Orienterande litteraturöversikt

TRYCKKAMMARBEHANDLING VID DIABETESFOTSÅR, STRÅLNINGSORSAKAD VÄVNADSDÖD I BEN ELLER INFLAMMATION I URINBLÅSA / ÄNDTARM

2019-12-12

Innehållsdeklaration

Detta HTA Skåne dokument är baserat på följande moment:

☒ Metodbeskrivning
☐ PICO
☐ Uttömmande litteratursökning
☒ Översiktlig litteratursökning
☐ Flödesschema
☒ Litteratursållning
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☐ Kunskapsluckor identifierade
☐ Jävsdeklaration inhämtad från projektdeltagarna

Innehållsförteckning

Bilaga 1
Yttrande från Prioriteringsrådet 2017-03-20, Dnr. 1402749

Orienterande litteraturöversikt

Inledning

Syftet med föreliggande arbete är att ge en orienterande överblick över den litteratur som publicerats i tryckkammarfrågan vid de tre tillstånden: diabetesorsakade fotsår (DFU), strålningsorsakad vävnadsdöd i ben (osteoradionekros, ORN) samt radiologiskt orsakad inflammation i urinblåsa och/eller ändtarm (cystit/proktit). Litteraturöversikten utgör således ett led i det förberedande arbetet inför beslut i Metod- och prioriteringsrådet huruvida ett HTA-projekt skall initieras.

2016 publicerade SBU:s Upplysningstjänst sina svar kring tryckkammarbehandling (Hyperbaric oxygen treatment, HBOT) vid de tre tillstånden. 2017 avgav Region Skånes dåvarande prioriteringsråd ett yttrande till koncernkontoret efter en värdering i ämnet av HTA Skåne (bilaga 1).

En sonderande litteratursökning, med tidsmässig början efter SBU:s litteratursökning och till med 191107 har nu gjorts i medicinska databaser samt på ett antal HTA-organisationers webbplatser (appendix 1). Likaså har sökningar efter planerade och pågående studier

genomförts. Resultatet, som inte är heltäckande, redovisas översiktligt, indelat efter typ av studier.
Refererad litteratur är en sammanställning av ett enklare sållningsförfarande. Något formellt PICO har inte tagits fram. Litteraturen är inte relevansbedömd, kvalitetsgranskad eller evidensgraderad.
Den avslutande analysen är således enkel till sin natur och grund till sin karaktär.

Frågeställare
Richard Frobell, FoU-chef Skånes sjukhus Nordväst.

Ärendebeskrivning och frågeställning från frågeställare
”HBOT (Hyperbaric oxygen treatment) är en kostsam och utrymmeskrävande behandlingsmetod där det vetenskapliga underlaget är oklart. RS prioriteringsråd yttrade sig 2017 om att Region Skåne inte bör tillhandahålla denna behandling. Vi önskar nu en förnyad litteratursökning och ett uppdaterat yttrande som även tar hänsyn till behandling av akuta tillstånd samt en förändrad kostnadskalkyl.

Frågeställningen är således huvudsakligen oförändrad med önskemål om ställningstagande till akuta behandlingstillstånd: Bör Region Skåne, inom ramen för rutinsjukvård, erbjuda tryckkammarbehandling av diabetesorsakade fotsår, strålningsorsakad vävnadsdöd i ben (osteoradionekros), radiologiskt orsakad inflammation i urinblåsa och/eller ändtarm (cystit och proktit) samt akuta tillstånd?”

Bakgrund
Under åren 2014 till 2017 har tryckkammarfrågan tagits upp vid ett flertal tillfällen i Region Skåne.

I mars 2017 gjorde Koncernkontorets Prioriteringsråd ett yttrande: ”Tryckkammarbehandling vid diabetessår och strålningsorsakad vävnadsdöd och inflammation” (Dnr. 1402749, bilaga 1). Frågeställningen var: ”Bör Region Skåne inom ramen för rutinsjukvård erbjuda tryckkammarbehandling vid diabetesorsakade fotsår, strålningsorsakad vävnadsdöd i ben (osteoradionekros) samt radiologiskt orsakad inflammation i urinblåsa och ändtarm (cystit och proktit)?” Prioriteringsrådets ställningstagande[*] löd: *”Region Skåne bör inte inom ramen för rutinsjukvård erbjuda tryckkammarbehandling vid diabetesorsakade fotsår (prioritet 9), osteoradionekros (prioritet 8) samt radiologiskt orsakad cystit och proktit (FoU)”.*

Sammanfattning av de tre svaren från SBU:s Upplysningstjänst 2016
För alla de tre svaren från SBU:s Upplysningstjänst nedan gäller att ”SBU har inte tagit ställning i sakfrågan eftersom de enskilda studiernas kvalitet inte bedömts och resultaten inte vägts samman”. Därför redovisar man endast de enskilda författarnas slutsatser.

Syfte:
”Är hyperbar syrgasbehandling effektivt som tillägg till konventionell behandling av svårläkta ben- och/eller fotsår hos vuxna patienter med diabetes typ 1 eller 2?”
För inkluderade artiklar: vg se nedan länk
Slutsatser:
”Enligt författarna till den ena HTA-rapporten förbättrade HBO sårläkning hos patienter med diabetiska fotsår. Författarna till Cochrane-översikten, publicerad år 2015, drog slutsatsen att HBO förbättrade läkningen under en uppföljningstid på upp till sex veckor men inte på längre

[*] Nationella prioriteringsmodellen, prioriteringsgrad 1-10 där 1 innebär högsta prioritet och 10 lägsta prioritet. Resurser bör i första hand fördelas till åtgärder med högst prioritet. Åtgärder med mycket låg evidens och/eller bristande klinisk erfarenhet hänvisas till forskning och utveckling, FoU.”

sikt. De fann också att behandlingen verkade minska risken för amputation över fotleden. Författarna till den senaste RCT:n rapporterade att HBO varken minskade risken för amputation eller förbättrade läkningen hos patienter med diabetessår."

Länk till publikationen:
https://www.sbu.se/contentassets/bb89a92f77f24ba7a428de66e1b3e13b/hyperbar-syrgasbehandling-av-diabetesrelaterade-fot--och-bensar.pdf

Syfte:
"Är hyperbar syrgasbehandling effektivt som tillägg till konventionell behandling av vävnadsdöd i ben orsakad av strålbehandling mot cancer?"
För inkluderade artiklar: vg se nedan länk
Slutsatser:
"Författarna till den senaste systematiska översikten kom fram till att hyperbar syrgasbehandling (HBO) ökade chansen att exponerat skelett i käken täcktes med tandkött samt minskade risken för sårruptur. Författarna bedömde att det vetenskapliga underlaget för båda slutsatserna var av måttlig kvalitet.
Sammantaget anser författarna till de tidigare systematiska översikterna att HBO-behandling troligen förbättrar behandling av strålningsorsakad benvävnadsdöd, men att fler randomiserade kontrollerade studier behövs."

Länk till publikationen:
https://www.sbu.se/contentassets/d11825195f5e48899a32513e1b359014/hyperbar-syrgasbehandling-av-vavnadsdod-i-ben-orsakad-av-stralbehandling.pdf

Syfte:
"Är hyperbar syrgasbehandling effektivt som tillägg till konventionell behandling av inflammation i urinblåsa respektive ändtarm orsakad av strålbehandling mot cancer?"
För inkluderade artiklar: vg se nedan länk
Slutsatser:
"Författarna till de tre senaste systematiska översikterna gjorde bedömningen att HBO verkar förbättra läkningen av strålningsorsakad proktit. Två av översikterna inkluderade även strålningsorsakad cystit, men kunde inte dra några slutsatser om effekten av HBO-behandling i denna patientgrupp.
Författarna till HTA-rapporten drog slutsatsen att HBO förbättrade läkningen hos patienter med strålningsorsakad proktit, men att det vetenskapliga underlaget var av låg kvalitet. De kunde inte heller dra några slutsatser angående effekten av HBO hos patienter med cystit."

Länk till svaret:
https://www.sbu.se/contentassets/ef5c222ca13043cb97b79532b24514d2/hyperbar-syrgasbehandling-av-stralningsorsakad-cystit-och-proktit.pdf

Aktuell litteratursökning av HTA Skåne

Litteratursökningarna (appendix 1) har utgått från 2016, då SBU:s Upplysningstjänst publicerade sina svar kring tryckkammarbehandling vid de tre tillstånden.

Frågeställningar har efter 2016 undersökts i tre HTA-rapporter: en tysk från Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen 2016, en kanadensisk från Health Quality Ontario 2017 samt en norsk från Folkehelseinstituttet 2019.

HTA-rapporter

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen 2016

Hyperbare Sauerstofftherapie bei diabetischem Fußsyndrom

Syfte:
Syftet med föreliggande undersökning är en nyttovärdering av HBO i jämförelse med varje annat behandlingsalternativ hos patienter med diabetiska fotsår beträffande patientrelevanta effektmått.
(översättning från tyska: R Steingrimsdottir)

För inkluderade artiklar: vg se nedan länk

Författarnas slutsatser:
Av den föreliggande nyttovärderingen framgår att det avseende effektmåttet sårläkning finns stöd för nyttan av tilläggsbehandling med HBOT vid DFU i jämförelse med enbart standard-sårvård.
Avseende de andra patientrelevanta effektmåtten mortalitet, amputation (mindre och större amputationer), oönskade effekter av behandlingen, hälsorelaterad livskvalitet och vistelsetid på sjukhus finns det inget stöd för nytta eller skada av tilläggsbehandling med HBOT vid DFU i jämförelse med andra behandlingsalternativ.
Avseende effektmåtten smärta, kardiovaskulär sjuklighet och beroende av hjälp utifrån eller vårdbehov kunde inget uttalande göras om nytta eller skada av tilläggsbehandling med HBOT vid DFU i jämförelse med andra behandlingsalternativ, då inga data för detta fanns.
Ett uttalande om nyttan utifrån undergrupper eller indikationer var på grund av avsaknad av data inte möjligt.
(översättning från tyska: R Steingrimsdottir)

Länk till rapporten:
http://ebm.i.skane.se/_layouts/15/WopiFrame.aspx?sourcedoc=&file=IQWiG_HBOT-DFU_20160420.pdf&action=default

Health Quality Ontario 2017

Hyperbaric Oxygen Therapy for the Treatment of Diabetic Foot Ulcers: A Health Technology Assessment

Syfte:
”In this health technology assessment, we compared the safety and effectiveness of standard wound care plus hyperbaric oxygen therapy versus standard wound care alone for patients with diabetic foot ulcers. We also looked at how much hyperbaric oxygen therapy costs and whether it is cost-effective (good value for money) and spoke with patients to learn about their experiences with hyperbaric oxygen therapy.”

För inkluderade artiklar: vg se nedan länk

Författarnas slutsatser:
”We found that hyperbaric oxygen therapy and standard wound care appear to be given in many different ways. Therefore, the findings of the studies we reviewed differed on how effective hyperbaric oxygen therapy was in terms of the rate of major amputations undergone by patients receiving standard wound care plus hyperbaric oxygen therapy versus standard wound care alone. However, our analysis showed that standard wound care plus hyperbaric oxygen therapy results in an improvement in ulcer healing compared with standard wound

care alone. The studies we reviewed found that standard wound care plus hyperbaric oxygen is as safe as standard wound care alone. The evidence makes it difficult to draw any definitive conclusions on the effectiveness of standard wound care plus hyperbaric oxygen therapy versus standard wound care alone for the treatment of diabetic foot ulcers. […] Patients with whom we spoke who had undergone hyperbaric oxygen therapy for the treatment of diabetic foot ulcers reported that they felt it was a highly effective treatment, they were satisfied with their wound healing, and they felt an improvement in their quality of life. Patients also said that although the process of receiving hyperbaric oxygen therapy was simple, it required a substantial time commitment and has associated costs."

