

ZNAČAJ DIJABETES MELITUSA U STOMATOLOŠKOJ PRAKSI

THE IMPORTANCE OF DIABETES MELLITUS IN DENTAL PRACTICE

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Sažetak

U ovom radu prikazane su osnovne karakteristike dijabetes melitusa, oboljenja od koga boluje oko 10% stanovništva, sa tendencijom daljeg rasta. Poseban fokus je na oralnim manifestacijama dijabetesa i na specifičnostima pacijenata sa dijabetesom koji se podvrgavaju različitim stomatološkim procedurama i intervencijama. U tom kontekstu, posebno su apostrofirane hiper i hipoglikemijske krize, koje mogu brzo uznapredovati do kome ukoliko se blagovremeno ne prepoznaju i ne leče. U cilju pravovremene dijagnostike prikazane su kliničke manifestacije i laboratorijski parametri akutnih komplikacija dijabetesa, kao i faktori rizika koji doprinose nastanku ovih komplikacija. Date su preporuke Američkog i Evropskog dijabetesnog udruženja, kao i Nacionalnog vodiča za dijagnozu i lečenje dijabetes melitusa Republike Srbije u pogledu potrebne preproceduralne evaluacije ovih pacijenata i opremljenosti stomatoloških ordinacija. Na taj način bi se uspešno predupredile i sprečile akutne komplikacije dijabetesa.

Ključne reči: dijabetes melitus, oralne manifestacije dijabetesa, stomatološke intervencije, akutne komplikacije dijabetesa, terapija akutnih komplikacija dijabetesa

Uvod

Dijabetes melitus (*Diabetes mellitus*, DM) je metaboličko oboljenje nastalo zbog nedovoljne produkcije insulina u pankreasu (DM tip 1) ili neadekvatne utilizacije insulina na periferiji (DM tip 2) ili kombinacijom oba mehanizma¹. Mnoge supstance različito utiču na sekreciju insulina, pa mogu dovesti do značajnog disbalansa nivoa glikemije, čak i do hipo (hiper) glikemijskih kriza. Glavni stimulatori sekrecije insulina su glukoza i fruktoza, a ostali stimulatori su aminokiseline, hormoni gastrointestinalnog trakta (gastrin, holecistokinin, sekretin, inkretini), acetil-holin i neki lekovi (agonisti β -adrenergičkih receptora). Najvažniji inhibitori sekrecije su stres-hormoni (tzv. kontraregulatorni hormoni), gde spadaju kateholamini (epinefrin i norepinefrin), kortizol, hormon rasta i glukagon. Citokini, kao i neki lekovi (na primer agonisti α -adrenergičkih receptora, glukokortikoidi i dr.) takođe inhibiraju sekreciju insulina².

Normalna vrednost glikemije je 3,5-6,0 mmol/L, a glikoziliranog hemoglobina 3,5-6%. Dijagnoza DM se postavlja na osnovu povišenih vrednosti glikemije, i to $\geq 7,0$ mmol/L ili $\geq 11,1$ mmol/L, 120 minuta nakon testa opterećenja glukozom (*Oral Glucose Tolerance Test*, OGTT). Od 2009. godine u kriterijume za dijagnozu DM je uvrštena i povišena vrednost glikoziliranog hemoglobina (HbA1c $\geq 6,5\%$) kao pokazatelja dugoročne metaboličke kontrole (oko tri meseca, odnosno 6-8 nedelja kod trudnica)³.

Učestalost DM je velika u svim razvijenim zemljama sveta, sa tendencijom daljeg rasta. Dok je 2000. godine bilo 6,4% obolelih, već 2014. broj se povećao na 8,3% svetske populacije, sa prognozom daljeg rasta, koja bi do 2040. mogla iznositi i više od 12%, po prognozi Svetske zdravstvene organizacije (*World Health Organisation*, WHO)⁴. Javlja se u svim uzrastima, najviše posle četrdesete godine života, više u nerazvijenim i zemljama u razvoju, gde je i veći broj nedijagnostikovanih slučajeva DM, i može iznositi i preko 40%⁵. U gerijatrijskoj populaciji učestalost DM je najveća ($> 20\%$), pri čemu je u starijem životnom dobu DM češće udružen sa hroničnim komplikacijama i drugim komorbiditetima, koji se

javljaju u vezi sa dijabetesom ili nezavisno od njega⁶. Prema podacima WHO trenutno ima oko 400 miliona registrovanih dijabetičara, a u Srbiji, prema podacima Instituta za javno zdravlje Srbije, oko 700.000.

Dijabetes ima i svoje oralne manifestacije koje su od značaja u stomatološkoj praksi⁷. Međutim, i bez oralnih manifestacija pacijenti sa DM zaslužuju posebnu pažnju stomatologa i zahtevaju pažljivu preproceduralnu evaluaciju jer je to posebno osetljiva grupa pacijenata u smislu mogućnosti razvoja nekih akutnih komplikacija. Stomatolozi moraju poznavati osnovne karakteristike dijabetesa, kako bi mogli pravovremeno i adekvatno da reaguju ako u stomatološkoj ordinaciji dođe do razvoja hiper ili hipoglikemijskih kriza. Tada je potrebno postupati u skladu sa preporukama Nacionalnog vodiča za dijagnozu i lečenje dijabetesa melitusa, koje je izdalo Ministarstvo zdravlja Republike Srbije⁸.

Specifične forme hiperglikemije

Stres-hiperglikemija (*Stress Hyperglycemia*, SHG) se definiše kao hiperglikemija kod prethodno euglikemičnih pacijenata, sa vrednostima glikemije $\geq 7,0$ mmol/L u dva sukcesivna merenja ili vrednosti glikemije $\geq 11,1$ mmol/L u nasumičnom merenju kod prethodno normoglikemičnih pacijenata. SHG se najčešće javlja u vezi sa nekim akutnim procesom, kao što je trauma ili neko drugo akutno oboljenje, pa tako i u stomatološkoj ordinaciji⁹. Prema različitim izveštajima, učestalost SHG iznosi od 3% do 80% slučajeva kada su u pitanju hospitalizovani pacijenti. Ovako velika varijabilnost se objašnjava nedovoljno precizno definisanom stres-hiperglikemijom, kao i zbog činjenice da je u velikom broju slučajeva DM već postojao, ali nije bio prepoznat i lečen².

Insulinska rezistencija predstavlja nemogućnost efikasnog iskorišćavanja insulina, iako ga ima dovoljno u organizmu, što može imati za posledicu hiperglikemiju. Ova rezistencija može biti uslovljena naslednim, genetskim faktorima ili uzrokovana nekim lekovima (kortikosteroidi). Ipak, najčešće se javlja u okviru stresnih stanja, kao što su infekcija, sepsa, kritično oboljenje i dr¹. Takođe se javlja u trudnoći, kod gojaznih osoba i osoba sa povišenim krvnim pritiskom, u sklopu hiperlipidemije (povišen holesterol i/ili trigliceridi) itd¹. Važnu ulogu u smanjenju odnosa insulin/glukoza ima oslobađanje stres-hormona i citokina. Insulin stimuliše apsorpciju glukoze u tkivima osetljivim na insulin (jetra, skeletni mišići i masno tkivo) i time smanjuje oslobađanje glukoze iz jetre².

