



## Kako spriječiti akutnu disfunkciju bubrega u intenzivnoj skrbi?

## How can we prevent acute renal dysfunction in intensive care?

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**A**kutno bubrežno zatajivanje predstavlja sindrom kojeg karakterizira naglo smanjenje glomerularne filtracije s posljedicom različitog stupnja nakupljanja dušikovih otpadnih spojeva i uremičkih toksina. Prema podacima *Acute Dialysis Quality Initiative* u 2002. godine postojalo je više od 35 definicija akutnog zatajivanja bubrega. Učestalost ovog stanja u Jedinicama intenzivne skrbi (ICU, prema engl. *Intensive Care Unit*) zbog toga varira od 1% do 25%. Akutno bubrežno zatajivanje najčešće nastaje kao posljedica druge osnovne bolesti — obično teškog stupnja sepse i septičkog šoka, pa stoga i ne čudi visoka smrtnost — od 15% do 60%.

Termin akutno bubrežno zatajivanje (ARF, prema engl. *acute renal failure*) uveden je 1951. godine. Moderna literatura termin ARF koristi za težeg stupnja zatajivanja bubrega (stupanj III prema RIFLE klasifikaciji), dok se za cijeli sindrom akutnog poremećaja bubrežne funkcije koristi termin akutno bubrežno oštećenje (AKI, prema engl. *acute kidney injury*). ARF značajno doprinosi stopi smrtnosti u ICU. Tradicionalno je razmišljanje da pacijenti umiru s ARF, a ne zbog ARF. Podaci od početka 90-tih godina prošlog stoljeća upućuju na činjenicu da su i blaži stupnjevi AKI povezani s lošijim ishodom liječenja mjereno dužim brojem dana liječenja, višom stopom smrtnosti, kao i češćom prelaskom ARF u kronično bubrežno zatajivanje. Sto-

**A**cute renal failure (ARF) is a syndrome characterized by a sudden reduction of glomerular filtration resulting in a different degree of accumulation of nitrogen waste compounds and uremic toxins. According to the data from the *Acute Dialysis Quality Initiative* in 2002, there were more than 35 definitions of ARF. The frequency of such a condition in the Intensive Care Units (ICU) for that reason varies from 1% to 25%. ARF frequently occurs as a consequence of another basic disease — usually serious degree of sepsis and septic shock, so therefore a high mortality rate is no wonder — from 15% to 60%.

The term of ARF was introduced in 1951. The modern literature uses the term ARF for a more serious degree of renal failure (class III according to RIFLE classification), but for the entire syndrome of acute renal failure, the term of acute kidney injury (AKI) is used. ARF considerably contributes to the death rate in ICU. There is traditional way of thinking that patients die with ARF, not because of ARF. The data since the beginning of 90-ies in the last century indicate the fact that even less severe degrees of AKI are connected with worse outcome of treatment measured by a longer number of days of treatment, higher death rate as well as more frequent transition of ARF into chronic renal failure. This is the reason why it is important to prevent every, even the lowest degree of AKI. There is a key me-



ga je važno spriječiti svaki, pa i najmanji stupanj AKI. Ključno je pitanje koji je mehanizam bubrežnog oštećenja — predbubrežni (smanjena perfuzija bubrega), bubrežni (glomerularni ili nglomerularni) ili poslijebubrežni (opstrukcija u mokraćnim putevima).

Mjerama prevencije AKI nastoji se očuvati funkcija bubrega, spriječiti smrtni ishod, spriječiti komplikacije (poremećaji tekućine, elektrolita i acidobaznog statusa) te spriječiti potrebu za kroničnom dijalizom. Konzervativne metode za sprječavanje AKI uključuju korekciju dehidracije, korekciju hipotenzije (održavanje tlaka perfuzije bubrega) te ograničenje izloženosti nefrotoksičnim tvarima. Izotonične otopine (fiziološka, Ringer i sl.) primijenjene intravenozno općenito su prihvaćen način sprječavanja AKI. Optimalna brzina i količina infuzijskih otopina nije definirana, te stoga mora biti prilagođena stanju pojedinog pacijenta. Niti srednji arterijski tlak nije definiran, a terapija vazopresornim lijekovima se treba započeti tek po nadoknadi volumena. Suprotno uvriježenom mišljenju, podaci iz studija ne ukazuju na činjenicu da je primjena norepinefrina povezana s većom učestalosti AKI. Vezano uz nefrotoksične lijekove naročito oprez je potreban kod primjene aminoglikozida (preporuča se primjena u jednoj dnevnoj dozi), amfotericina i kontrastnih sredstava.