Länk till rapporten:
http://www.hqontario.ca/Evidence-to-Improve-Care/Journal-Ontario-Health-Technology-Assessment-Series

Folkehelseinstituttet 2019
Hyperbar oksygenbehandling av osteonekrose

Syfte:
"Vi har oppsummert forskning om effekt og sikkerhet av HBO i behandlingen av osteonekrose. Vi har også vurdert kostnadseffektivitet og budsjettvirkninger av HBO-behandling."

Notera att denna HTA-rapport handlar om effekt av HBO-behandling "ved strålerelatert osteonekrose, medikamentrelatert osteonekrose" samt "ved osteonekrose i hofta" – varav enbart den första av de tre är av intresse utifrån våra frågeställningar – således bortser vi här från de delar av rapporten som rör de övriga två.

För inkluderade artiklar: vg se nedan länk

Författarnas slutsatser:
• "HBO-behandling kan føre til at flere pasienter med strålerelatert osteonekrose oppnår fullstendig slimhinnedekning av kjevebeinet.

• Det er uklart om HBO-behandling har bedre effekt enn annen behandling av strålerelatert osteonekrose, medikamentrelatert osteonekrose eller idiopatisk osteonekrose i hofteleddet.

• Det er uklart i hvilken grad uønskede hendelser kan knyttes til HBO-behandling."

Länk till rapporten:
https://www.fhi.no/publ/2019/hyperbar-oksygenbehandling-av-osteonekrose/

Riktlinjer och rekommendationer
Var god se appendix 3

Sammanfattning av identifierade originalstudier
(för författare, titel, tidskrift och abstrakt, vg se appendix 2)

Ämnesområde	Syst. översikter	Originalstudier
DFU	4	16
ORN	2	4
Cystit/proktit	3	5

DFU: Efter en översiktlig publikationssållning återstod 20 st vetenskapliga arbeten, av dessa var fyra stycken systematiska översikter och de återstående var originalstudier. Då mer kvalificerad utvärdering av publikationerna inte är genomförd begränsas analysen till författarnas egna konklusioner (detta gäller även nedan ämnesområden för tryckkammarbehandling).

I tre av de fyra systematiska översikterna konkluderades att HBOT inte kunde förbättra sårläkning eller minska antalet större amputationer.

Av originalstudierna var fyra st RCT:er, däribland en studie som var dubbelblind randomiserad och där kontrollgruppen genomgick placebobehandling. Övriga studier var kohortstudier (med eller utan jämförelsegrupp) eller registerstudier. I den dubbelblindade placebokontrollerade RCT:n förelåg ingen skillnad mellan HBOT (inkl sedvanlig behandling) och patienter behandlade med sedvanlig behandling avseende sårläkning eller amputation. I en separat studie, men på samma patienter, kunde man inte heller finna någon skillnad mellan grupperna avseende hälsorelaterad QoL. I en öppen RCT rapporterades att tilläggsbehandling med HBOT kunde signifikant förbättra sårläkningen och minska amputationsfrekvensen. I ytterligare en öppen RCT kunde sårstorleken påverkas med HBOT som tilläggsbehandling (amputationsfrekvens inte rapporterad).

Resultaten från de övriga originalstudierna var blandade, med övervikt för att HBOT kunde positivt påverka sårläkning.

ORN: Två systematiska översikter och fyra originalarbeten identifierades. De två översikterna kom till olika slutsatser; den ena fann att HBOT kunde förebygga ORN och att symptomatiska besvär såsom exempelvis muntorrhet kunde framgångsrikt behandlas med HBOT. Den andra systematiska översikten fann inte att det förelåg någon evidens för att HBOT varken kunde förebygga eller behandla ORN.

I de fyra originalarbetena (ingen av dessa var RCT:er) konkluderade författarna att HBOT kunde, med vissa reservationer, ha positiva effekter.

Cystit/proktit: Efter det enkla sållningsförfarandet återstod åtta arbeten, tre var systematiska översikter och fem var originalarbeten varav en var en RCT. De systematiska översikterna fann att HBOT var en effektiv behandling vid cystit/proktit, i den ena översikten kommenterades att kostnaden för HBOT var hög och dess tillgänglighet låg.

I en oblindad RCT utan placebogrupp (nordisk multicenterstudie med utgångspunkt från Gbg) fann man att man kunde nå en signifikant förbättring med HBOT i ett självrapporterat scoring-system. I de övriga icke-RCT originalstudierna såg man även förbättringar med HBOT.

Pågående studier och studieprotokoll
En sökning av planerade och pågående studier har genomförts i Clinical Trials.

Avseende diabetesfotsår pågår en större prospektiv registerstudie som beräknas vara färdig i februari 2025: The Diabetic Foot Ulcer Registry (DFUR)
Länk till studieprotokollet: https://clinicaltrials.gov/ct2/show/study/NCT02813161

Beträffande cystit/proktit pågår en prospektiv icke-randomiserad pilotstudie som beräknas vara färdig i oktober 2020: Hyperbaric Oxygen Therapy for Inflammatory Conditions of the Urinary Bladder (HBOTCICrUTI)
Länk till studieprotokollet: https://clinicaltrials.gov/ct2/show/study/NCT03143920

I fråga om osteoradionekros har inga pågående studier identifierats.

Enkel analys

DFU: Rapporterade data är divergerande.

I majoriteten av de systematiska översikterna konkluderades att HBOT inte tillför något substantiellt för DFU-patienterna. I SoS nationella riktlinjer från 2018 avseende diabetes och svårläkta kroniska fotsår får HBOT rekommendationsgrad 9, dvs *kan i undantagsfall erbjudas.* I samma SoS publikation har en hälsoekonomisk utvärdering genomförts; denna konkluderade att: ”kostnaden för hyperbar syrgas bedöms vara omkring 90 000 kronor per patient i Sverige för en behandlingssession omfattande 40 tillfällen”.

Dock bör det framhållas att i Svensk Förening för Anestesi och Intensivvård från 2017 avges följande riktlinje: ”Patienter som är kärlutredda, rökfria och trots optimal glykemisk kontroll och sårvård, har refraktära, ischemiska, ofta infekterade sår bör remitteras till HBO-enhet för bedömning”.

I de nyligen publicerade originalarbetena utmärker sig den enda RCT:n som var designad med dubbelblind randomisering och placebobehandling. Resultaten visade (uppföljning: 3 m) att inget talade för att HBOT tillför något, vare sig för sårläkning eller amputations prevention (Fedorko et al, 2016).

ORN: Rapporterade data är motsägelsefulla.

Cystit/proktit: Inom detta sjukdomsområde förefaller det som om HBOT kan ha en plats i den terapeutiska arsenalen.

Ingen pågående RCT har identifierats i Clinical Trials för något av ämnesområdena ovan. I förhållande till sammanfattningarna från SBU Upplysningstjänst från oktober 2016 avseende DFU, cystit/proktit och ORN förefaller det inte som nya vetenskapliga data tillkommit som väsentligt förändrat kunskapsläget, mer än möjligen för ämnesområdet DFU där således en placebokontrollerad dubbelblind RCT publicerats.

För inget av de undersökta ämnesområdena har vi identifierat några studier vars värde är så potentiellt stort att man bör invänta deras svar.

Denna enkla analys, med reservationen att den inte är baserad på en fullständig HTA-rapport, gör att HTA Skåne slutsats blir att vi inte ser ett omedelbart behov att revidera Koncernkontorets yttrande från 2017.

Vidare har denna litteraturöversikt inte besvarat frågeställarens frågor kring hälsoekonomi vid HBOT eller HBOT-behandling vid akuta tillstånd. Orsaken till detta är att hälsoekonomiska aspekter är bortom vad denna enklare HTA-produkt erbjuder. Angående akut HBOT-behandling; inga sökningar har gjorts på de akuta tillstånden i det här skedet. HTA Skåne har tolkat frågeställarens ”akuta tillstånd” som akut dykarsjuka och akut kolmonoxidförgiftning. Vid dessa två tillstånd råder tydlig och klar vetenskap samt beprövad erfarenhet över HBOT:s terapeutiska plats, varför dessa frågeställningar lämnats därhän.

Om Metod- och Prioriteringsrådet är i behov av lokalt förankrad analys av hälsoekonomi, etiska och organisatoriska aspekter samt en fördjupad medicinsk (inkluderande akuta tillstånd samt övriga nya rön) analys rekommenderas en fullständig HTA-rapport.

För HTA Skåne
Jan Holst, HTA-handledare, docent och överläkare
Kristina Arnebrant, informationsspecialist
Ranka Steingrimsdottir, informationsspecialist

Appendix 1

Litteratursökning

Följande HTA-organisationers webbsidor genomsöktes:

- SBU – Statens beredning för medicinsk och social utvärdering
- HTA-centrum VGR – Västra Götalandsregionen
- Metodrådet SLL & Region Gotland
- CAMTÖ - Centrum för evidensbaserad medicin och utvärdering av medicinsk metodik, Region Örebro län
- Regionala metodrådet, Sydöstra sjukvårdsregionen
- DACEHTA, Danmark
- Folkehelseinstituttet, Norge
- FinOHTA, Finland
- CRD – Centre for Reviews and Dissemination, University of York, UK
- CADTH – Canadian Agency for Drugs and Technologies in Health, Canada
- NICE - National Institute for Health and Care Excellence, UK

Sökningar gjordes - utifrån sökstrategierna i de tre svaren fån SBU:s Upplysningstjänst - i databaserna Medline och PubMed. Sökningar gjordes även i Cochrane Library. Vidare gjordes en sökning efter pågående studier i Clinicaltrials.gov.