Oralne manifestacije dijabetesa melitusa

Brojnim radovima je pokazana povezanost između DM i parodontalnih bolesti¹⁰. Pacijenti sa dijabetesom često imaju osećaj žarenja i pečenja u usnoj duplji, kao i neprijatan zadah iz usta (*fetor ex ore*). Oralna mukoza je edematozna, tamnije prebojena, a moguće su i ulceracije usne duplje.

Jezik je takođe edematozan, crven, sa atrofičnim papilama (*lingua geografica*). Gingiva pokazuje sklonost ka krvarenju i infekcijama (posebno kandidijazom), a pljuvačne žlezde sklonost ka nastanku kalkuloze. Parodontopatija i parodontalni apscesi su čest nalaz kod osoba sa dijabetesom, a češći su i težeg oblika u mlađem uzrastu¹¹. Usled nedostatka vitamina B, prisutni su stomatodinija i stomatopiroza, što može biti dodatno pogoršano kandidijazom¹².

Patofiziologija oralnih manifestacija dijabetesa nije u potpunosti razjašnjena, ali je poznata povezanost sa pojavom karijesa¹³. Kod osoba sa dijabetesom je povišena vrednost glukoze u pljuvački (glikosilija), a pH pljuvačke je smanjen (acidoza). Takođe je prisutna hiposekrecija pljuvačke (*xerostomia*), što otežava žvakanje i gutanje hrane i onemogućava adekvatno samočišćenje usne duplje, čime se stvaraju povoljni uslovi za razvoj mikroorganizama i infekcije. Dokazano je da su parodontopatija i oralna oboljenja češći kod obolelih od dijabetesa nego kod zdravih osoba^{11,12}.

Oralni krvni sudovi osoba sa DM imaju povećanu permeabilnost usled mikroangiopatije, što dovodi do deponovanja mukopolisaharida i glikoproteina u oralnim tkivima. Krvni sudovi gingive su aterosklerotično i ateromatozno promeњeni, suženog lumena. Prisutne su mikrotromboze, mikroangiopatije, što ima za posledicu stazu, poremećaje ishrane i oksigenacije oralnih tkiva, kao i otežanu eliminaciju štetnih metaboličkih produkata. Alveolarna kost podležu obilnoj resorpciji i formiranju džepova koji supuriraju, pa postoji tendencija ka stvaranju apscesa¹⁴. U parodontcijumu dolazi do progresivne destrukcije svih komponenti, povećane kolagenolize i smanjene sinteze novog kolagena¹¹.

Parodontitis je hronična upala desni uzrokovana inflamatornom bolešću, što može biti ne samo uzrok gubitka zuba, već se razmatra i mogućnost da je parodontitis modifikujući faktor koji utiče na celokupno sistemsko zdravlje organizma^{14,15}. Novije studije su pokazale povezanost parodontitisa sa hroničnim bolestima, kao što su Alchajmerova bolest, karcinom, reumatoidni artritis i dr^{13,16}. Osim toga što je poznato da DM ima uticaja na pojavu i ishod lečenja pacijenata sa korona virusom, radovima Santane i drugih autora je pokazano da udruženost dijabetesa i parodontalnih bolesti povećava rizik od infekcije virusom COVID 19¹⁷⁻²¹. Brojni radovi ukazuju na povezanost dijabetesa i ishoda stomatoloških implantata^{22,23}. Takođe, dosta radova se bavilo uticajem lokalne anestezije na nivo glikemije kod osoba sa dijabetesom prilikom stomatoloških procedura (lidokain sa epinefrinom 1:100.000). Međutim, nema dokaza da lokalni anestetik sa dodatkom adrenalina signifikantno menja nivo glikemije^{24,25}.

Iz napred navedenog, nedvosmisleno proizilazi da se stomatolozi često susreću sa pacijentima koji imaju dijabetes jer je to vulnerabilna populacija po pitanju bolesti usta i zuba. Iako je dobro poznata povezanost dijabetesa i povećane učestalosti bolesti usta i zuba, nažalost ne postoje posebni protokoli i preporuke kojima bi se osiguralo bezbedno

okruženje za ove pacijente u stomatološkoj ordinaciji. I dalje je fokus stomatologa prilikom izvođenja intervencija kod ovih pacijenata na eventualnoj pojavi hipo i hiperglikemije, na njihovoj prevenciji i adekvatnom kupiranju²⁶.

Evaluacija i priprema pacijenata sa dijabetesom pre stomatološke intervencije

Sa stomatološkog stanovišta, najvažniji elementi preproceduralne evaluacije pacijenata sa DM su: sagledavanje dužine trajanja bolesti i režima lečenja, prisustvo komplikacija DM i/ili drugih komorbiditeta i uvid u laboratorijske analize (glikemija, glikolizirani hemoglobin, a po potrebi i druge analize) (tabela 1). Obim preproceduralne evaluacije zavisi od složenosti i hitnosti stomatološke intervencije, procenjene dužine njenog trajanja, vremena proteklog od poslednjeg obroka (i poslednje doze antidijabetesne terapije), kao i očekivanog nivoa stresa, što je u velikoj meri subjektivna kategorija i zavisi od strukture ličnosti pacijenta. Ipak, najvažnije pitanje je, da li je dijabetes dobro kontrolisan. Za veće stomatološke intervencije, posebno hirurške intervencije, obavezno je mišljenje endokrinologa ili anesteziologa².

Tabela 1. Elementi preproceduralne evaluacije pacijenata sa DM

Elementi preoperativne evaluacije	Obratiti pažnju na
1. Karakteristike DM	Tip DM; Dužina trajanja bolesti Režim lečenja-terapija (OH, insulin, kombinovano)
2. Prisustvo komplikacija DM	Akutne (DKA, HHS, hipoglikemija) Hronične (mikro i makro-angiopatije, posebno DAN)
3. Prisustvo drugih komorbiditeta koji mogu (ali ne moraju) biti povezani sa DM	Hipertenzija i druge bolesti KVS, NAFLD
4. Laboratorijske analize	Glikemija i HbA1c obavezno, a po potrebi: ureja, kreatinin, elektroliti, urin-analiza (albumini, ketoni)
5. Procena disajnog puta	Mogućnost potrebe za hitnom intubacijom traheje, koja je kod dijabetičara često otežana

Legenda: OH (Oral Hypoglycemic) - oralni hipoglikemici; DKA (Diabetic Ketoacidosis) - dijabetična ketoacidoza; HHS (Hyperglycemic Hyperosmolar State) - hiperglikemijsko hiperosmolalno stanje; DAN (Diabetic Autonomic Neuropathy) - dijabetična autonomna neuropatija; NAFLD (Non-Alcoholic Fatty Liver Disease) - nealkoholna masna bolest jetre.

