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Bubreg i kontrastna sredstva

The kidney and contrast agents

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Kontrastna sredstva (KS) primjenjuju se u medicinskoj radiologiji od samih početaka. Međutim, ni danas nema potpuno sigurnih sredstava koja će dati pojačano zasjenjenje ili prozirnost tkiva. Broj pretraga u kojima se koriste KS je u porastu, a primijeni se preko 60 milijuna doza godišnje. KS su vodeći uzročnik bubrežnog zatajenja u bolnicama. Nema drugog sredstva koje se daje u tako visokim dozama: prosječna doza od 100 ml kontrasta koncentracije 300 mg I/ml sadrži 30 g joda!

U klasičnoj radiologiji razlikujemo pozitivna (barijevi i jodni preparati) i negativna (kisik, ugljični dioksid, helij, ksenon) KS. Pozitivna KS su netopiva i topiva. Netopiva se primjenjuju za prikaz šupljih organa, uglavnom probavnog sustava - barijev sulfat ($BaSO_4$). Ulju slični preparati su danas izbačeni iz upotrebe osim u intervencijama — embolizacijama. Topiva su spojevi koji sadrže jod, uglavnom derivati trijodbenzena. Natrijev meglumin diatrizoat se primjenjuje u CT dijagnostici uz dodatak anisova ulja (radi okusa) i kod pregleda probavnog sustava kada postoji mogućnost izlijevanja u okolicu (trbušna šupljina, prsište i sl.). Isti spoj se koristi(o) i za intravenske preglede mokraćnog sustava kao i za CT, angiografije i intervencijske postupke.

Vodotopljiva jodna KS, s obzirom na osmolalnost mogu biti niskoosmolarna (hipotonična, hipoosmolalna) i visokoosmolarna (hipertonična, hiperosmolalna). Osmolalnost je proporcionalna s odnosom atoma joda i broja čestica u otopini KS. Kod većine hiperosmolalnih KS taj odnos je 3:2, dok je kod hipoosmolalnih 3:1. Hiperosmolarna KS imaju osmolalitet 1400-1800 mosmol/kg (jotalamat, diatrizoat), hipoosmoloarna 500-850 mosmol/kg (joksaglat, jopamidol, joheksol, joversol, jopromid), a izoosmolalna oko 290 mosmol/kg (jotrolan, jodiksanol). S obzirom na molekularnu strukturu možemo ih dijeliti na monomere i dimere, a prema električnom naboju na ionska i neionska.

Danas su u upotrebi uglavnom preparati koji su manje osmolalnosti i vrlo rijetkih nuspojava i alergijskih reakcija. Nuspojave se dijele na blage (mučnina, povraćanje, svrbež kože, osip, bol u rukama), srednje (urtikarija, edem lica, hipotenzija, bronhospazam)i teške (šok, edem larinksa, konvulzije, respiratorni i kardijalni arest).

Za magnetsku rezonanciju koriste se KS koja sadrže ione gadolinija, koji se mogu dati bolesnicima alergičnim na jodne kontraste. Ni ona nisu bezopasna. Sve više je opisa sistemske nefrogene skleroze uzrokovane gadolinijem.

Kontrastom izazvana nefropatija je reverzibilna, neoligurična forma akutnog zatajenja bubrežne funkcije, koje se definira porastom kreatinina u serumu za 44 μmol/L ili 25% osnovne vrijednosti kreatinina. Porast kreatinina nastupa u prvih 48-72 sata od primjene KS, a oporavak unutar

Contrast agents (CA) have been used in medical radiology since the very beginning. However, today there are still no sure agents that can provide increased shade effects or transparency of the tissues. The numbers of tests where contrast agents are used are increasing, with over 60 million doses administered annually. Contrast agents are a leading cause of kidney failure in hospitals. There is no other substance that is administered in such high doses: an average dose of 100 ml of contrast agent concentration 300 mg I/ml contains 30 g of iodine!

In classical radiology, we distinguish CA between positive (barium and iodine solutions) and negative (oxygen, carbon dioxide, helium, xenon). Positive CA are insoluble and soluble. Insoluble are used for showing hollow organs, mainly the digestive tract — barium sulfate ($BaSO_4$). Oil solutions have today been thrown out of use except in interventions — embolisations. Soluble are those compounds which contain iodine, mainly derived from three-iodine benzene. Sodium-meglumine-diatrizoate is applied in CT diagnostics with the additive anise oil (for taste reasons) and for tests of the gastrointestinal tract when there exists a possibility of emissions into surrounding areas (abdominal cavity, thorax and so on). The same compound is/was also used for intravenous examinations of the urinary tract as well as CTs, angiographs and intervention procedures.