Söktermer:
”Hyperbaric Oxygenation” [MeSH], ”Oxygen/therapeutic use” [MeSH], hyperbaric oxygenation, hyperbaric oxygen, HBO therapy, Oxygen therapy, Topical oxygen

”Diabetic Foot” [MeSH], ”Leg Ulcer” [MeSH], ”Diabetes Mellitus” [MeSH], diabetic feet, diabetes, diabetic, leg ulcer, foot ulcer, lower extremity ulcer*, chronic wound, chronic ulcer*

”Proctitis” [MeSH], ”Cystitis” [MeSH], proctitis, cystitis, pelvis, tissue injur*, ”Pelvis/injuries” [MeSH], ”Radiation injuries” [MeSH], radiation injury, irradiat*, radiation, radiotherap*

“Osteoradionecrosis” [MeSH], late radiation tissue injury, osteonecrosis, bone necrosis, radiation injury, irradiat*, radiation, radiotherap*

Appendix 2

Riktlinjer & rekommendationer

Nationella riktlinjer

Titel: Nationella riktlinjer för diabetesvård
Avsändare: Socialstyrelsen
Datum: 2018-10-25
Länk: https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/nationella-riktlinjer/2018-10-25.pdf
Tillstånd som omfattas: diabetesfotsår
Ur innehållet:

s. 111

Rad	Tillstånd och åtgärd	Motivering till rekommendation	Rekommendation
E34	Diabetes och kroniska svårläkta fotsår Behandling med hyperbar syrgas	Avgörande för rekommendationen är att underlaget är otillräckligt för avgörande effektmått (amputation). Åtgärdens effekt på sårläkning och att tillståndet har stor svårighetsgrad motiverar rangordning. Kommentar: Det finns en osäkerhet om kostnadseffektiviteten. En detaljerad kostnadssammanställning är svår då resursförbrukning beror på många faktorer såsom sårets ursprungliga skick, graden av infektion och personalens erfarenhet och kompetens. Kostnaden för hyperbar syrgas bedöms vara omkring 90 000 kronor per patient i Sverige för en behandlingssession omfattande 40 tillfällen.	9

Titel: Clinical Commissioning Policy: Hyperbaric oxygen therapy for diabetic lower limb ulceration (diabetic foot ulcer) (all ages)
Avsändare: NHS (National Health Service), England
Datum: 2019-04-12
Länk: https://www.england.nhs.uk/wp-content/uploads/2019/04/Hyperbaric-oxygen-therapy-for-diabetic-lower-limb-ulceration-all-ages.pdf
Tillstånd som omfattas: diabetesfotsår
Ur innehållet:
p. 5
"**Policy Statement**
NHS England will not routinely commission hyperbaric oxygen therapy for diabetic lower limb ulceration in accordance with the criteria outlined in this document."
p. 6
"**About the treatment**
In addition to the standard care for diabetic foot ulcer, Hyperbaric oxygen therapy (HBOT) has been suggested as a potential additional therapy in cases where the normal treatment has failed to heal the wound. HBOT involves the inhalation of pure oxygen at a pressure higher than normal atmospheric pressure, usually 2 to 3 atmospheres absolute (ATA). During HBOT, the patient is in a pressure chamber, and when used for the treatment of diabetic foot ulcers, this is usually for 45 to 120 minutes on most days for several weeks.
What we have decided
NHS England has carefully reviewed the evidence to treat diabetic lower limb ulceration with hyperbaric oxygen therapy. We have concluded that there is not enough evidence to make the treatment available at this time."

Titel: HSE National Wound Management Guidelines 2018

Avsändare: HSE (Health Service Executive), Irland
Datum: 2018
Länk: https://www.hse.ie/eng/services/publications/nursingmidwifery%20services/wound-management-guidelines-2018.pdf
Tillstånd som omfattas: diabetesfotsår
Ur innehållet:
p. 79
"Clinical Question 39: What is the recommendation for the use of hyperbaric oxygen therapy (HBOT) in the management of wounds?"
"**Evidence Statement**
A Cochrane Review "Hyperbaric oxygen therapy for chronic wounds" (Kranke et al., 2015) addressed this question.
This review included 12 trials (n=577) and the authors concluded that in people with diabetic foot ulcers, HBOT significantly improved the ulcer healing in the short term. More trials are needed to properly evaluate HBOT in people with chronic wounds. These trials must be adequately powered and designed to minimise bias.
Recommendations
39.1 Hyperbaric oxygen therapy should be considered for patients with chronic wounds and used in combination with conventional wound treatments. Application is dependent on availability, suitability and based on comprehensive patient and wound assessment.
HSE Recommendation Evidence Grade: A"
p.110
"Clinical Question 62: What interventions enhance the healing of chronic ulcers of the foot in diabetes?"
"**Evidence Statement**
A Cochrane Review (Wu et al., 2015) "Dressings for treating foot ulcers in people with diabetes: an overview of systematic reviews" addressed this question. In total this review found 13 eligible systematic reviews relevant pertaining to this topic, which contained a total of 17 relevant RCTs. The authors concluded that there is currently no robust evidence for differences between wound dressings for any outcome in foot ulcers in people with diabetes (treated in any setting) and that practitioners may want to consider the unit cost of dressings, their management properties and patient preference when choosing dressings.
Recommendation"
(…) […]
62.4 Consider the use of systemic hyperbaric oxygen therapy, even though further blinded and randomised trials are required to confirm its cost-effectiveness and to identify the population most likely to benefit from its use. HSE Recommendation Evidence Grade: C"

Riktlinjer från professionen

Titel: SFAI riktlinje hyperbar oxygenbehandling 171204
Avsändare: SFAI **(**Svensk Förening för Anestesi och Intensivvård)
Datum: 171204
Länk: https://sfai.se/riktlinje/medicinska-rad-och-riktlinjer/intensivvard/sfai-riktlinje-hyperbar-oxygenbehandling-171204/
Tillstånd som omfattas: diabetesfotsår, osteoradionekros, cystit/proktit
Ur innehållet:
"BÖR remitteras till HBO-behandling"
"Fotsår hos diabetiker
Vid diabetes utvecklas ofta kärlkomplikationer, i stora (makroangiopati) såväl som små (mikroangiopati) kärl. Mikroangiopati leder till en dålig vävnadsperfusion och hypoxi, vilket medför försämrat immunförsvar och sårläkning. Studier har visat att HBO kan accelerera sårläkning via kapillärnybildning och immunomodulerande mekanismer. Efter 30–40 behandlingar får man en kvarstående förbättring av sårläkningen som kan fortsätta även efter avslutad behandlingsserie.

Patienter som är kärlutredda, rökfria och trots optimal glykemisk kontroll och sårvård, har refraktära, ischemiska, ofta infekterade sår bör remitteras till HBOenhet för bedömning. Behandlingstabell/protokoll: 2,4 - 2,5 bar, ca 100 min, vanligen behandlingsserier om 30–40 behandlingar."

"BÖR remitteras till HBO-behandling"

"Skador i mjukdelsvävnad efter strålbehandling Kronisk strålskada (duration >6mån) i mjukdelar orsakas av strålningsinducerad inflammation som med tiden leder till fibros. Hypoxiska biverkningar med vävnadssönderfall, svårläkta fibrotiska sår, irritation och/eller blödningar ses ibland månader till år efter avslutad strålbehandling av cancer. Vanliga lokalisationer är urinblåsa (strålcystit) och ändtarm (strålproktit) men även mjukdelar som svalg (laryngit) och bröst (mastit) kan drabbas.
Patienter med kroniskt strålskadad vävnad bör remitteras till HBO-enhet för bedömning. Behandlingstabell/protokoll: 2,4 - 2,5 bar, ca 100 min, vanligen behandlingsserier om 30–40 behandlingar"

"KAN remitteras till HBO-behandling"

"Osteoradionekros (ORN)
Osteoradionekros definieras som ett benområde (ex i mandibeln) som inte läker inom 2 mån efter strålterapi utan tecken på tumörrecidiv.
HBO-behandling kan ges vid manifest sjukdom eller som profylax vid tandextraktion eller kirurgi.
Behandlingstabell/protokoll: 2,4 - 2,5 bar, ca 100 min, vanligen behandlingsserier om 30-40 behandlingar."

Titel: Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment.
Avsändare: Daniel Mathieu, Alessandro Marroni, Jacek Kot
Datum: 2017-03
Länk: http://www.echm.org/documents/DHM%202017-Mathieu%20D-Tenth%20European%20Consensus%20Conference%20on%20Hyperbaric%20Medicine.pdf
Tillstånd som omfattas: diabetesfotsår, osteoradionekros, cystit/proktit
Ur innehållet:

"Abstract
The tenth European Consensus Conference on Hyperbaric Medicine took place in April 2016, attended by a large delegation of experts from Europe and elsewhere. The focus of the meeting was the revision of the European Committee on Hyperbaric Medicine (ECHM) list of accepted indications for hyperbaric oxygen treatment (HBOT), based on a thorough review of the best available research and evidence-based medicine (EBM). For this scope, the modified GRADE system for evidence analysis, together with the DELPHI system for consensus evaluation, were adopted. The indications for HBOT, including those promulgated by the ECHM previously, were analysed by selected experts, based on an extensive review of the literature and of the available EBM studies. The indications were divided as follows: Type 1, where HBOT is strongly indicated as a primary treatment method, as it is supported by sufficiently strong evidence; Type 2, where HBOT is suggested as it is supported by acceptable levels of evidence; Type 3, where HBOT can be considered as a possible/optional measure, but it is not yet supported by sufficiently strong evidence. For each type, three levels of evidence were considered: A, when the number of randomised controlled trials (RCTs) is considered sufficient; B, when there are some RCTs in favour of the indication and there is ample expert consensus; C, when the conditions do not allow for proper RCTs but there is ample and international expert consensus. For the first time, the conference also issued 'negative' recommendations for those conditions where there is Type 1 evidence that HBOT is not indicated. The conference also gave consensus-agreed recommendations for the standard of practice of HBOT."
p. 28

“We recommend HBOT in the treatment of haemorrhagic radiation cystitis (Type 1 recommendation, Level B evidence).”
“We recommend HBOT in the treatment of radiation proctitis (Type 1 recommendation, Level A evidence).”
“We recommend HBOT in the treatment of mandibular osteoradionecrosis (Type 1 recommendation, Level B evidence).”
p. 29
“We suggest using HBOT in the treatment of diabetic foot lesions (Type 2 recommendation, Level B evidence).”
“We recommend HBOT in ischaemic lesions (ulcers or gangrene) without surgically treatable arterial lesions or after vascular surgery:
a. In the diabetic patient, the use of HBOT is recommended in the presence of a chronic critical ischaemia as defined by the European Consensus Conference on Critical Ischemia (see note below), if TCOM readings under hyperbaric conditions (253 kPa, 100% oxygen) are higher than 100 mmHg (Type 1 recommendation, level A evidence).
b. In the arteriosclerotic patient, HBOT is recommended in case of a chronic critical ischaemia (see note below), if TCOM readings under hyperbaric conditions (253 kPa, 100% oxygen) are higher than 50 mmHg (Type 2 recommendation, Level B evidence).
c. Note: Chronic critical ischaemia can be recognised when there is: periodic pain, persistent at rest, needing regular analgesic treatment for more than two weeks, or ulceration or gangrene of foot or toes with ankle systolic pressure < 30 mmHg in the diabetic.11
d. However, despite the strong agreement on the validity of the criteria listed above to properly select patients for HBOT, the jury acknowledges the fact not all hyperbaric centres are able to perform TCOM under hyperbaric conditions (253 kPa, 100% oxygen). Therefore, owing to this limitation, we suggest HBOT in diabetic foot ulcers (grade 3 and above of Wagner classification, stage B, grade 3 and above of University of Texas classification) that have failed to respond to adequate basic wound care after four weeks (Type 2 recommendation, Level B evidence).
• For the same reason as above, it would be reasonable to use HBOT in delayed-healing (chronic), nondiabetic wounds and in recurrent, multiple non-healing wounds due to vasculitis (especially those who have not responded to immunosuppressive therapy) (Type 3 recommendation, Level C evidence).”

Appendix 3

Artiklar publicerade från och med 2016
(som inte ingår i svaren från SBU:s Upplysningstjänst)

TRYCKKAMMARBEHANDLING VID DFU:

Andrade, S. M. d. and I. C. R. V. Santos (2016). **Hyperbaric oxygen therapy for wound care.** Oxigenoterapia hiperbarica para tratamento de feridas. 37(2): e59257.

> OBJECTIVE: To describe the most common types of wounds indicated for hyperbaric oxygen therapy and the results., METHOD: Cross-sectional study at a Hyperbaric Centre in the city of Salvador, Bahia, Brazil. The medical records of 200 patients treated with hyperbaric oxygen were reviewed from January to November 2013. The variables of the persons, clinical, indications, number of sessions and wound care were analysed by means of descriptive statistics and the chi-square test of association incorporating Yates's correction with a level of 5%., RESULTS: The wounds that were most frequently indicated for hyperbaric oxygen therapy were venous ulcers, traumatic injury and diabetic foot. Patients with chronic wounds had fewer sessions (61.1%) and their wounds healed or were reduced (62.0%) compared to those with acute wounds., CONCLUSION: Hyperbaric oxygen therapy is an effective treatment for patients with chronic wounds.