Osnovni ciljevi preproceduralne procene i pripreme pacijenata sa DM su: izbeći hiperglikemiju (> 10 mmol/L), hipoglikemiju (< 3,8 mmol/L), kao i velike varijacije glikemije i gubitak elektrolita. Američka dijabetesna asocijacija (*American Diabetes Association*, ADA) dala je preporuke 2014. godine, koje su i danas na snazi, da bi ciljne vrednosti glikemije za pacijente koji su planirani za invazivne dijagnostičke i terapijske procedure ili hirurške intervencije trebalo da budu što bliže fiziološkoj granici, ali obavezno < 10 mmol/L. Sa time se slažu i Kanadska i Australijska dijabetesna asocijacija, kao i većina autora^{2, 27}. HbA1C kao pokazatelj dugoročne metaboličke kontrole je važniji laboratorijski parametar od vrednosti glikemije jer se ona menja u toku dana (u zavisnosti od doba dana, obroka, stresa...)¹⁻³.

Preproceduralna priprema pacijenata sa DM za stomatološke procedure svakako obuhvata i evaluaciju komplikacija dijabetesa (akutnih i hroničnih) i drugih komorbiditeta koji ne moraju biti nužno u vezi sa DM. Ipak, potrebno je imati na umu da je, od drugih komorbiditeta, hipertenzija prisutna kod 40-50% dijabetičara, i može biti povezana sa aterosklerozom, a okultnu infekciju ima oko 17% pacijenata sa dijabetesom. Često je prisutna i bolest koronarnih arterija, posebno kod mladih (što je atipično), kao i kongestivna srčana bolest, steatoza jetre i dr².

Osim toga, od značaja su i činjenice (naročito kada su u pitanju stomatološke operacije) da pacijenti sa DM imaju povećanu sklonost ka infekciji²⁸, da je kod njih usporeno i odloženo zarastanje rana. Takođe, sklone su dehidraciji (zbog osmotske diureze u hiperglikemiji) i razvoju hiperosmolalnosti²⁶. Nisu retke ni teške komplikacije poput dijabetesne ketoacidoze (zbog ketogeneze), tromboembolije (zbog hiperviskoznosti i povećane trombogeneze) ili edema mozga.

Bez obzira o kojoj vrsti stomatološke intervencije kod osoba sa DM se radi, stomatolozi bi trebalo da budu upoznati sa osnovnim karakteristikama dijabetesa pre početka tretmana. Iako mnogi autori preporučuju skrining pacijenata sa rizikom od dijabetesnih komplikacija, nisu ponuđeni jasni protokoli za postupanje sa rizičnim pacijentima u stomatološkoj ordinaciji. Smatra se da rizik od komplikacija imaju svi pacijenti sa vrednostima glikemije > 16 mmol/L, bez obzira da li su prisutne alarmantne kliničke manifestacije hiperglikemije, poput glavobolje, znojenja, vrtoglavice, drhtanja, zamagljenog vida i dr²⁶. U cilju izbegavanja akutnih komplikacija dijabetesa, preporuka je da se stomatološke intervencije kod pacijenata sa DM izvode u jutarnjim časovima, posle doručka i primene insulina ili jutarnje doze oralnih hipoglikemika. Takođe, potrebno je izmeriti vrednost glikemije pre i posle intervencije⁸.

Komplikacije dijabetesa melitusa

Komplikacije dijabetesa mogu biti akutne i hronične, a sa stomatološkog stanovišta svakako su značajnije akutne. U akutne komplikacije DM spadaju one povezane sa teškom hiperglikemijom: dijabetesna ketoacidoza (*Diabetic Ketoacidosis*, DKA), hiperglikemijsko hiperosmolalno stanje (*Hyperglycemic Hyperosmolar State*, HHS) i kombinovani poremećaji (DKA/HHS), kao i one povezane sa hipoglikemijom, koja može biti različitog stepena. I hiper i hipoglikemijske komplikacije mogu brzo uznapredovati do kome ako se brzo ne dijagnostikuju i hitno ne spreče. Ukoliko su prisutne akutne komplikacije DM, sve elektivne procedure i intervencije, uključujući svakako i elektivne operacije, jesu kontraindikovane. Mogu se izvoditi samo hitne intervencije, iz vitalnih indikacija²⁹.

Hiperglikemija nastaje kao rezultat zbirnog delovanja tri procesa: povišene glukoneogeneze, ubrzane glikolize i smanjenog iskorišćavanja glukoze od strane perifernih tkiva.

U DKA dolazi i do lipolize (povećanog oslobađanja masnih kiselina iz masnog tkiva u cirkulaciju), što dovodi do nekontrolisane oksidacije masti u jetri, sa posledičnim stvaranjem ketonskih tela (ketonemija i metabolička acidoza)^{29,30}. Hiperglikemija se javlja u prisustvu faktora rizika (među kojima je najznačajniji infekcija, koja je odgovorna za > 20% nastalih hiperglikemija) ili kao posledica stresa (stres-hiperglikemija) (tabela 2).

Tabela 2. Precipitirajući faktori za nastanak hiperglikemijskih kriza

Precipitirajući faktori	Objašnjenja
Infekcija	pneumonija, urinarni trakt, sepsa
Neadekvatna antidijabetesna Th	insulinska, oralni hipoglikemici
Endokrini poremećaji	Kušingov sindrom, tireotoksikoza, akromegalija
Druge bolesti	akutni pankreatitis, akutne intestinalne opstrukcije, AMI, CVI, toplotni udar
Lekovi	kortikosteroidi, tijazidni diuretici, β-blokeri, hlorpromazin, fenitoin

Legenda: AMI (Acute Myocardial Infarction) - akutni infarkt miokarda; CVI (Cerebrovascular Insult) - cerebrovaskularni insult; Th (Therapy) - terapija.

Dijabetesna ketoacidoza je najčešća hiperglikemijska komplikacija sa incidencom oko 4,6-8,0 na 1.000 (odraslih) pacijenata sa DM godišnje i smrtnošću oko 1-5%. U dečjem uzrastu učestalost DKA je mnogo veća, a u oko 40% (u rasponu od 26% do 67%) novootkrivenih slučajeva DM kod dece prezentuje se kao DKA, i taj rizik je utoliko veći ukoliko su deca mlađa. Mortalitet u dečjem uzrastu iznosi 0,15-0,30%. Učestalost HHS je mnogo manja (oko 1:1.000 pacijenata), ali je mortalitet znatno veći nego kod DKA (5-20%), a naročito je visok među mladim gojaznim bolesnicima i kod bolesnika sa komorbiditetima^{29,31}.