Water soluble iodine contrast agents, with regard to its osmolality, can be low-osmolar (hypotonic, hypoosmolar) and highly osmolar (hypertonic, hyperosmolar). Osmolality has a proportional relationship to the iodine atom and the number of particles in the contrast agent solution. For a majority of hyper-osmolar contrast agents, this relationship is 3:2 while for hypoosmolar it is 3:1. Hyperosmolar contrast agents indicate osmolality of 1400-1800 mosmol/kg (iotalamate, diatrizoate), hypoosmolar 500-850 mosmol/kg (ioksaglat, iopamidol, iohexol, ioversol, iopromide), while isoosmolar around 290 mosmol/kg (iotrolan, iodixanol). Considering the molecular structure, we can divide them into monomers and dimers, and according to the electrical charge into ionic or non-ionic.

Today, mainly products in use are those with less osmolality, very rare negative side-effects and allergic reactions. The side-effects are categorized as mild (nausea, vomiting, itchy skin, rash, pain in the hands), medium (urticaria, face edema, hypotension, bronchospasm) and severe (shock, laryngeal edema, convulsions, respiratory and cardiac arrest).

Contrast agents are used for magnetic resonance imaging, which contain the ions gadolinium, which can be given to patients allergic to iodine contrast agents. These too are not harmless. There is an increasing occurrence of systematic nephrogenic sclerosis caused by gadolinium.

3-5 dana. Prema brojnim radovima učestalost nastanka je 0-50%. Perzistentno zatajenje možemo očekivati prvenstveno u dijabetičara i kod pacijenata kojima je rađena koronarografija.

Točan mehanizam nastanka je nepoznat, a osnovne teorije su 1. medularna hipoksemija, 2. direktni citotoksični utjecaj kontrasta. Diferencijalno dijagnostički treba misliti na ishemičku akutnu tubularnu nekrozu, akutni intersticijski nefritis, emboliju renalne arterije.

Postoje brojni čimbenici rizika za razvoj kontrastne nefropatije o kojima moramo voditi računa kada šaljemo pacijenta na kontrastne pretrage. To su: prisutno zatajenje bubrežne funkcije (kreatinin u serumu >132 μmol/L ili glomerularna filtracija <60 ml/min/1,73 m^2), šećerna bolest s oštećenjem bubrežne funkcije, srčano zatajenje, dehidracija, dob iznad 70 godina, multipli mijelom, uzimanje potencijalno nefrotoksičnih lijekova, nesteroidnih antireumatika (NSAR), cisplatine, aminoglikozidnih antibiotika, ACE inhibitora i primjena jodnog kontrasta u posljednjih 72 sata.

Kako bi se smanjio broj slučajeva kontrastom izazvane nefropatije potrebno je provoditi mjere prevencije, a to su:

• korištenje drugih radioloških metoda, ako je klinički moguće, u visokorizičnih bolesnika (UZV, MRI, CT bez kontrasta),

• upotreba niskoosmolarnih ili izoosmolarnih KS,

• korištenje manjih doza KS (npr. za prikaz A-V fistule sigurno je ako se primijeni <10 ml KS) i ne ponavljanje kontrastnih pretraga unutar 72 sata,

• izbjegavanje uzimanja potencijalno rizičnih lijekova,

• dobra hidracija pacijenta, na usta ili davanjem infuzija,

• primjena acetilcisteina.

Preporuka je 48 sati prije pretrage prestati uzimati metformin, 24-48 sata prije pretrage stopirati unos aminoglikozidnih antibiotika, NSAR, cisplatine, metotreksata, ACE inhibitora, ARB, manitola, diuretika.

Uzimanjem tekućine na usta može se postići zadovoljavajuće hidracija pacijenta, kao i infuzijama 0,45% ili 0,9% natrijeva klorida (izotonična otopina ima povoljnije djelovanje). Infuzije treba davati visokorizičnim pacijentima, u količini od 1-1,5 ml/kg/sat, 6-12 sati prije pretrage i isto toliko nakon pretrage. Infuzija natrijeva bikarbonata 154 mEq/L (=154 ml 8,4% $NaHCO_3$) u 5% glukozi 3 ml/kg/sat pokazala je bolje rezultate, koji su dovedeni u pitanje najnovijim istraživanjima, pa će konačni stav tek trebati definirati.

Acetilcistein je antioksidans, u Listi lijekova HZZO-a nije specificiran, označen je za korištenje u bolnicama samo za liječenje otrovanja s paracetamolom. Međutim, najčešće se primjenjuje kao sekretolitik, a koristi se i kod liječenja ovisnosti na kokain jer poništava kemijske promjene u mozgu izazvane kokainom. Za prevenciju kontrastom izazvane nefropatije primjenjuje se najčešće u dozi od 600 mg 2 puta dnevno tijekom 2 dana (dan prije i dan poslije ili dan prije i na dan primjene kontrasta).