Chen, C.-Y., et al. (2017). **Adjunctive Hyperbaric Oxygen Therapy for Healing of Chronic Diabetic Foot Ulcers:**

A Randomized Controlled Trial. Journal of wound, ostomy, and continence nursing: official publication of The Wound, Ostomy and Continence Nurses Society 44(6): 536-545.

PURPOSE: The purpose of this study was to compare the effect of standard wound care with adjunctive hyperbaric oxygen therapy (HBOT) to standard wound care alone on wound healing, markers of inflammation, glycemic control, amputation rate, survival rate of tissue, and health-related quality of life in patients with diabetic foot ulcers (DFUs)., DESIGN: Prospective, randomized, open-label, controlled study., SUBJECTS AND SETTING: The sample comprised 38 patients with nonhealing DFUs who were deemed poor candidates for vascular surgery. Subjects were randomly allocated to an experimental group (standard care plus HBOT, n = 20) or a control group (standard care alone, n = 18). The study setting was a medical center in Kaohsiung City, Taiwan., METHODS: Hyperbaric oxygen therapy was administered in a hyperbaric chamber under 2.5 absolute atmospheric pressure for 120 minutes; subjects were treated 5 days a week for 4 consecutive weeks. Both groups received standard wound care including debridement of necrotic tissue, topical therapy for Wagner grade 2 DFUs, dietary control and pharmacotherapy to maintain optimal blood glucose levels. Wound physiological indices were measured and blood tests (eg, markers of inflammation) were undertaken. Health-related quality of life was measured using the Medical Outcomes Study 36-Item Short Form., RESULTS: Complete DFU closure was achieved in 5 patients (25%) in the HBOT group (n = 20) versus 1 participant (5.5%) in the routine care group (n = 18) (P = .001). The amputation rate was 5% for the HBOT group and 11% for the routine care group (chi = 15.204, P = .010). The HBOT group showed statistically significant improvements in inflammation index, blood flow, and health-related quality of life from pretreatment to 2 weeks after the last therapy ended (P < .05). Hemoglobin A1c was significantly lower in the HBOT group following treatment (P < .05) but not in the routine care group., CONCLUSIONS: Adjunctive HBOT improved wound healing in persons with DFU. Therapy also reduced the risk of amputation of the affected limb. We assert that at least 20 HBOT sessions are required to be effective.

Eggert, J. V., et al. (2016). **Cost and mortality data of a regional limb salvage and hyperbaric medicine program for Wagner Grade 3 or 4 diabetic foot ulcers.** Undersea & hyperbaric medicine : journal of the Undersea and Hyperbaric Medical Society, Inc 43(1): 1-8.

We obtained costs and mortality data in two retrospective cohorts totaling 159 patients who have diabetes mellitus and onset of a diabetic foot ulcer (DFU). Data were collected from 2005 to 2013, with a follow-up period through September 30, 2014. A total of 106 patients entered an evidence-based limb salvage protocol (LSP) for Wagner Grade 3 or 4 (WG3/4) DFU and intention-to-treat adjunctive hyperbaric oxygen (HBO2) therapy. A second cohort of 53 patients had a primary lower extremity amputation (LEA), either below the knee (BKA) or above the knee (AKA) and were not part of the LSP. Ninety-six of 106 patients completed the LSP/HBO2with an average cost of USD $33,100. Eighty-eight of 96 patients (91.7%) who completed the LSP/HBO2had intact lower extremities at one year. Thirty-four of the 96 patients (35.4%) died during the follow-up period. Costs for a historical cohort of 53 patients having a primary major LEA range from USD $66,300 to USD $73,000. Twenty-five of the 53 patients (47.2%) died. The difference in cost of care and mortality between an LSP with adjunctive HBO2therapy vs. primary LEA is staggering. We conclude that an aggressive limb salvage program that includes HBO2 therapy is cost-effective.

Elraiyah, T., et al. (2016). **A systematic review and meta-analysis of adjunctive therapies in diabetic foot ulcers.** Journal of vascular surgery 63(2 Suppl): 46S-42.

BACKGROUND: Multiple adjunctive therapies have been proposed to accelerate wound healing in patients with diabetes and foot ulcers. The aim of this systematic review is to summarize the best available evidence supporting the use of hyperbaric oxygen therapy (HBOT), arterial pump devices, and pharmacologic agents (pentoxifylline, cilostazol, and iloprost) in this setting., METHODS: We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Web of Science, and Scopus through October 2011. Pairs of independent reviewers selected studies and extracted data. Predefined outcomes of interest were complete wound healing and amputation., RESULTS: We identified 18 interventional studies; of which 9 were randomized, enrolling 1526 patients. The risk of bias in the included studies was moderate. In multiple randomized trials, the addition of HBOT to conventional therapy (wound care and offloading) was associated with increased healing rate (Peto odds ratio, 14.25; 95% confidence interval, 7.08-28.68) and reduced major amputation rate (odds ratio, 0.30; 95% confidence interval, 0.10-0.89), compared with conventional therapy alone. In one small trial, arterial pump devices had a favorable effect on complete healing compared with HBOT and in another small trial compared with placebo devices. Neither iloprost nor pentoxifylline had a significant effect on amputation rate compared with

conventional therapy. No comparative studies were identified for cilostazol in diabetic foot ulcers., CONCLUSIONS: There is low- to moderate-quality evidence supporting the use of HBOT as an adjunctive therapy to enhance diabetic foot ulcer healing and potentially prevent amputation. However, there are only sparse data regarding the efficacy of arterial pump devices and pharmacologic interventions.

Ennis, W. J., et al. (2018). **Impact of Hyperbaric Oxygen on More Advanced Wagner Grades 3 and 4 Diabetic Foot Ulcers: Matching Therapy to Specific Wound Conditions.** Advances in wound care 7(12): 397-407.

Objective: The goal of this research was to identify a population of diabetic foot ulcer patients who demonstrate a significant response to hyperbaric oxygen therapy (HBOT) using a large sample size to provide guidance for clinicians when treating these complicated patients. Approach: The effect of HBOT on diabetic foot ulcers, Wagner grades 3 and 4, was evaluated using a retrospective observational real-world data set. The study reported on the overall healing rate, (74.2%) at the population level, for >2 million wounds. Results: When a subgroup of patients of only foot ulcers with a Wagner grade 3 or 4 were considered, the healing rate was only 56.04%. The use of HBOT, without filtering for the number of treatments received, improved the healing rate to 60.01% overall. Healing rates for this same subgroup, however, were improved to 75.24% for patients who completed the prescribed number of hyperbaric treatments. Innovation: This observational study discusses the importance of reporting at the population level, specific wound etiology level, a risk-stratified level, and to then overlay the effect of treatment adherence on those outcomes to provide clinicians with a comprehensive understanding of when to prescribe an advanced modality such as hyperbaric oxygen. Conclusion: The authors provide healing outcomes data from several prior HBOT studies as well as other advanced modalities that have been used in diabetic foot ulcer care for comparison and context.

Erdogan, A., et al. (2018). **Efficacy of Hyperbaric Oxygen Therapy in Diabetic Foot Ulcers Based on Wagner Classification.** The Journal of foot and ankle surgery: official publication of the American College of Foot and Ankle Surgeons 57(6): 1115-1119.

Diabetic foot ulcer is a common chronic complication of diabetes mellitus. In addition to conventional primary therapy, there are adjuvant therapy methods such as hyperbaric oxygen therapy for the healing of diabetic foot ulcer wounds. The present study aimed to determine the efficacy of hyperbaric oxygen therapy in diabetic foot ulcers based on Wagner classification. It was performed retrospectively from prospectively collected data. One hundred thirty patients with diabetic foot ulcers were assessed in 2 groups: 1 group received hyperbaric oxygen therapy; the other group did not. Patients were examined according to age, sex, ulcer grade based on Wagner classification; ulcer healing status; whether hyperbaric oxygen therapy was received; duration of diabetes in years; HbA1C, sedimentation, C-reactive protein levels; and presence of accompanying diseases, including peripheral arterial disease, chronic obstructive pulmonary disease, hypertension, chronic kidney disease, neuropathy, and retinopathy. The mean follow-up period was 19.5+/-4.45 months (range 12 to 28 months). Seventy-one (54.6%) patients received hyperbaric oxygen therapy, and 59 (45.4%) patients did not. All patients in Wagner grade 2 healed in both groups. In the group that received hyperbaric oxygen therapy for grade 3 and 4 patients, 35 (87.5%) and 11 (84.6%) healed, respectively. In total, 60 (84.5%) patients in the group that received hyperbaric oxygen therapy healed. The subgroup comparison conducted according to Wagner classification revealed no differences between the 2 groups of grades 2 and 5 patients. It also revealed that treatment had higher levels of efficacy in the healing of ulcers in grade 3 and 4 patients.

Fedorko, L., et al. (2016). **Hyperbaric Oxygen Therapy Does Not Reduce Indications for Amputation in Patients With Diabetes With Nonhealing Ulcers of the Lower Limb: A Prospective, Double-Blind, Randomized Controlled Clinical Trial.** Diabetes care 39(3): 392-399.

OBJECTIVE: Hyperbaric oxygen therapy (HBOT) is used for the treatment of chronic diabetic foot ulcers (DFUs). The controlled evidence for the efficacy of this treatment is limited. The goal of this study was to assess the efficacy of HBOT in reducing the need for major amputation and improving wound healing in patients with diabetes and chronic DFUs., RESEARCH DESIGN AND METHODS: Patients with diabetes and foot lesions (Wagner grade 2-4) of at least 4 weeks' duration participated in this study. In addition to comprehensive wound care, participants were randomly assigned to receive 30 daily sessions of 90 min of HBOT (breathing oxygen at 244 kPa) or sham (breathing air at 125 kPa). Patients, physicians, and researchers were blinded to group assignment. At 12 weeks postrandomization, the primary outcome was freedom from meeting the criteria for amputation as assessed by a vascular surgeon. Secondary

outcomes were measures of wound healing., RESULTS: One hundred fifty-seven patients were assessed for eligibility, with 107 randomly assigned and 103 available for end point adjudication. Criteria for major amputation were met in 13 of 54 patients in the sham group and 11 of 49 in the HBOT group (odds ratio 0.91 [95% CI 0.37, 2.28], P = 0.846). Twelve (22%) patients in the sham group and 10 (20%) in the HBOT group were healed (0.90 [0.35, 2.31], P = 0.823). All other indices of wound healing were also not statistically significantly different between groups., CONCLUSIONS: HBOT does not offer an additional advantage to comprehensive wound care in reducing the indication for amputation or facilitating wound healing in patients with chronic DFUs. Copyright © 2016 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered.

Game, F. L., et al. (2016). **Effectiveness of interventions to enhance healing of chronic ulcers of the foot in diabetes: a systematic review.** Diabetes/metabolism research and reviews 32 Suppl 1: 154-168.