Hipoglikemija je najčešća, pa time i najznačajnija akutna komplikacija DM iz vizure stomatologa. Češća je kod DM tip 1, čak se smatra da jedna četvrtina do jedne trećine pacijenata na insulinu doživi bar jednom godišnje težu hipoglikemiju. Generalno, hipoglikemija je teži poremećaj od hiperglikemije, jer neke ćelije/tkiva mogu koristiti isključivo glukozu kao energetski supstrat (npr. mozak)³². Javlja se u prisustvu faktora rizika kao što su: propušten obrok ili dugotrajno gladovanje, pothranjenost, cirkulatorni poremećaji, septični šok, insuficijencija jetre i/ili bubrega i/ili nadbubrega, češće kod gerijatrijskih bolesnika, pacijenata bez svesti, a pojavi hipoglikemije mogu doprineti i hipopituitarizam, imobilizacija i dr. Ponekad je dovoljan samo jedan propušten obrok, promena antidijabetesne terapije ili mesta aplikacije insulina za nastanak hipoglikemije. Klinička slika i tretman hipoglikemije zavise od njene težine, koja se kreće u rasponu od lake do veoma teške³³ (tabela 3).

Tabela 3. Težina hipoglikemije

Nivo (težina) glikemije	Vrednost glikemije	Napomene
Nivo 1 Laka hipoglikemija	< 3,9	Dovoljno niska vrednost za tretman brzo delujućim ugljenim hidratima
Nivo 2 Klinički signifikantna hipoglikemija	< 3,0	Dovoljno niska vrednost, koja je indikativna za razvoj teških, klinički značajnih komplikacija hipoglikemije
Nivo 3 Teška hipoglikemija	nema specifičnog praga; obično < 2,3	Težak akcident praćen promenom mentalnog i/ili somatskog statusa i zahteva tretman radi oporavka

Hronične komplikacije DM su često prisutne, posebno kod pacijenata kod kojih je bolest dugo trajala i kod onih sa loše regulisanim dijabetesom^{2,34}. Tu spadaju makro i mikrovaskularne komplikacije (dijabetična nefropatija, retinopatija, polineuropatija). Od posebnog značaja u periproceduralnom periodu je prisustvo DAN.

Karakteristike DAN, kao što su: tiha (*silent*) kardijalna ishemija, ortostatska hipotenzija, gastropareza, disfunkcija mokraćne bešike, izostanak znojenja (poremećaj termoregulacije) i dr. mogu za posledicu imati brojne komplikacije, naročito tokom većih stomatoloških operacija u opštoj anesteziji, kao na primer: razvoj akutnog infarkta miokarda, hipotenzije, aspiracije gastričnog sadržaja u pluća (zbog usporenog i odloženog gastričnog pražnjenja), urinarne retencije, ileusa i dr².

Dijagnoza i tretman akutnih komplikacija DM u stomatološkoj ordinaciji

Klinička slika akutnih komplikacija DM nije specifična²⁹. Simptomi i znaci hiperglikemijskih kriza imaju dosta sličnosti kako među sobom, tako i sa hipoglikemijom, ali i sa nekim drugim oboljenjima i stanjima, pa je za dijagnozu ključna laboratorijska potvrda. Zbog toga je važno da se u stomatološkim ordinacijama poštuju preporuke različitih udruženja (američkih, evropskih i drugih) i što je najvažnije, Nacionalnog vodiča za dijagnozu i lečenje DM koje je izdalo Ministarstvo zdravlja republike Srbije^{8,30,35}. Ovi vodiči, između ostalog, preporučuju da na mestima na kojima se izvode bilo kakve procedure i/ili intervencije uvek bude dostupan pribor za merenje glikemije u kapilarnoj krvi^{8,36}.

Terapija hipoglikemije bi trebalo da bude usklađena sa stepenom izraženosti simptoma i znakova. Laka hipoglikemija je praćena simptomima kao što su glad, pospanost, gađenje, slabost, laka ošamućenost, glavobolja. Kod umerene hipoglikemije dolazi do tahikardije, uznemirenosti, konfuzije, nekooperativnosti, a prisutni su i znojenje, bledilo, drhtavica, dok je teška hipoglikemija praćena hipotenzijom i gubitkom svesti. U skladu sa našim Nacionalnim vodičem za dijagnozu i tretman DM, za stepen 1-2 (laka/umerena hipoglikemija) potrebno je primeniti 2-4 tablete dekstroze ili dve kafene kašičice (10 g) šećera, meda ili džema ili mala bočica soka koji sadrži šećer. Za stepen 3-4 (teška hipoglikemija) preporučena terapija je parenteralna: intravenski spori bolus ili infuzija glukoze (25 mL 50% ili 100 mL 20%). Ova terapija podiže nivo šećera za 12,5 mmol/L u roku od pet minuta, pa je to najbolji način kupiranja teške hipoglikemije,

ali je potreban oprez jer paravensko davanje može izazvati nekrozu. Alternativa glukozu je glukagon (1 mg = 1 jedinica), koji se može primeniti intravenski, intramuskularno ili supkutano, ali će ova terapija biti bez efekta ako je pacijent duže vreme gladovao ili unosio alkohol (jer su depoi glikogena za mobilizaciju glukoze iscrpljeni). Zbog toga je neophodno da stomatološke ordinacije budu opremljene u skladu sa preporukama Nacionalnog vodiča i da su u njima uvek dostupni (pored pribora za merenje glikemije u kapilarnoj krvi): kocka čokolade ili šećera, voćni sok ili drugi zaslađeni napitak, i komplet za davanje injekcije glukagona^{8, 37}. Preporučuje se da se kod pacijenata sa DM tokom izvođenja stomatološke procedure sve vreme održava verbalni kontakt, a ako je došlo do hipoglikemije (koja je uspešno kupirana) – da se takav pacijent najmanje još sat vremena nadgleda u stomatološkoj ordinaciji.

Terapija dijabetesne ketoacidoze je kompleksna. Ukoliko je u pitanju lakša forma DKA (svestan pacijent, dobrog opšteg stanja) može se pokušati sa peroralnom rehidracijom i supkutanim injekcijama regularnog ili brzodelujućeg insulina. Kod težih formi DKA terapija je isključivo parenteralna (intravenska), sprovodi se uz laboratorijski i drugi monitoring, pa se ne može primenjivati u stomatološkoj ordinaciji, već zahteva hospitalizaciju. Zato je važno da se blagovremeno posumnja na DKA u stomatološkoj ordinaciji, kako bi se organizovao transport pacijenta u bolnicu. Nažalost, simptomi i znaci nisu naročito specifični, pa je neophodna laboratorijska potvrda. DKA se manifestuje osećajem suvoće u ustima, prisutni su žeđ, opšta slabost, malaksalost, iscrpljenost, anoreksija, smanjeno znojenje, a mogući su i mučnina i povraćanje, kao i različiti poremećaji svesti, u zavisnosti od težine DKA. Međutim, težinu DKA je teško proceniti bez

laboratorijskih analiza, pre svega gasnih analiza (pH krvi i bikarbonati u serumu), pa je glavni vodič u kliničkoj proceni težine DKA – stanje svesti^{27, 29}.

