U našem Zavodu određuju se: ciklosporin od 1998. g. (FPIA), takrolimus od 2002. g. (MEIA), everolimus (FPIA) od 2006.-2008. g., sirolimus od 2008. g. (MEIA) i mikofenolat od 2006. g. (EMIT).
Od 300 OLT-a, ukupno jednogodišnje preživljenje je 85% te višegodišnje preživljavanje od 80%, što je usporedivo s drugim transplantacijskim centrima u Europi. Transplantacije jetre su izvršene uz poštivanje svih kriterija Eurotransplanta (odabir pacijenata), u bolesnika različitih jetrenih oboljenja: alkoholne bolesti jetre, oboljenja izazvanih infekcijom hepatitis C virusom, primarnom bilijarnom cirozom, kriptogenim oboljenjima jetre, hepatocelularnim karcinomom, metaboličkim deficitom alfa-1-antitripsina, sindroma Budd Chiari, mezenhimalnog hemangioendotelioma, nealkoholnog steatohepatitisa, autoimunog hepatitisa, Wilsonove bolesti.
Konačni nam je cilj uz rutinski follow-up gore navedene imunosupresivne terapije koja se primjenjuje u bolesnika transplantiranih u Kliničkoj bolnici „Merkur" ponuditi „optimalni algoritam" imunosupresivne terapije po bolesniku u korelaciji sa kliničkom efikasnošću u predviđanju akutnog ili kroničnog odbacivanja presadka.
Na osnovu dobivene dijagnostičke efikasnosti određivanja „kritičnih lijekova", tj. imunosupresiva eventualno doprinjeti postavljanju konačnog cilja kako za kliničara tako i za medicinskog biokemičara, a to je dobar ishod transplantiranog bolesnika.

e-pošta: iozvald@gmail.com

enable the alternative to the standard immunosuppressive therapy); as well as estimation of nucleotide synthesis inhibitors: micofenolate, applied as combination of mono- or polyvalent therapy.
By its selective and specific impact on cells of immune system, especially on T-lymphocytes immunosuppressives provide tolerance to these cells to the transplant. Due to strong variability in bioavailability and distribution it is necessary continuously to measure drug concentrations in circulation, because every immunosuppressive has its therapeutic range within narrow limits and the dosage is titrated by the measured levels in circulation.
Mentioned tests cannot differ between changes caused by acute rejection and transplant dysfunction of other etiology, nor can they determine the severity of rejection. Therefore, the final answer is provided by histological test method as golden standard which is not always possible. That is what makes the follow-up of a transplantation outcome an interdisciplinary task.
In our Department we determine levels of: cyclosporin since 1998 (FPIA), tacrolimus since 2002 (MEIA), everolimus (FPIA) 2006-2008, sirolimus since 2008 (MEIA) and micofenolat since 2006 (EMIT).
From 300 OLT the overall one year survival rate was 85% and survival rate for several years was 80% what concurs with results from other European transplantation centers. Liver transplantations were performed completely in concordance with Eurotransplant criteria (patient selection) on patients with different liver diseases: alcohol-induced liver disease, liver diseases caused by Hepatitis C virus infection, primary biliary cirrhosis, criptogen liver disease, hepatocellular carcinoma, metabolic alpha 1 antitripsin deficiency, Budd-Chiari syndrome, mesenchymal hemangioendothelioma, nonalcoholic steatohepatitis, autoimmune hepatitis, Wilson's disease.
Our final goal is supported by routine follow-up of immunosuppressive therapy which is already in usage in Merkur University Hospital to offer the "optimal algorithm" of immunosuppressive therapy for a patient in correlation with clinical efficiency in prediction of acute or chronic transplant rejection.
Based on diagnostic efficiency in determination of "critical drugs", i.e. immunosuppressives, we would like to contribute to the final goal setting for clinicians as well as for medical biochemists and this goal is a successful outcome of a transplantation.

e-mail: iozvald@gmail.com