The outcome of management of diabetic foot ulcers remains a challenge, and there remains continuing uncertainty concerning optimal approaches to management. It is for these reasons that in 2008 and 2012, the International Working Group of the Diabetic Foot (IWGDF) working group on wound healing published systematic reviews of the evidence to inform protocols for routine care and to highlight areas, which should be considered for further study. The same working group has now updated this review by considering papers on the interventions to improve the healing of chronic ulcers published between June 2010 and June 2014. Methodological quality of selected studies was independently assessed by two reviewers using Scottish Intercollegiate Guidelines Network criteria. Selected studies fell into the following ten categories: sharp debridement and wound bed preparation with larvae or hydrotherapy; wound bed preparation using antiseptics, applications and dressing products; resection of the chronic wound; oxygen and other gases, compression or negative pressure therapy; products designed to correct aspects of wound biochemistry and cell biology associated with impaired wound healing; application of cells, including platelets and stem cells; bioengineered skin and skin grafts; electrical, electromagnetic, lasers, shockwaves and ultrasound and other systemic therapies, which did not fit in the aforementioned categories. Heterogeneity of studies prevented pooled analysis of results. Of the 2161 papers identified, 30 were selected for grading following full text review. The present report is an update of the earlier IWGDF systematic reviews, and the conclusion is similar: that with the possible exception of negative pressure wound therapy in post-operative wounds, there is little published evidence to justify the use of newer therapies. Analysis of the evidence continues to present difficulties in this field as controlled studies remain few and the majority continue to be of poor methodological quality. Copyright © 2015 John Wiley & Sons, Ltd.

Jagadish, M., et al. (2016). **Diabetic Foot Ulcers: The Importance of Patient Comorbidity Recognition and Total Contact Casting in Successful Wound Care.** The American surgeon 82(8): 733-736.

Diabetic foot ulcers (DFUs) are a major burden on the health-care system. The purpose of this study is to investigate factors affecting the healing rate of DFU in a university wound care center. Records of DFU patients treated between July 2013 and February 2015 were reviewed. Demographics, comorbidities, wound characteristics, and treatment modalities including offloading, hyperbaric oxygen treatment, total contact casting, and bioengineered skin were investigated. All patients underwent weekly debridement regardless of treatment modality. A total of 114 patients ages 18 to 98 comprised the study population. Total contact casting was the only treatment associated with increased healing (P = 0.02). Smoking (P = 0.004) and deep vein thrombosis history (P = 0.001) significantly decreased the likelihood of wound healing. Patients with past vascular event trended toward longer healing times (P = 0.07). Total contact casting in combination with weekly wound debridement showed benefit in DFU wound healing, whereas patients with a history of deep vein thrombosis and smoking were less likely to heal.

Kaplan, S. T., et al. (2017). **Amputation predictors in diabetic foot ulcers treated with hyperbaric oxygen.** Journal of wound care 26(7): 361-366.

OBJECTIVE: Although hyperbaric oxygen therapy (HBOT) has long been used for diabetic foot ulcers (DFUs), its effectiveness is still controversial. The aim of this study was to investigate the efficacy of HBOT in the management of DFUs and identify amputation predictors., METHOD: Patients with chronic DFUs (Wanger grade 2-5) were included in the study, which took place between January 2010 and December 2012. HBOT, 100% oxygen, 2.4 atmosphere absolute (ATA) for 120 minutes, was administered to all patients in addition to standard treatment. DFUs were monitored for at least 3 years, or until healing or amputation occurred., RESULTS: Patients with a total of 146 chronic DFUswere recruited. Complete

healing (69.6%) and significant improvement (17.9%) was observed in 87.5% of the patients. The cases with no improvement resulted in amputation (minor amputation: 15.0%; major amputation: 8.2%). The duration of diabetes (p=0.037), new wound formation (p=0.045), C-reactive protein (p=0.001) and Wagner grade (p=0.0001) were correlated with amputation in multiple regression analysis. Mortality was higher in the amputation group than in the non-amputation group (47.1 % versus 21.4 %, p=0.007)., CONCLUSION: The inclusion of HBOT with standard treatment and a multidisciplinary approach may be useful in the treatment of DFUs. We found the most important predictors of amputation to be Wagner grade and wound infection. Multicentre, prospective, randomised studies are needed to provide more evidence.

Katz, D. E., et al. (2016). **Diabetic foot infection in hospitalized adults.** Journal of infection and chemotherapy: official journal of the Japan Society of Chemotherapy 22(3): 167-173.

BACKGROUND: Acute infections of the diabetic foot (DFI) are a common and complex condition. Patients are generally managed in the ambulatory setting and epidemiological data pertaining to hospitalized patients is lacking. The aim of this study was to analyze the epidemiology, microbiology and outcomes of hospitalized patients with DFI, who are managed at a referral center equipped with hyperbaric oxygen (HBO) therapy., METHODS: A retrospective cohort study of adult patients admitted to a tertiary referral center with DFI over a six-month period in 2013 was undertaken. Predictors of clinical outcomes and efficacy of treatment modalities were analyzed by Cox regression., RESULTS: Sixty-one patients with DFI were identified. Most patients were elderly (67 +/- 13 years), with long-standing (17 +/- 9 years), poorly controlled (HbA1c 9 +/- 3%) diabetes. Most patients had polymicrobial infection (80%); specifically, anaerobic (39%) and multi or extensively-drug resistant organisms (61%). Administration of appropriate antimicrobials was delayed for >48 h in 83%. Advanced age was associated with worse outcomes. Sicker patients with severe peripheral vascular disease were managed with HBO. The use of HBO was associated with higher costs and increased functional deterioration, and did not prevent future limb amputation., CONCLUSIONS: Our study illustrates the descriptive epidemiology of hospitalized adults with DFI predominantly of polymicrobial etiology. MDROs and anaerobic organisms are common causative pathogens, and appropriate antibiotics were frequently delayed. HBO treatment may delay the need for limb amputation, but not obviate this eventual outcome. Copyright © 2015 Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

Kawecki, M., et al. (2018). **Computerized planimetry evaluation of hyperbaric oxygen therapy in the treatment of diabetic foot.** Advances in clinical and experimental medicine: official organ Wroclaw Medical University 27(1): 39-44.

BACKGROUND: Diabetic foot ulcer is one of the major complications of diabetes mellitus in adults., OBJECTIVES: The aim of the study was to conduct a planimetry evaluation of the effectiveness of hyperbaric oxygen therapy (HBOT) in the treatment of patients with vascular disorders caused by diabetic foot., MATERIAL AND METHODS: The study included 94 patients, 30 females (32%) and 64 males (68%), aged 33-76 years, with diabetes lasting 1.5-32 years, who underwent HBOT due to diabetic foot. All patients from that group underwent vascular procedures prior to HBOT. In qualifying patients for hyperbaric oxygen therapy, transcutaneous oximetry method was applied (30-60 exposures in hyperbaric oxygen at pressure of 2.5 ATA). Progress in wound healing was evaluated by computerized planimetry system IRIS 4., RESULTS: In 26 patients the wounds were completely closed and in 37 patients the topical state was significantly improved - the wound surface decreased by 34% in average. During the treatment, in 11 patients amputation of fingers and metatarsal necrotic bones was performed, while in 9 patients amputation was prevented., CONCLUSIONS: A planimetry evaluation showed that the application of HBOT in the treatment of diabetic foot enhances foot ulcer healing, reduces tissue damage, contributes to the reduction of complications related to soft tissue and bone infections.

Lalieu, R. C., et al. (2019). **Hyperbaric Oxygen Therapy for Non-Ischemic Diabetic Ulcers: A Systematic Review.** Wound repair and regeneration: official publication of the Wound Healing Society [and] the European Tissue Repair Society.

Diabetic foot ulcers are a common complication of diabetes, which affects 25% of patients and may ultimately lead to amputation of affected limbs. Research suggests hyperbaric oxygen therapy improves healing of these ulcers. However, this has not been reflected in previous reviews, possibly because they did not differentiate between patients with and without peripheral arterial occlusive disease. Therefore, we performed a systematic review of published literature in the MEDLINE, Embase and Cochrane

CENTRAL databases on non-ischemic diabetic foot ulcers with outcome measures including complete ulcer healing, amputation rate (major and minor) and mortality. Seven studies were included, of which two were randomized clinical trials. Two studies found no difference in major amputation rate, whereas one large retrospective study found 2% more major amputations in the hyperbaric oxygen group. However, this study did not correct for baseline differences. Two studies showed no significant difference in minor amputation rate. Five studies reporting on complete wound healing showed no significant differences. In conclusion, the current evidence suggests that hyperbaric oxygen therapy does not accelerate wound healing and does not prevent major or minor amputations in patients with a diabetic foot ulcer without peripheral arterial occlusive disease. Based on the available evidence, routine clinical use of this therapy cannot be recommended. However, the available research for this specific subgroup of patients is scarce, and physicians should counsel patients on expected risks and benefits. Additional research, focusing especially on patient selection criteria, is needed to better identify patients that might profit from this therapy modality. This article is protected by copyright. All rights reserved. Copyright This article is protected by copyright. All rights reserved.

Li, G., et al. (2017). **Relationship between hyperbaric oxygen therapy and quality of life in participants with chronic diabetic foot ulcers: data from a randomized controlled trial.** Acta diabetologica 54(9): 823-831.

AIMS: To investigate the effect of hyperbaric oxygen therapy on health-related quality of life (HRQoL) in participants with diabetes and chronic foot ulcers., METHODS: Using data from a randomized controlled trial, we included 103 participants (49 in hyperbaric oxygen therapy group and 54 in sham group) for analyses. The primary outcome was HRQoL as measured by the EQ-5D-3L instrument, while secondary outcomes included quality of life evaluated by the Short Form 36 (SF-36) and Diabetic Foot Ulcers Scale-Short Form (DFS-SF). We used the analysis of covariance to assess whether the EQ-5D index values in hyperbaric oxygen therapy group differed from the sham group. Logistic regression was used to assess the relationship between hyperbaric oxygen therapy and the responses of 'problems' for the EQ-5D health states., RESULTS: No significant differences in EQ-5D index values were found between the hyperbaric oxygen therapy and sham groups: 0.01 (95% CI -0.25, 0.28; p = 0.93) at week 12; 0.07 (95% CI -0.21, 0.34; p = 0.64) at week 6. Hyperbaric oxygen therapy was found to be associated with fewer participants reporting 'problems' in mobility (OR 0.24, 95% CI 0.07, 0.85 at week 12) and pain or discomfort (OR 0.20, 95% CI 0.07, 0.61 at week 6; OR 0.32, 95% CI 0.11, 0.97 at week 12), compared with the sham group. No significant differences in SF-36 or DFS-SF were observed., CONCLUSIONS: No significant effect of hyperbaric oxygen therapy on HRQoL measured by EQ-5D index value was found in this study. Due to the potential insufficient power to assess statistical difference, more large-scale research is needed to further evaluate the effect of hyperbaric oxygen therapy on HRQoL in participants with chronic diabetic foot ulcers.

Nik Hisamuddin, N. A. R., et al. (2019). **Use of hyperbaric oxygen therapy (HBOT) in chronic diabetic wound - A randomised trial.** The Medical journal of Malaysia 74(5): 418-424.