Terapija DKA, u skladu sa Nacionalnim vodičem, uključuje rehidraciju, nadoknadu elektrolita (pre svega kalijuma), aplikaciju insulina i druge mere⁸. Nadoknada tečnosti i elektrolita mora se vršiti lagano, u dužem vremenskom periodu, jer nije cilj postići normoglikemiju momentalno (a to nije ni moguće, jer su broj i senzitivnost insulinskih receptora ograničeni)²⁹. U toku terapije DKA obavezno je često ponavljati laboratorijske analize, a neophodno je i praćenje elektrokardiograma (EKG) ako je vrednost kalijuma suviše niska ili visoka (< 3 mmol/L ili > 6 mmol/L). U terapiji DKA mogu se primeniti frakcionisane bolus-doze kratkododelujućeg insulina, ali se preporučuje kontinuirana intravenska infuzija ovog insulina. Nadoknada bikarbonata u lečenju DKA bi trebalo da bude veoma oprezna i limitirana na slučajeve kada je metabolička acidoza veoma izražena (nivo bikarbonata < 8 mmol/L ili je pH < 7,0)⁸. Osnovni uslov za uspešno lečenje DKA je stalno praćenje i nega bolesnika tokom prvih 24 časa terapije.

Svakako, najvažnija je prevencija ovih komplikacija, i u tom kontekstu potrebno je da u sklopu preproceduralne pripreme za stomatološke intervencije pacijenti dobiju savet o značaju redovnih kontrola kod endokrinologa, pravilnog dijetetskog režima, naročito kada su u pitanju posebno vulnerabilne kategorije pacijenata sa dijabetesom, kao što su deca, trudnice i pacijenti starijeg životnog doba³⁸⁻⁴⁰.

Zaključak

Dijabetes melitus je najčešći endokrini/metabolički poremećaj od koga boluje oko 10% populacije sa tendencijom daljeg rasta. Ovako velika učestalost podrazumeva da se i stomatolozi veoma često susreću sa osobama sa DM u svojoj praksi. Dijabetes ima različite oralne manifestacije koje mogu biti razlog dolaska u stomatološku ordinaciju. Neophodno je da svaki stomatolog poznaje osnovne karakteristike dijabetesa, a naročito njegove akutne komplikacije, kako bi ih blagovremeno prepoznao i bio u mogućnosti da primeni odgovarajuće terapijske mere. Pre bilo koje stomatološke procedure ili intervencije neophodna je evaluacija pacijenata sa DM različitog obima, u zavisnosti od vrste, hitnosti i planirane dužine trajanja stomatološke intervencije. Najvažnije je da dijabetes bude dobro kontrolisan, što se najbolje potvrđuje normalnim (ili prihvatljivim) vrednostima glikoziliranog hemoglobina. Sve dijagnostičke i terapijske mere koje se preduzimaju u pravcu prevencije i lečenja akutnih komplikacija DM moraju biti u skladu sa preporukama Nacionalnog vodiča za dijagnostiku i terapiju DM. Svaka stomatološka ordinacija mora posedovati pribor za merenje glikemije iz kapilarne krvi, kao i preporučena sredstva za terapiju hipoglikemije, dok se pacijenti sa dijabetesnom ketoacidozom ili drugim hiperglikemijskim komplikacijama moraju hospitalizovati.

Abstract

This paper presents the basic characteristics of diabetes mellitus, a disease that affects about 10% of the population, with a tendency to further increase in frequency. There is a special focus on the oral manifestations of diabetes and the specifics of diabetic patients undergoing various dental procedures and interventions. In this context, hyper and hypoglycemic crises, which can quickly progress to coma, if not recognized and treated promptly, are especially apostrophized. With the goal of timely diagnosis, clinical manifestations and laboratory parameters of acute diabetic complications are presented, as well as risk factors that contribute to the occurrence of these complications. The recommendations of the American and European Diabetes Associations, as well as the Serbian National Guide for the Diagnosis and Treatment of Diabetes mellitus, are given regarding the necessary pre-procedural evaluation of these patients and the equipment of dental offices, to successfully prevent and treat acute complications of diabetes.

Keywords: diabetes mellitus, oral manifestations of diabetes, dental interventions, acute complications of diabetes, therapy of acute complications of diabetes

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THE IMPORTANCE OF DIABETES MELLITUS IN DENTAL PRACTICE

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Abstract

This paper presents the basic characteristics of diabetes mellitus, a disease that affects about 10% of the population, with a tendency to further increase in frequency. There is a special focus on the oral manifestations of diabetes and the specifics of diabetic patients undergoing various dental procedures and interventions. In this context, hyper and hypoglycemic crises, which can quickly progress to coma, if not recognized and treated promptly, are especially apostrophized. With the goal of timely diagnosis, clinical manifestations and laboratory parameters of acute diabetic complications are presented, as well as risk factors that contribute to the occurrence of these complications. The recommendations of the American and European Diabetes Associations, as well as the Serbian National Guide for the Diagnosis and Treatment of Diabetes mellitus, are given regarding the necessary pre-procedural evaluation of these patients and the equipment of dental offices, to successfully prevent and treat acute complications of diabetes.

Keywords: diabetes mellitus, oral manifestations of diabetes, dental interventions, acute complications of diabetes, therapy of acute complications of diabetes

Introduction

Diabetes mellitus (DM) is a metabolic disorder caused by insufficient insulin production in the pancreas (Type 1 DM), inadequate insulin utilization in the periphery (Type 2 DM), or a combination of both mechanisms¹. Many substances have different effects on insulin secretion, which can lead to significant imbalances in blood glucose levels, even to hypo- or hyperglycemic crises. The main stimulators of insulin secretion are glucose and fructose, while other stimulators include amino acids, gastrointestinal hormones (gastrin, cholecystokinin, secretin, incretins), acetylcholine, and certain medications (β -adrenergic receptor agonists). The most important inhibitors of secretion are stress hormones (known as counterregulatory hormones), including catecholamines (epinephrine and norepinephrine), cortisol, growth hormone, and glucagon. Cytokines, as well as some medications (such as α -adrenergic receptor agonists, glucocorticoids, etc.), also inhibit insulin secretion².

The normal range for fasting blood glucose levels is 3.5-6.0 mmol/L, and for glycosylated hemoglobin (HbA1c) it is 3.5-6%. The diagnosis of diabetes mellitus (DM) is established based on elevated blood glucose levels, specifically ≥ 7.0 mmol/L or ≥ 11.1 mmol/L, 120 minutes after an Oral Glucose Tolerance Test (OGTT). Since 2009, the criteria for diagnosing DM have also included an elevated level of glycosylated hemoglobin (HbA1c $\geq 6.5\%$) as an indicator of long-term metabolic control (around three months, or 6-8 weeks in pregnant women)³.