Rezultati kliničke primjene medikamena, kao temelja farmakološke strategije sprječavanja AKI, su razočaravajući. Primjena diuretika Henleove petlje korisna je za liječenje prekomjernog volumena, ali ne kod liječenja oligurije i u prevenciji AKI. Ukoliko se želi primijeniti diuretik ove skupine u oliguričnog bolesnika prije liječenja dijalizom valja to učiniti oprezno, a ukoliko se ne postigne adekvatna diureza potrebno je odmah prekinuti primjenu lijeka da bi se spriječila ototoksičnost. Također, niti primjena manitola, dopamina ili antagonista kalcija nije klinički djelotvorna u prevenciji AKI. Primjena N-acetilcisteina, te hidracije intravenozno uz otopinu bikarbonata može smanjiti učestalost AKI nakon primjene kontrastnih sredstava, poglavito u osoba sa od prije poznatim oštećenjem bubrežne funkcije, dijabetesom i poznatom bolesti krvožilnog sustava ili jetre. Uloga teofilina i profilaktičke hemofiltracije u svrhu sprječavanja nefropatije izazvane kontrastom zahtjeva daljnja istraživanja.

Osoblje u ICU ima ključnu ulogu u otklanjanju uzroka i sprječavanju dodatnog oštećenja bubrežne funkcije, ukoliko se AKI prepozna dovoljno rano. Po osiguranju adekvatne funkcije vitalnih organa, odnosno hemodinamskoj i respiratornoj potpori, potrebno je dijagnosticirati uzrok, a potom se usredotočiti na praćenje i korekciju volumena, pratiti diurezu i ukoliko postoji indikacija primijeniti neku od metoda nadomještanja bubrežne funkcije. Ohrabruje podatak da u većine preživjelih pacijenata s ARF slijedi oporavak bubrežne funkcije.

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chanism as to which is the renal damage mechanism — pre-renal (reduced kidney perfusion), renal (glomerular or non-glomerular) or post-renal (obstruction in urinary tracts).

The prevention measures of AKI are applied as to preserve the renal function, prevent deathly outcome, prevent complications (disorders of fluids, electrolytes and acidobase status) and eliminate a need for chronic dialysis. Conservative methods applied for preventing AKI includes a correction of dehydration and hypotension (maintaining of pressure of renal perfusion) and limitation of exposure to nephrotoxic substances. Isotonic solutions (saline solution, Ringer etc.) applied intravenously are generally accepted method of AKI prevention. Optimum speed and quantity of infusion solutions has not been defined, and so it must be adapted to the condition of a particular patient. Hardly has middle arterial pressure been defined, the therapy with vasopressive medications need to start only upon compensation of the volume. Contrary to the traditional opinion, the data from the studies does not indicate the fact that the administration of norepinephrine is connected with ever greater frequency of AKI. Related with nephrotoxic medications, special precautionary measures are to be taken when administering aminoglycosides (administering in one daily dose is recommended), amphotericins and contrast agents.

The findings of clinic application of medications, as a foundation of pharmacologic strategy of AKI prevention are disappointing. The administration of loop diuretics is useful for treatment of excessive volume, but not when treating oliguria and for the AKI prevention. If a diuretic of this group in oliguric patients prior to treatment by using dialysis is to be changed, this should be done carefully, and if no adequate diuresis has been achieved, it is necessary to interrupt the administration of the medication immediately as to prevent ototoxicity. Even the application of mannitol, dopamine or calcium antagonists has not been clinically efficient in AKI prevention. The application of N-acetylcysteine and hydration intravenously with the solution of bicarbonates may reduce the frequent occurrence of AKI after application of contrast agents, especially in persons with earlier renal function damage, diabetes and known disease of cardiovascular system or liver. The role of theophyllines and prophylactic hemofiltration for the purpose of prevention of contrast nephropathy requires further investigation.

Personnel in the ICU have a key role in elimination of the cause and prevention of additional renal function damage if AKI is recognized early enough. After making sure that vital organs perform their vital functions or after having secured hemodynamic and respiratory support, it is necessary to diagnose a cause and focus on monitoring and correction of volume, monitor diuresis and in case of any indications, it is necessary to change some of the methods of compensating the renal function. The data which is encouraging is that with the greatest number of survived patients with ARF there follows convalescence of the renal function.