INTRODUCTION: The purpose of this study was to investigate the effect of hyperbaric oxygen therapy (HBOT) towards diabetic foot ulcer (DFU) patients in addition to the standard wound care management., METHODS: Fifty-eight diabetic patients with ulcers at Wagner Grade 2 and above involved in this study after presented at two study centres of tertiary teaching hospitals. The assigned patients received conventional wound care with additional HBOT given at 2.4 ATA for 90 minutes. Patients in the control group who received conventional wound care only were treated and observed for 30 days. The progress of wound healing was observed and measured at day 0, 10, 20 and 30 of study. The data collected were analysed using SPSS software (ver. 22) to study the association of HBOT towards healing of the diabetic foot ulcers., RESULTS: Repeated Measures ANOVA analysis with Greenhouse-Geisser correction indicated that the means of wound size over time points (Day 0, 10, 20 and 30) among patients under HBOT group were statistically significantly different [$F(1,61)=30.86$, $p<0.001$)] compared to conventional therapy group. Multiple logistic regression analysis showed that HBOT group has nearly 44 times higher odds to achieve at least 30% wound size reduction within the study period (95%CI: 7.18, 268.97, $p<0.001$)., CONCLUSION: The results obtained in this study indicated that as an adjunctive therapy to conventional wound care, HBOT affected the rate of healing in diabetic foot ulcers significantly in terms of wound size reduction when compared to administering the conventional wound care alone.

Perren, S., et al. (2018). **Hyperbaric Oxygen Therapy in Ischaemic Foot Ulcers in Type 2 Diabetes: A Clinical Trial.** The open cardiovascular medicine journal 12: 80-85.

Background and Aims: Several treatment modalities and protocols for ischaemic foot ulcers are available.

However, little consensus exists on optimal treatment. The aim of this study was to compare Standard Wound Care (SWC) alone vs. SWC with adjunct hyperbaric oxygen therapy (HBOT) in the treatment of ischaemic Diabetic Foot Ulcers (DFUs)., Patients and Methods: Twenty-six patients with Type 2 Diabetes Mellitus (T2DM) presenting with a newly diagnosed ischaemic foot ulcer were included. These were divided into group A (SWC with adjunct HBOT) and group B (SWC only). Participants were followed every week for 4 weeks and their ulcers were measured for their surface area and depth to assess any change in wound size., Results: Both treatment arms succeeded in reducing ulcer area and depth ($p<0.001$). However, ulcer area ($p<0.001$) and depth ($p<0.001$) exhibited superior improvement in group A., Conclusion: Adjunctive HBOT appears to improve wound healing in ischaemic DFUs and merits further study.

Salama, S. E., et al. (2019). **Adjuvant Hyperbaric Oxygen Therapy Enhances Healing of Nonischemic Diabetic Foot Ulcers Compared With Standard Wound Care Alone.** The international journal of lower extremity wounds 18(1): 75-80.

Recent systematic reviews and meta-analyses have produced conflicting results about the efficacy of hyperbaric oxygen therapy (HBOT) in improving the healing rate for chronic diabetic foot wounds. This study aimed to assess the efficacy of systemic HBOT in healing of chronic nonischemic diabetic foot ulcer. Thirty adult patients having Wagner's grade 2 or 3 chronic diabetic foot ulcers, in whom the response to 30 days of standard wound care was not favorable, were prospectively randomized to have either HBOT (20-40 sessions) plus conventional treatment (n = 15) or conventional treatment alone (n = 15). Ischemic wounds and patients with contraindications to systemic HBOT were excluded. The primary end point was complete healing of the target ulcer. Secondary endpoints included the following: rate of ulcer healing at the end of treatment period and at 4 and 8 weeks thereafter as well as rate of amputation. A significantly greater percentage of HBOT-treated wounds (33.3%, 5/15) achieved complete closure than conventional therapy-treated wounds (0%, 0/15; P = .014) at the end of treatment. This significant difference was maintained throughout the 8 weeks of follow-up. Complications frequency was nonsignificantly different between both groups. Our study showed that HBOT plus conventional therapy appears as safe as and probably more effective than conventional therapy alone for the healing of chronic nonischemic diabetic foot wounds. Larger studies are required to confirm its specific indications.

Santema, K. T. B., et al. (2018). **Hyperbaric Oxygen Therapy in the Treatment of Ischemic Lower- Extremity Ulcers in Patients With Diabetes: Results of the DAMO2CLES Multicenter Randomized Clinical Trial.** Diabetes care 41(1): 112-119.

OBJECTIVE: Conflicting evidence exists on the effects of hyperbaric oxygen therapy (HBOT) in the treatment of chronic ischemic leg ulcers. The aim of this trial was to investigate whether additional HBOT would benefit patients with diabetes and ischemic leg ulcers., RESEARCH DESIGN AND METHODS: Patients with diabetes with an ischemic wound (n = 120) were randomized to standard care (SC) without or with HBOT (SC+HBOT). Primary outcomes were limb salvage and wound healing after 12 months, as well as time to wound healing. Other end points were amputation-free survival (AFS) and mortality., RESULTS: Both groups contained 60 patients. Limb salvage was achieved in 47 patients in the SC group vs. 53 patients in the SC+HBOT group (risk difference [RD] 10% [95% CI -4 to 23]). After 12 months, 28 index wounds were healed in the SC group vs. 30 in the SC+HBOT group (RD 3% [95% CI -14 to 21]). AFS was achieved in 41 patients in the SC group and 49 patients in the SC+HBOT group (RD 13% [95% CI -2 to 28]). In the SC+HBOT group, 21 patients (35%) were unable to complete the HBOT protocol as planned. Those who did had significantly fewer major amputations and higher AFS (RD for AFS 26% [95% CI 10-38])., CONCLUSIONS: Additional HBOT did not significantly improve complete wound healing or limb salvage in patients with diabetes and lower-limb ischemia.

Vinkel, J., et al. (2019). **The clinical use of hyperbaric oxygen in the treatment of Danish patients with diabetic foot ulcers.** Danish medical journal 66(2).

INTRODUCTION: Patients with diabetic foot ulcers (DFU) suffer from diabetes-related complications and comor-bidities. Hyperbaric oxygen therapy (HBOT) is a treatment modality with limited capacity used in the treatment of DFUs. It is important to ensure that HBOT is offered to patients who are suitable for this treatment regarding effect, compliance and life expectancy. The objective of the present study was to describe the population of patients with DFU who were referred to HBOT in Denmark in the 1999-2016 period., METHODS: All patients with DFU who were treated at the HBOT chamber in Copenhagen during the study period were considered. Patients with an invalid social security number or an incorrect

diagnosis were excluded. Data on comor-bidities, amputation and death were extracted from the Danish National patient Registry and the Danish Civil Registration System. Continuous data were described as median values and binary data were described as proportions. The probability estimate for survival and amputation was investigated by constructing Kaplan-Meier curves., RESULTS: The cohort included 148 patients. Patients were mainly referred from the Capital Region (92%) and multi-disciplinary wound care centres were the primary referring departments (67%). Comorbidity rates were high with an initial median Charlson Comorbidity Index score of five. The five-year amputation and mortality estimates after referral were 73.5% and 51.8%, respectively., CONCLUSIONS: The study showed that Danish DFU patients who are offered HBOT are in advanced stages of their disease, and the referral hinges on local factors such as geography and the referring source rather than on standardised procedures., FUNDING: none., TRIAL REGISTRATION: not relevant. Copyright Articles published in the DMJ are "open access". This means that the articles are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits any non-commercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

Zhao, D., et al. (2017). **Efficacy and Safety of Hyperbaric Oxygen Therapy Used in Patients With Diabetic Foot: A Meta-analysis of Randomized Clinical Trials.** Clinical therapeutics 39(10): 2088-2094.e2082.

PURPOSE: The efficacy and safety profile of hyperbaric oxygen therapy (HBOT) in patients with diabetic foot ulcer have been controversial in recent years. Our meta-analysis was undertaken to evaluate the efficacy and safety profile of HBOT in patients with diabetic foot ulcer., METHODS: We searched the PubMed, Cochrane Library, EMBASE, and Clinical Trials.gov databases for controlled trials. The efficacy end points included the incidence of healed ulcers, major amputations, minor amputations, and reduction in the ulcer wound area. The tolerability end point was the incidence of adverse events., FINDINGS: Nine randomized clinical trials involving 526 patients met the inclusion criteria. No difference was found in the incidence of healed ulcers (risk ratio [RR] = 2.22; 95% CI, 0.87-5.62; P = 0.32; I2 = 81%), minor amputations (RR = 0.95; 95% CI, 0.39-2.29; P = 0.91; I2 = 74%), major amputations (RR = 0.47; 95% CI, 0.17-1.28; P = 0.14; I2 = 61%), and adverse events (RR = 1.00; 95% CI, 0.64-1.56; P = 0.99; I2 = 26%) between the HBOT and standard therapy (ST) groups. HBOT was associated with a greater reduction in the ulcer wound area versus ST (standard mean difference = 1.12; 95% CI, 0.20-2.04; P = 0.04; I2 = 70%)., IMPLICATIONS: No differences existed between HBOT and ST with respect to the incidence of healed ulcers, risk of minor or major amputations, and adverse events. HBOT was associated with a greater reduction in the ulcer wound area than ST. HBOT is a clinically meaningful adjuvant therapy for patients with diabetic foot ulcer.

TRYCKKAMMARBEHANDLING VID ORN:

Borab, Z., et al. (2017). **Systematic review of hyperbaric oxygen therapy for the treatment of radiation-induced skin necrosis.** Journal of plastic, reconstructive & aesthetic surgery: JPRAS 70(4): 529-538.

Every year, 1.2 million cancer patients receive radiation therapy in the United States. Late radiation tissue injury occurs in an estimated 5-15% of these patients. Tissue injury can include skin necrosis, which can lead to chronic nonhealing wounds. Despite many treatments available to help heal skin necrosis such as hyperbaric oxygen therapy, no clinical guidelines exist and evidence is lacking. The purpose of this review is to identify and comprehensively summarize studies published to date to evaluate the effectiveness of hyperbaric oxygen therapy for the treatment of radiation-induced skin necrosis. Adhering to PRISMA guidelines, a systematic review of currently published articles was performed, evaluating the use of hyperbaric oxygen to treat skin necrosis. Eight articles were identified, including one observational cohort, five case series, and two case reports. The articles describe changes in symptoms and alteration in wound healing of radiation-induced skin necrosis after treatment with hyperbaric oxygen therapy. Hyperbaric oxygen therapy is a safe intervention with promising outcomes; however, additional evidence is needed to endorse its application as a relevant therapy in the treatment of radiation-induced skin necrosis.

Chen, J.-A., et al. (2016). **Osteoradionecrosis of mandible bone in patients with oral cancer--associated factors and treatment outcomes.** Head & Neck 38(5): 762-768.

BACKGROUND: The purpose of this study was to investigate factors associated with osteoradionecrosis (ORN) of the mandible bone in a large cohort of patients with oral cancer., METHODS: We reviewed the

medical records of patients with oral cancer and identified those with ORN of the mandible bone. Variables of patients with and without ORN were compared and associated factors were investigated by logistic regression model., RESULTS: A total of 1692 patients were included in the final analysis and 105 patients (6.2%) developed ORN in the mandible bone. Primary site, including mouth floor, buccal mucosa, retromolar trigone, or gum, segmental mandibulectomy, and total radiation dose to the primary site >=75 Gy were independent factors associated with ORN. After aggressive treatment using surgical intervention with/without hyperbaric oxygen, 93.3% of the patients healed completely., CONCLUSION: Among patients with oral cancer after radiation, ORN is an uncommon and dreaded complication. Recognition of associated factors can help physicians to identify those at risk. Copyright © 2015 Wiley Periodicals, Inc.

Dieleman, F. J., et al. (2017). **The efficacy of hyperbaric oxygen therapy related to the clinical stage of osteoradionecrosis of the mandible.** International journal of oral and maxillofacial surgery 46(4): 428-433.