The prevalence of diabetes mellitus is high in all developed countries worldwide, with a tendency for further growth. While in 2000 there were 6.4% of affected individuals, by 2014 the number increased to 8.3% of the world's population, with a forecast for further growth. According to the World Health Organization (WHO), this could exceed 12% by 2040⁴. Diabetes mellitus occurs in all age groups, with the highest prevalence observed after the age of forty, especially in underdeveloped and developing countries where there is a higher number of undiagnosed cases of DM, reaching over 40%⁵. In the geriatric population, the prevalence of DM is highest ($>20\%$), with diabetes being more commonly associated with chronic complications and other comorbidities in older age, whether related to diabetes or independent of it⁶. According to WHO data, there are currently around 400 million registered diabetics worldwide, and in Serbia, according to the Institute of Public Health of Serbia, there are approximately 700,000 cases.

Diabetes also has oral manifestations that are significant in dental practice⁷. However, even without oral manifestations, patients with diabetes deserve special attention

from dentists and require careful pre-procedural evaluation because they are a particularly sensitive group of patients in terms of the possibility of developing acute complications. Dentists must be familiar with the basic characteristics of diabetes to be able to react promptly and adequately if hyperglycemic or hypoglycemic crises occur in the dental office. In such cases, it is necessary to act following the recommendations of the National Guideline for the Diagnosis and Treatment of Diabetes Mellitus issued by the Ministry of Health of the Republic of Serbia⁸.

Specific forms of hyperglycemia

Stress hyperglycemia (SHG) is defined as hyperglycemia in previously euglycemic patients, with blood glucose levels ≥ 7.0 mmol/L in two successive measurements or blood glucose levels ≥ 11.1 mmol/L in random measurements in previously normoglycemic patients. SHG most commonly occurs concerning an acute process, such as trauma or another acute illness, including situations in the dental office⁹. According to various reports, the frequency of SHG ranges from 3% to 80% of cases among hospitalized patients. This wide variability is explained by the imprecise definition of stress hyperglycemia and the fact that in a large number of cases, diabetes mellitus already existed but was unrecognized and untreated².

Insulin resistance represents the inability to effectively utilize insulin, despite sufficient levels present in the body, which can result in hyperglycemia. This resistance may be influenced by genetic factors or caused by certain medications (such as corticosteroids). However, it most commonly occurs within the context of stressful conditions, such as infection, sepsis, critical illness, and others¹. It also occurs during pregnancy, in obese individuals, and in those with high blood pressure, as part of hyperlipidemia (elevated cholesterol and/or triglycerides), etc¹. The release of stress hormones and cytokines plays an important role in reducing the insulin/glucose ratio. Insulin stimulates glucose uptake in insulin-sensitive tissues (liver, skeletal muscles, and adipose tissue), thereby reducing glucose release from the liver².

Oral manifestations of diabetes mellitus

Numerous studies have demonstrated an association between diabetes mellitus (DM) and periodontal diseases¹⁰. Patients with diabetes often experience a burning sensation and discomfort in the oral cavity, as well as bad breath (*fetor ex ore*). The oral mucosa may appear swollen, and darker in color, and ulcerations in the oral cavity are possible. The tongue may also appear swollen, red, with atrophic papillae (lingua geografica). The gingiva tends to bleed easily and is prone to infections (especially candidiasis), while the salivary glands are prone to calculus formation. Periodontal disease and periodontal abscesses are common findings in

individuals with diabetes, and they are more frequent and severe in younger age groups¹¹. Due to a deficiency in vitamin B, stomatodynia and stomatopyrosis may be present, which can be further aggravated by candidiasis¹².

The pathophysiology of oral manifestations of diabetes is not fully elucidated, but there is a known association with the occurrence of dental caries¹³. In individuals with diabetes, there is an elevated glucose level in saliva (glycosylation), and saliva pH is decreased (acidosis). Additionally, there is reduced saliva secretion (xerostomia), which complicates chewing and swallowing food and prevents adequate self-cleaning of the oral cavity, creating favorable conditions for the development of microorganisms and infections. It has been demonstrated that periodontal disease and oral disorders are more common in individuals with diabetes compared to healthy individuals^{11,12}.

In individuals with diabetes, oral blood vessels exhibit increased permeability due to microangiopathy, leading to the deposition of mucopolysaccharides and glycoproteins in oral tissues. Gingival blood vessels are affected by atherosclerosis and atheromatous changes, resulting in narrowed lumens. Microthromboses and microangiopathies are present, leading to stasis, disturbances in the nourishment and oxygenation of oral tissues, as well as impaired elimination of harmful metabolic byproducts. Alveolar bone undergoes significant resorption and the formation of pockets that suppurate, thus predisposing to the development of abscesses¹⁴. In the periodontium, there is progressive destruction of all components, increased collagenolysis, and reduced synthesis of new collagen¹¹.

Periodontitis is a chronic inflammation of the gums caused by an inflammatory disease, which can not only lead to tooth loss but also is considered a modifying factor that affects overall systemic health^{14,15}. Recent studies have shown an association between periodontitis and chronic diseases such as Alzheimer's disease, cancer, rheumatoid arthritis, and others^{13,16}. In addition to the known impact of DM on the occurrence and outcome of treatment in patients with the coronavirus, studies by Santana and other authors have shown that the combination of diabetes and periodontal diseases increases the risk of COVID-19 infection¹⁷⁻²¹. Numerous studies indicate a connection between diabetes and the outcome of dental implants^{22,23}. Also, many studies have examined the impact of local anesthesia on glycemic levels in individuals with diabetes during dental procedures (lidocaine with epinephrine 1:100.000). However, there is no evidence that a local anesthetic with the addition of adrenaline significantly alters glycemic levels^{24,25}.

From the aforementioned, it unequivocally emerges that dentists often encounter patients with diabetes because they constitute a vulnerable population concerning oral and dental diseases. Although the association between diabetes and increased prevalence of oral and dental diseases is well-known, unfortunately, there are no specific protocols

and recommendations to ensure a safe environment for these patients in dental practices. The focus of dentists when performing interventions in these patients still lies on the potential occurrence of hypo- and hyperglycemia, their prevention, and appropriate management²⁶.