Nephropathy caused by contrast agent is a reversible, neoliguric form of acute renal failure, which is defined by an increase in creatinine in serum by 44 μmol/L or 25% of the basic value of creatinine. The increase in creatinine occurs in the first 48-72 hours from administering CA, and recovery lasts 3-5 days. Based on literature data, the frequency of occurrence is 0-50%. Persistent failure can be expected primarily in diabetics and those patients where a coronarography has been carried out.

The exact cause is not known, but the basic theories are: (1) medullar hypoxemia (2) direct cytotoxic impact of the CA. Differential diagnostics should consider ischemic acute tubular necrosis, acute interstitial nephritis, renal artery embolism.

There are a number of risk factors in the development of nephropathy which we must take into account when sending patients on contrast examinations. They are: kidney failure (creatinine in serum >132 μmol/L or glomerular filtration <60 ml/min/1.73 m^2), diabetes along with kidney failure, heart failure, dehydration, older than 70 years, multiple myeloma, consumption of potentially nephrotoxic drugs, non-steroidal antirheumatic drugs, cisplatine, aminoglycoside antibiotics, ACE inhibitors and the administration of a contrast agent in the last 72 hours.

In order to reduce the number of events nephropathy caused by contrast agents, it is necessary to implement preventive measures, such as:

• Use of other radiological methods, if clinically possible, in high risk patients (ultrasound, MRI, CT without contrast agents),

• Use of low osmolar or iso-osmolar contrast agents,

• Using smaller doses of contrast agents (e.g. sure enough for showing the A-V fistula if using <10 ml of contrast agent) and not repeating contrast examinations within a period of 72 hours,

• Avoiding the use of potentially risky medication,

• Good hydration of patients, orally or through infusion,

• Use of acetylcysteine.

It is recommended that 48 hours prior to the examination a patient is to cease taking metformin, 24-48 hours prior to the examination cease intake of aminoglycoside antibiotics, NSAR, cisplatin, methotrexate, ACE inhibitors, ARB, mannitols, diuretics.

Oral consumption of liquids can achieve proper hydration in patients, as well as infusions 0.45% or 0.9% sodium chloride (isotonic solution has a more favorable effect). Infusions are to be given to high-risk patients, in amounts of 1-1.5 ml/kg/hour, 6-12 hours prior to the examination and also following the examination. Infusion of sodium biocarbonate 154 mEq/L (=154 ml 8.4% $NaHCO_3$) in 5% of glucose 3 ml/kg/hour has shown better results, which have been brought into question in the latest research, hence the final decision is still to be determined.

Acetylcysteine is antioxidant, in the list of medications at the Croatian Institute for Health Insurance it is not specified, and is designated for use in hospitals only for treating paracetamol poisoning. However, most often it is administered as secrotolytic, and is also used in healing ad-

Ostali primjenjivani lijekovi (blokatori kalcijevih kanala, teofilin, dopamin, fenoldopamin, antagonisti receptora endotelina) nisu dokazali povoljno djelovanje u prevenciji.

KS se lako odstranjuju i hemodijalizom i peritonejskom dijalizom. Primjena dijalize je potrebna samo u slučaju većeg porasta kreatinina (ako je kreatinin u serumu veći od 352 μmol/L). Hemodijaliza se ne preporuča kao rutinska metoda, a hemodijafiltracija ima povoljniji uspjeh ali je potrebna dodatna potvrda korisnosti i opravdanosti primjene.

Nakon primjene KS dolazi do pojave lažno pozitivnog nalaza na proteinuriju (do 1,5-2 g/L). Zbog toga ne treba testirati na proteinuriju barem 24 sata nakon davanja KS.

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diction to cocaine, because it eliminates chemical changes in the brain caused by cocaine. In preventing nephropathy caused by CA, it is most often used in doses of 600 mg twice daily during a period of 2 weeks (the day before and day after or the day before and on the day of administering the contrast agent).

Other administrable medication (calcium channel blockers, teofiline, dopamine, fenoldopamin, antagonists of endothelin receptors) have not shown favorable preventive effects.

CA are easily removed by hemodialysis and peritoneal dialysis as well. Use of dialysis is necessary only in the event of a larger increase of creatinine (if creatinine in serum is greater than 352 μmol/L). Hemodialysis is not recommended as a routine method, while hemodiafiltration has a favorable result, but it is necessary to further confirm its usability and justify its administration.

Following the administration of contrast agents there occur false positive results in proteinuria (till 1.5-2 g/L). Therefore, there is no need to test for proteinuria at least 24 hours after administering contrast agents.