This study aimed to evaluate the success of hyperbaric oxygen therapy (HBOT) and surgery in the treatment of mandibular osteoradionecrosis (ORN) in relation to the extent of the ORN. Twenty-seven patients with ORN were identified from a total of 509 patients with a history of primary oral or base of the tongue cancer; these patients had been treated with radiation therapy with curative intent between 1992 and 2006, with a radiation dose to the mandible of >=50Gy. The ORN was staged according to the classification of Notani et al. The time from completion of radiation therapy to the development of ORN varied (median 3 years). Forty HBOT sessions were offered. After HBOT alone, 3 of 11 stage I lesions, 0 of 8 stage II lesions, and 0 of 8 stage III lesions had healed (P=0.0018). An absolute incidence of 5.3% ORN was found in this population. Of all sites irradiated in this study, the floor of the mouth was most associated with ORN (8.6%), whereas the cheek was least associated (0%). Based on the results of this study, HBOT can be recommended for stage I and II ORN and for selected cases of stage III ORN. Copyright © 2017 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Gavriel, H., et al. (2017). **Hyperbaric oxygen therapy for maxillary bone radiation-induced injury: A 15-year single-center experience.** Head & Neck 39(2): 275-278.

BACKGROUND: Although hyperbaric oxygen therapy (HBOT) is used to treat chronic radiation tissue injury, clinical evidence supporting its use in maxillary bone osteoradionecrosis (ORN) is lacking. Therefore, the purpose of this study was to report our results of collected patient outcomes from a single center's large experience using HBOT to treat maxillary bone ORN., METHODS: From 1999 to 2015, 21 patients received treatment for maxillary bone ORN at our center. The medical records were retrospectively reviewed for the following variables: age, sex, comorbidities, tumor stage and site, previous surgery, previous radiotherapy or chemoradiation therapy, HBOT data, response to treatment and further management., RESULTS: A positive clinical outcome from HBOT occurred in 85.7% of patients with ORN and was proven radiologically in 14 of 15 patients (93.3%). In 5 patients, reconstructive surgery was required thereafter., CONCLUSION: Controversy exists regarding the management of ORN of the maxillofacial skeleton. Our large, single-center experience probably supports the efficacy of HBOT for maxillary bone ORN. © 2016 Wiley Periodicals, Inc. Head Neck 39: 275-278, 2017. Copyright © 2016 Wiley Periodicals, Inc.

Ravi, P., et al. (2017). **The role of hyperbaric oxygen therapy in the prevention and management of radiation-induced complications of the head and neck - a systematic review of literature.** Journal of Stomatology, Oral and Maxillofacial Surgery 118(6): 359-362.

Radiation therapy for the treatment of head and neck cancer can injure normal tissues and have devastating side effects. Hyperbaric oxygen (HBO) is known to reduce the severity of radiation-induced injury by promoting wound healing. While most of the research in literature has focused on its efficacy in osteonecrosis, HBO has other proven benefits as well. The aim of this review was to identify the various benefits of hyperbaric oxygen therapy in patients who have undergone radiation for head and neck cancer. An electronic database search was carried out to identify relevant articles and selected articles were reviewed in detail. The quality of evidence for each benefit, including preserving salivary gland function, preventing osteonecrosis, dental implant success, and overall quality of life, was evaluated. Evidence showed that HBO was effective in improving subjective symptoms of xerostomia, swallowing, speech and overall quality of life. There was no conclusive evidence to show that HBO improved implant survival, prevented osteonecrosis, or improved salivary gland function. The high costs and accessibility of HBO therapy must be weighed against the potential benefits to each patient. Copyright © 2017 Elsevier

Sultan, A., et al. (2017). **The Use of Hyperbaric Oxygen for the Prevention and Management of Osteoradionecrosis of the Jaw: A Dana-Farber/Brigham and Women's Cancer Center Multidisciplinary Guideline.** The oncologist 22(3): 343-350.

BACKGROUND: Osteoradionecrosis of the jaw (ORN) is an infrequent yet potentially devastating complication of radiation therapy to the head and neck region. Treatment options include antimicrobial therapy, local sequestrectomy, resection, and the use of hyperbaric oxygen (HBO). Published data on ORN are difficult to compare because of the lack of a universally accepted classification and staging system, and the literature on the use of HBO to either prevent or successfully manage ORN is controversial and inconclusive. Therefore, we aimed to establish a standard approach for using HBO at our institution., MATERIALS AND METHODS: A literature search was conducted of articles published in the English language between January 1980 and January 2016. Retrieved articles were evaluated by two independent reviewers. Isolated case reports, abstracts, case series, review articles, and cohort studies without a control group were excluded; summary data were extracted from the remaining studies. A panel of experts from Head and Neck Oncology and Oral Medicine from the Dana-Farber Cancer Institute and Brigham and Women's Hospital reviewed the summary data and established multidisciplinary guidelines on the use of HBO for the prevention and management of ORN., RESULTS: Seven studies were evaluated and reviewed by the multidisciplinary panel. There was no consistent evidence in support of HBO for either the prevention or management of ORN., CONCLUSION: Based on the available evidence and expert opinion, routine use of HBO for the prevention or management of ORN is not recommended and is rarely used at our institution. The Oncologist 2017;22:343-350 IMPLICATIONS FOR PRACTICE: The Division of Head and Neck Oncology of Dana-Farber/Brigham and Women's Cancer Center does not recommend the routine use of HBO for the prevention or management of ORN. Adjunctive HBO may be considered for use on a case-by-case basis in patients considered to be at exceptionally high risk who have failed conservative therapy and subsequent surgical resection.

Bowen, J. M., et al. (2019). **Systematic review of agents for the management of cancer treatment-related gastrointestinal mucositis and clinical practice guidelines.** Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer 27(10): 4011-4022.

PURPOSE: The aim of this study was to update the clinical practice guidelines for the use of agents for the prevention and/or treatment of gastrointestinal mucositis (GIM)., METHODS: A systematic review was conducted by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society for Oral Oncology (MASCC/ISOO). The body of evidence for each intervention, in each cancer treatment setting, was assigned an evidence level. Based on the evidence level, one of the following three guideline determinations was possible: Recommendation, Suggestion, and No Guideline Possible., RESULTS: A total of 78 papers across 13 interventions were examined of which 25 were included in the final review. No new guidelines were possible for any agent due to inadequate and/or conflicting evidence. Existing guidelines for probiotics and hyperbaric oxygen were unchanged., CONCLUSIONS: Of the agents studied for the prevention and treatment of GIM, the evidence continues to support use of probiotics containing Lactobacillus spp. for prevention of chemoradiotherapy and radiotherapy-induced diarrhea in patients with pelvic malignancy, and hyperbaric oxygen therapy to treat radiation-induced proctitis. Additional well-designed research is encouraged to enable a decision regarding palifermin, glutamine, sodium butyrate, and dietary interventions, for the prevention or treatment of GIM.

Cardinal, J., et al. (2018). **Scoping Review and Meta-analysis of Hyperbaric Oxygen Therapy for Radiation-Induced Hemorrhagic Cystitis.** Current Urology Reports 19(6): 38.

PURPOSE OF REVIEW: To critically review and summarize existing literature assessing the effectiveness of hyperbaric oxygen therapy (HBOT) for the treatment of radiation-induced urologic injury., RECENT FINDINGS: Though 5 of the included 13 studies were published in the last 2-3 years, the only randomized controlled study was performed in 2012. Recent studies have confirmed the safety and efficacy of HBOT as well as identified risk factors for success vs. failure of HBOT for hemorrhagic radiation cystitis (HRC). Of the 602 patients that received HBOT for HRC, 84% had a partial or complete resolution. In the 7 studies that utilized RTOG/EORTC, 75% of patients saw an improvement in hematuria of at least one grade (out of possible 5 total). Of the 499 patients with documented follow-up, 14% experienced recurrence, with a median time to recurrence of 10 months (6 to 16.5 months).

Chong, V. and M. Rice (2016). **The effectiveness of hyperbaric oxygen therapy (HBOT) in radiation-induced haemorrhagic cystitis.** The New Zealand medical journal 129(1446): 79-83.

INTRODUCTION: Radiation cystitis is one of the possible complications from pelvic radiotherapy. Hyperbaric oxygen (HBOT) improves tissue oxygenation and healing of scarred tissue., AIMS: To assess the efficacy of hyperbaric oxygen therapy (HBOT) in the management of radiation-induced haemorrhagic cystitis in patients with urological cancers., METHODS: This is a retrospective review on all patients with macroscopic haematuria secondary to radiation induced haemorrhagic cystitis who were treated with hyperbaric oxygen therapy (HBOT) between 2009 and 2013. The primary outcome is symptomatic assessment (either complete resolution, partial resolution or no change)., RESULTS: A total of 12 patients with radiation-induced cystitis secondary to urological cancer were included in this study with a mean follow-up of 443 days. The mean age was 78 years. Complete resolution of haematuria was seen in six out of 12 patients. Partial response was achieved in two patients where one required two courses of HBOT and one required three courses of HBOT. As a result, the overall improvement of haematuria after HBOT was 67%. A total of four patients had no response to HBOT., CONCLUSION: Radiation-induced cystitis is a difficult clinical problem to treat. HBOT is not a magic bullet but it may be another alternative treatment option we have at this point in time.

Dellis, A., et al. (2017). **Hyberbaric oxygen as sole treatment for severe radiation - induced haemorrhagic cystitis.** International braz j urol : official journal of the Brazilian Society of Urology 43(3): 489-495.

PURPOSE: To examine the safety and efficacy of hyperbaric oxygen as the primary and sole treatment for severe radiation-induced haemorrhagic cystitis., MATERIALS AND METHODS: Hyperbaric oxygen was prospectively applied as primary treatment in 38 patients with severe radiation cystitis. Our primary endpoint was the incidence of complete and partial response to treatment, while the secondary endpoints included the duration of response, the correlation of treatment success-rate to the interval between the onset of haematuria and initiation of therapy, blood transfusion need and total radiation

dose, the number of sessions to success, the avoidance of surgery and the overall survival., RESULTS: All patients completed therapy without complications with a mean follow-up of 29.33 months. Median number of sessions needed was 33. Complete and partial response rate was 86.8% and 13.2%, respectively. All 33 patients with complete response received therapy within 6 months of the haematuria onset. One patient needed cystectomy, while 33 patients were alive at the end of follow-up., CONCLUSIONS: Our study suggests the early primary use of hyperbaric oxygen for radiation-induced severe cystitis as an effective and safe treatment option. Copyright by the International Brazilian Journal of Urology.

Mougin, J., et al. (2016). **Evaluation of Hyperbaric Oxygen Therapy in the Treatment of Radiation-induced Hemorrhagic Cystitis.** Urology 94: 42-46.

OBJECTIVE: To evaluate the efficacy of hyperbaric oxygen therapy (HBO) in the treatment of postradiation hematuria (PRH) and to identify the predictive factors for a successful outcome., MATERIALS AND METHODS: We conducted a retrospective study and included all patients with PRH treated with HBO in a university hospital center between January 2003 and December 2013. We studied the patients' clinical characteristics, radiotherapy indication, treatments preceding HBO, the grade of hematuria diagnosed based on the Common Terminology Criteria for Adverse Events classification v 4.03 and the efficacy of HBO. The success of HBO was defined as the total or partial resolution of hematuria., RESULTS: We included 71 patients with a median age of 72 (39-87) years. PRHs were severe (grade >=3) in 50 (70.4%) of the cases. Radiotherapy was indicated in the treatment of prostate cancer in 61 (85.9%) patients. The median length of time between hematuria and HBO was 8 (1-154) months. Prior to HBO, 46 (64.8%) patients underwent electrocoagulation of the bladder. HBO sessions were compounded by 9 cases of barotraumatic otitis, 5 cases of transient visual disturbance, and 1 case of finger paresthesia. On average, 29 (3-50) sessions were carried out. Treatment was effective in 46 (64.8%) patients, 37 (52.1%) of whom were completely cured. A hematuria grade of less than 3 was a predictive factor in the successful treatment (P = .027). Median follow-up was 15 (1-132) months., CONCLUSION: HBO completely resolves PRH in 52.1% of cases. Prolonged patient follow-up is required to confirm the efficacy of this treatment.