Evaluation and preparation of patients with diabetes before dental interventions

From a dental perspective, the most important elements of pre-procedural evaluation of patients with diabetes mellitus (DM) include: assessing the duration of the disease and treatment regimen, the presence of DM complications and/or other comorbidities, and reviewing laboratory tests (blood glucose levels, glycosylated hemoglobin, and other necessary analyses) (Table 1). The extent of pre-procedural evaluation depends on the complexity and urgency of the dental intervention, estimated duration of the procedure, the time elapsed since the last meal (and last dose of antidiabetic therapy), as well as the expected level of stress, which is largely a subjective category and depends on the patient's personality structure. However, the most important question is whether diabetes is well controlled. For major dental

Table 1. Elements of pre-procedural evaluation of patients with DM

Elements of preoperative evaluation	Pay attention to:
1. DM characteristics	Type of DM; Duration of illness Treatment regimen-therapy (oral hypoglycemic agents, insulin, combined)
2. Presence of DM complications	Acute (DKA, HHS, hypoglycemia) Chronic (micro and macroangiopathies, especially DAN)
3. Presence of other comorbidities that may (but not necessarily) be associated with DM	Hypertension and other diseases CV, NAFLD
4. Laboratory analyses	Glycemia and HbA1c are mandatory, and as needed: urea, creatinine, electrolytes, urine analysis (albumin, ketones)
5. Assessment of the airway	Possibility of the need for emergency tracheal intubation, which is often difficult in diabetics

Legend: OH - Oral Hypoglycemic; DKA - Diabetic Ketoacidosis; HHS - Hyperglycemic Hyperosmolar State; DAN - Diabetic Autonomic Neuropathy; NAFLD - Non-Alcoholic Fatty Liver Disease.

interventions, especially surgical procedures, consultation with an endocrinologist or anesthesiologist is mandatory².

The primary goals of pre-procedural assessment and preparation of patients with DM are to avoid hyperglycemia (> 10 mmol/L), and hypoglycemia (< 3.8 mmol/L), as well as large fluctuations in blood glucose levels and electrolyte loss. The American Diabetes Association (ADA) issued recommendations in 2014, which are still in effect today, stating that the target glucose values for patients scheduled for invasive diagnostic and therapeutic procedures or surgical interventions should be as close to the physiological range as possible, but definitely < 10 mmol/L. This is also supported by the Canadian and Australian Diabetes Associations, as well as the majority of authors^{2, 27}. HbA1C, as an indicator of long-term metabolic control, is a more

important laboratory parameter than blood glucose levels because blood glucose levels fluctuate throughout the day (depending on the time of day, meals, stress...)¹⁻³.

Preprocedural preparation of patients with diabetes mellitus for dental procedures certainly includes evaluation of diabetes complications (acute and chronic) and other comorbidities that may not necessarily be related to diabetes mellitus. However, it is important to keep in mind that among other comorbidities, hypertension is present in 40-50% of diabetics and may be associated with atherosclerosis, while approximately 17% of patients with diabetes have occult infections. Coronary artery disease is often present, especially in young individuals (which is atypical), as well as congestive heart failure, hepatic steatosis, and others².

Furthermore, it is important to consider that patients with diabetes mellitus have an increased susceptibility to infection²⁸, particularly concerning dental surgeries. Additionally, they experience delayed wound healing. They are also prone to dehydration due to osmotic diuresis in hyperglycemia, leading to the development of hyperosmolality²⁶. Serious complications such as diabetic ketoacidosis (due to ketogenesis), thromboembolism (due to increased blood viscosity and thrombogenesis), or cerebral edema are not uncommon.

Regardless of the type of dental intervention being performed on individuals with DM, dentists should be familiar with the basic characteristics of diabetes before starting treatment. Although many authors recommend screening patients at risk of diabetic complications, clear protocols for managing high-risk patients in dental offices have not been provided. It is considered that all patients with blood glucose levels > 16 mmol/L are at risk of complications, regardless of whether alarming clinical manifestations of hyperglycemia, such as headache, sweating, dizziness, tremors, blurred vision, etc., are present²⁶. To avoid acute complications of diabetes, it is recommended that dental procedures for patients with DM be performed in the morning, after breakfast and administration of insulin or the morning dose of oral hypoglycemic agents. Additionally, it is necessary to measure blood glucose levels before and after the intervention⁸.

Complications of diabetes mellitus

Complications of diabetes can be acute or chronic, with acute complications being more significant from a dental perspective. Acute complications of diabetes include those associated with severe hyperglycemia: diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS), combined disorders (DKA/HHS), as well as those associated with hypoglycemia, which can vary in severity. Both hyperglycemic and hypoglycemic complications can quickly progress to coma if not promptly diagnosed and urgently prevented. If acute complications of diabetes are present, all elective procedures and interventions, including elective surgeries,

are contraindicated. Only emergency interventions, for vital indications, should be performed²⁹.

Hyperglycemia occurs as a result of the combined action of three processes: increased gluconeogenesis, accelerated glycolysis, and reduced utilization of glucose by peripheral tissues. In DKA is also lipolysis (increased release of fatty acids from adipose tissue into circulation), leading to uncontrolled oxidation of fats in the liver, resulting in

Table 2. Precipitating factors for the onset of hyperglycemic crises

Precipitating factors	Explanations
Infection	pneumonia, urinary tract infection, sepsis
Inadequate anti-diabetic Th	insulin, oral hypoglycemics
Endocrine disorders	Cushing's syndrome, thyrotoxicosis, acromegaly
Other diseases	Acute pancreatitis, acute intestinal obstruction, AMI, CVI, heat stroke
Medications	Corticosteroids, thiazide diuretics, β-blockers, chlorpromazine, phenytoin

Legend: AMI - Acute Myocardial Infarction; CVI - Cerebrovascular Insult; Th - Therapy.

the formation of ketone bodies (ketonemia and metabolic acidosis)^{29, 30}. Hyperglycemia occurs in the presence of risk factors (among which infection is the most significant, responsible for > 20% of hyperglycemic events) or as a result of stress (stress hyperglycemia) (Table 2).

Diabetic ketoacidosis is the most common hyperglycemic complication, with an annual incidence of approximately 4.6-8.0 per 1.000 (adult) diabetic patients and a mortality rate of about 1-5%. In pediatric populations, the incidence of DKA is much higher, with around 40% (ranging from 26% to 67%) of newly diagnosed cases of diabetes in children presenting as DKA, especially among younger children. The mortality rate in pediatric patients is approximately 0.15-0.30%. The frequency of HHS is much lower (around 1 per 1.000 patients), but the mortality rate is significantly higher than that of DKA (5-20%), especially among young obese patients and those with comorbidities^{29, 30}.

Hypoglycemia is the most common and therefore the most significant acute complication of diabetes mellitus from the perspective of dentists. It is more common in type 1 diabetes mellitus, with estimates suggesting that one-quarter to one-third of insulin-treated patients experience severe hypoglycemia at least once a year. Generally, hypoglycemia is a more severe disorder than hyperglycemia because some cells/tissues can exclusively use glucose as an energy substrate (e.g., the brain)³². Hypoglycemia occurs in the presence of risk factors such as missed meals or

prolonged fasting, malnutrition, circulatory disorders, septic shock, liver and/or kidney and/or adrenal insufficiency, more frequently in geriatric patients, unconscious patients, and hypoglycemia can also be contributed by hypopituitarism, immobilization, and others. Sometimes, just missing one meal, changing antidiabetic therapy, or the site of insulin injection is enough to cause hypoglycemia. The clinical presentation and treatment of hypoglycemia depend on its severity, ranging from mild to very severe³³ (Table 3).

Chronic complications of DM are often present, especially in patients with long-standing disease and those with poorly controlled diabetes^{2, 34}. These include macrovascular and microvascular complications (diabetic nephropathy, retinopathy, polyneuropathy). Of particular importance in the perioperative period is the presence of DAN (diabetic autonomic neuropathy).

Characteristics of DAN, such as silent cardiac ischemia, orthostatic hypotension, gastroparesis, bladder dysfunction, lack of sweating (thermoregulation disorder), and others, can result in numerous complications, especially during major dental surgeries under general anesthesia, such as acute myocardial infarction, hypotension, aspiration of gastric contents into the lungs (due to delayed gastric emptying), urinary retention, ileus, and others².

Diagnosis and treatment of acute complications DM in the dental office

The clinical picture of acute complications of DM is not specific²⁹. Symptoms and signs of hyperglycemic crises have many similarities among themselves, as well as with hypoglycemia, but also with some other diseases and conditions, so laboratory confirmation is crucial for diagnosis. Therefore, it is important to adhere to the recommendations of various associations (American, European, and others) in dental offices and, most importantly, to the National Guide for the Diagnosis and Treatment of DM issued by the Ministry of Health of the Republic of Serbia^{8, 30, 35}. These guidelines, among other recommendations, suggest that equipment for measuring capillary blood glucose should always be available at sites where any procedures and/or interventions are performed^{8, 36}.

The treatment of hypoglycemia should be tailored to the severity of symptoms and signs. Mild hypoglycemia is characterized by symptoms such as hunger, drowsiness, nausea, weakness, mild dizziness, and headache. Moderate

Table 3. Severity of hypoglycemia

Level (severity) of glycemia	Value of glycemia	Notes
Level 1 Mild hypoglycemia	< 3.9	Sufficiently low value for treatment with rapidly acting carbohydrates
Level 2 Clinically significant hypoglycemia	< 3.0	Sufficiently low value indicative of the development of severe, clinically significant complications of hypoglycemia
Level 3 Severe hypoglycemia	there is no specific threshold; usually < 2.3	Severe accident accompanied by a change in mental and/or somatic status and requiring treatment for recovery

hypoglycemia presents with tachycardia, restlessness, confusion, and irritability, accompanied by sweating, pallor, and tremors. Severe hypoglycemia is marked by hypotension and loss of consciousness. According to our National Guidelines for the Diagnosis and Treatment of Diabetes Mellitus, for grades 1-2 (mild/moderate hypoglycemia), the recommended treatment is to administer 2-4 glucose tablets or two teaspoons (10 g) of sugar, honey, or jam, or a small bottle of juice containing sugar. For grades 3-4 (severe hypoglycemia), the recommended therapy is parenteral: slow intravenous bolus or infusion of glucose (25 mL of 50% or 100 mL of 20% solution). This therapy raises the blood sugar level by 12.5 mmol/L within five minutes, making it the best way to manage severe hypoglycemia. However, caution is needed as extravascular administration can cause necrosis. An alternative to glucose is glucagon (1 mg = 1 unit), which can be administered intravenously, intramuscularly, or subcutaneously. However, this therapy may be ineffective if the patient has been fasting or consuming alcohol for an extended period (as glycogen stores for glucose mobilization may be depleted). Therefore, it is necessary for dental offices to be equipped following the recommendations of the National Guide and to always have available (in addition to the equipment for measuring blood glucose levels in capillary blood): a sugar cube or chocolate, fruit juice, or another sweetened beverage, and a glucagon injection kit^{8, 37}. It is recommended that during dental procedures in patients with diabetes, verbal contact should be maintained continuously, and if hypoglycemia has occurred (which has been successfully managed), such patients should be monitored in the dental office for at least another hour.

The therapy for DKA is complex. In cases of milder DKA (conscious patient, good general condition), attempts can be made with oral rehydration and subcutaneous injections of regular or rapid-acting insulin. However, for severe forms of DKA, therapy is exclusively parenteral (intravenous) and requires laboratory and other monitoring, making it unsuitable for administration in a dental office. Hospitalization is necessary in such cases. Therefore, it is important to promptly suspect DKA in a dental to arrange for the patient's transport to the hospital. Unfortunately, the symptoms and signs of DKA are not particularly specific, necessitating laboratory confirmation. DKA presents with a sensation of dryness in the mouth, thirst, general weakness, fatigue, exhaustion, anorexia, decreased sweating, and possible nausea and vomiting. Various levels of consciousness disturbances may also occur, depending on the severity of DKA. However, assessing the severity of DKA without laboratory analysis, particularly gas analysis (blood pH and serum bicarbonate), is difficult. Therefore, the primary guide in the clinical assessment of DKA severity is the patient's level of consciousness^{27, 29}.

The treatment for DKA, as per the National Guidelines, involves rehydration, electrolyte replacement (primarily potassium), insulin administration, and other measures⁸. Fluid and electrolyte replacement must be done slowly over an

extended period because the goal is not to achieve normoglycemia instantly (which is not possible anyway, as the number and sensitivity of insulin receptors are limited)²⁹. During DKA therapy, it's essential to frequently repeat laboratory tests, and monitoring of electrocardiogram (EKG) is necessary if potassium levels are too low or too high (< 3 mmol/L or > 6 mmol/L). Fractionated bolus doses of short-acting insulin can be used in DKA therapy, but continuous intravenous infusion of this insulin is recommended. Bicarbonate replacement in DKA treatment should be very cautious and limited to cases where metabolic acidosis is severe (bicarbonate level < 8 mmol/L or pH < 7.0)⁸. The fundamental requirement for successful DKA treatment is continuous monitoring and care of the patient during the first 24 hours of therapy.

Certainly, the most important aspect is the prevention of these complications, and in this context, as part of the pre-procedural preparation for dental interventions, patients should receive advice on the importance of regular check-ups with an endocrinologist, maintaining a proper dietary regimen, especially for particularly vulnerable categories of diabetic patients such as children, pregnant women, and elderly patients³⁸⁻⁴⁰.

Conclusion

Diabetes mellitus is the most common endocrine/metabolic disorder affecting approximately 10% of the population with a tendency for further growth. Such a high prevalence implies that dentists frequently encounter individuals with diabetes in their practice. Diabetes has various oral manifestations that may be the reason for a visit to the dental office. Every dentist needs to be familiar with the basic characteristics of diabetes, especially its acute complications, to recognize them promptly and apply appropriate therapeutic measures. Before any dental procedure or intervention, an evaluation of patients with diabetes of varying extent is necessary, depending on the type, urgency, and planned duration of the dental intervention. The most important aspect is that diabetes is well-controlled, best confirmed by normal (or acceptable) levels of glycosylated hemoglobin. All diagnostic and therapeutic measures aimed at preventing and treating acute complications of diabetes must be in line with the recommendations of the National Guidelines for the Diagnosis and Treatment of Diabetes. Every dental office must have equipment for measuring blood glucose from capillary blood, as well as the recommended means for treating hypoglycemia, while patients with diabetic ketoacidosis or other hyperglycemic complications must be hospitalized.

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