Niezgoda, J. A., et al. (2016). **Outcomes of Radiation Injuries Using Hyperbaric Oxygen Therapy: An Observational Cohort Study.** Advances in Skin & Wound Care 29(1): 12-19.

BACKGROUND: The late effects of radiation therapy following the treatment of cancer are a well-known consequence. Evidence increasingly supports the use of hyperbaric oxygen (HBO) as an adjunctive treatment in a variety of radiation injuries., OBJECTIVE: To present the findings of a new registry of radiation injuries that was developed to evaluate the outcomes and treatment parameters of HBO treatment (HBOT) when applied to patients experiencing the late effects of radiation therapy., DESIGN: Observational cohort., SETTING: Hyperbaric oxygen clinical treatment facilities in the United States., PATIENTS: A total of 2538 patients with radiation-induced injuries., MEASUREMENTS: Injury type, patient age, gender, diabetes, end-stage renal disease, collagen vascular disease, coronary artery disease/peripheral vascular disease, on anticoagulant medication, on systemic steroid medication, patient is current smoker, patient abuses alcohol, symptoms reported, duration of symptoms, symptom progression prior to HBOT, transfusion units, HBOT time, HBOT count, HBO chamber pressure, HBO time in chamber, and patient outcomes., RESULTS: A total of 2538 patient entries with 10 types of radiation injuries were analyzed. The 5 most common injuries were osteoradionecrosis (33.4%), dermal soft tissue radionecrosis (27.5%), radiation cystitis (18.6%), radiation proctitis (9.2%), and laryngeal radionecrosis (4.8%). Clinical outcomes following HBOT were positive with symptoms that improved or resolved varying from 76.7% to 92.6%, depending on injury type. Overall, although the mean symptom improvement score between some groups is statistically significant, the differences are probably not clinically meaningful. Patients with osteoradionecrosis had the highest mean symptom improvement score (3.24) compared with a mean of 3.04 for laryngeal radionecrosis., LIMITATIONS: Limited data were available on patient comorbidities and symptom severity., CONCLUSIONS: Outcomes from a large patient registry of radiation-induced injuries support the continued therapeutic use of HBOT for radiation injuries.

Oscarsson, N., et al. (2019). **Radiation-induced cystitis treated with hyperbaric oxygen therapy (RICH-ART): a randomised, controlled, phase 2-3 trial.** The Lancet. Oncology 20(11): 1602-1614.

BACKGROUND: Late radiation cystitis is an adverse effect of cancer treatment with radiotherapy in the pelvic region. Symptoms of late radiation cystitis can be assessed with the Expanded Prostate Index

Composite Score (EPIC). Previous reports indicate that hyperbaric oxygen therapy reduces symptoms from late radiation cystitis, but the evidence is predominantly based on non-randomised and retrospective studies. We aimed to assess whether hyperbaric oxygen therapy would mitigate symptoms of late radiation cystitis., METHODS: We did a randomised, controlled, phase 2-3 trial (RICH-ART [Radiation Induced Cystitis treated with Hyperbaric oxygen-A Randomised controlled Trial]) at five Nordic university hospitals. All patients aged 18-80 years, with pelvic radiotherapy completed at least 6 months previously, a score of less than 80 in the urinary domain of the Expanded Prostate Index Composite Score (EPIC), and referred to participating hyperbaric clinics due to symptoms of late radiation cystitis, were eligible for inclusion. Exclusion criteria were ongoing bleeding requiring blood transfusion exceeding 500 mL in the past 4 weeks, permanent urinary catheter, bladder capacity less than 100 mL, fistula in the urinary bladder, previous treatment with hyperbaric oxygen therapy for late radiation injuries, and contraindications to hyperbaric oxygen therapy. After computer-generated 1:1 randomisation with block sizes of four for each stratification group (sex, time from radiotherapy to inclusion, and previous invasive surgery in the pelvic area), patients received hyperbaric oxygen therapy (30-40 sessions, 100% oxygen, breathed at a pressure of 240-250 kPa, for 80-90 min daily) or standard care with no restrictions for other medications or interventions. No masking was applied. The primary outcome was change in patient-perceived urinary symptoms assessed with EPIC from inclusion to follow-up at visit 4 (6-8 months later), measured as absolute change in EPIC urinary total score. RICH-ART closed enrolment on Dec 31, 2017; the last follow-up data will be compiled in 2023. RICH-ART is registered with ClinicalTrials.gov, number NCT01659723, and with the European Medicines Agency, number EudraCT 2012-001381-15., FINDINGS: Of 223 patients screened between May 9, 2012, and Dec 20, 2017, 87 patients were enrolled and randomly assigned to either hyperbaric oxygen therapy (n=42) or standard care (n=45). After excluding eight patients who withdrew consent directly after randomisation (one in the hyperbaric oxygen therapy group and seven in the standard care group), 79 were included in the intention-to-treat analyses (n=41 in the hyperbaric oxygen therapy group, n=38 in the standard care group). Median time from randomisation to visit 4 was 234 days (IQR 210-262) in the hyperbaric oxygen therapy group and 217 days (195-237) in the standard care group. The difference between change in group mean of EPIC urinary total score at visit 4 was 10.1 points (95% CI 2.2-18.1; p=0.013; 17.8 points [SD 18.4] in the hyperbaric oxygen therapy group vs 7.7 points [15.5] in the standard care group). 17 (41%) of 41 patients in the hyperbaric oxygen therapy group experienced transient grade 1-2 adverse events, related to sight and hearing, during the period of hyperbaric oxygen therapy., INTERPRETATION: Our results suggest that hyperbaric oxygen therapy relieves symptoms of late radiation cystitis. We conclude that hyperbaric oxygen therapy is a safe and well tolerated treatment., FUNDING: The regional research fund of Region Vastra Gotaland, Sweden, the regional Health Technology Assessment Centre at Sahlgrenska University Hospital, Sweden, and Lions Cancer Research Fund of Western Sweden.

Villeirs, L., et al. (2019). **Hyperbaric oxygen therapy for radiation cystitis after pelvic radiotherapy: Systematic review of the recent literature.** International journal of urology: official journal of the Japanese Urological Association.

The present study assessed the efficacy of hyperbaric oxygen therapy in reducing symptoms of radiation cystitis, a specific type of iatrogenic injury to the bladder, by systematic review of recent literature. The MEDLINE, Embase and Web of Science databases were searched using combinations of the terms "radiation," "cystitis" and "hyperbaric oxygen" to identify articles evaluating patients with radiation cystitis, treated with hyperbaric oxygen therapy. Only recent (<=10 years) original studies were included. Data were extracted and pooled in order to calculate descriptive weighted averages. Articles were evaluated on their level of evidence. A total of 20 papers were obtained, resulting in a cohort of 815 patients who were treated with hyperbaric oxygen therapy for radiation cystitis. Overall and complete response rates varied from 64.8% to 100% and 20% to 100%, respectively. The weighted average overall and complete response rates were 87.3% and 65.3%, respectively. Adverse events were observed in 9.6% of the patients, but permanent side-effects were rare. The most prominent limitations were high cost and low availability. Hyperbaric oxygen therapy is effective in the treatment of radiation-induced cystitis, with minimal adverse events, but low availability and high cost. At present, evidence is low; therefore, more prospective studies are required.

Referenser

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Koncernkontoret
Prioriteringsrådet

Yttrande

Datum 2017-03-20
Dnr. 1402749

Tryckkammarbehandling vid diabetessår och strålningsorsakad vävnadsdöd och inflammation

Frågeställning
Bör Region Skåne inom ramen för rutinsjukvård erbjuda tryckkammarbehandling av diabetesorsakade fotsår, strålningsorsakad vävnadsdöd i ben (osteoradionekros), samt radiologiskt orsakad inflammation i urinblåsa och ändtarm (cystit och proktit)?

Prioriteringsrådets ställningstagande

Region Skåne bör inte inom ramen för rutinsjukvård erbjuda tryckkammarbehandling vid diabetesorsakade fotsår (prioritet 9), osteoradionekros (prioritet 8) samt radiologiskt orsakad cystit och proktit (FoU)[1].

Bakgrund
Tryckkammarbehandling eller hyperbar oxygenbehandling (HBO) innebär att en patient får andas 100 % syrgas i en tryckkammare under tryck som motsvarar 14-18 meters vattendjup. Behandlingen genomförs vanligen som dagliga behandlingstillfällen om 60-90 minuter vid upp till totalt 30-40 behandlings-tillfällen motsvarande 6-8 veckors behandlingstid. Den grundläggande principen vid HBO-terapi är att öka syrgastransporten till olika vävnader i kroppen för att härigenom förbättra läkning. I Region Skåne har HBO använts sedan 80-talet för behandling av patienter med diabetesorsakade fotsår, osteoradionekros i käken och radiologiskt orsakad cystit och proktit. 2015 utfördes totalt 2 019 enskilda behandlingar av totalt 64 patienter. Behandling av patienter med osteonekros stod

[1] Nationella prioriteringsmodellen, prioriteringsgrad 1-10 där 1 innebär högsta prioritet och 10 lägsta prioritet. Resurser bör i första hand fördelas till åtgärder med högst prioritet. Åtgärder med mycket låg evidens och/eller bristande klinisk erfarenhet hänvisas till forskning och utveckling, FoU.

Postadress: 291 89 Kristianstad
Organisationsnummer: 23 21 00-0255

Telefon (växel): 044-309 30 00 Fax: 044-309 32 98
Internet: skane.se

för cirka 60 procent. Akut tryckkammarbehandling t.ex. vid dykarsjuka utförs inte i Region Skåne sedan 2006.

Bedömning av patientnytta
Prioriteringsrådets bedömning av patientnytta baseras på relevanta studier som identifierats via SBU's upplysningstjänst[2]. För effekt av HBO på läkning av diabetessår har sju litteratursammanställningar och en separat randomiserad studie värderats. HBO som tillägg till ordinarie sårvård har enligt vissa studier en måttlig effekt på läkning av diabetessår ett år efter avslutad HBO-behandling. Det vetenskapliga underlaget är emellertid begränsat. HBO har ingen säker effekt på andelen patienter som måste genomgå amputation ett år efter avslutad behandling. Det vetenskapliga underlaget för detta är otillräckligt. Avseende osteoradionekros finns det ett fåtal mindre studier som tyder på att HBO kan vara ett värdefullt tillägg till kirurgi för att uppnå läkning. Effekten är måttlig och det vetenskapliga underlaget är begränsat. För strålningsorsakad proktit och cystit bedöms nyttan av HBO som låg och det vetenskapliga underlaget är otillräckligt.

Etisk bedömning
De beskrivna sjukdomstillstånden är förenade med stort lidande och komplikationer och behandlingen ges till patienter när annan konventionell behandling inte varit framgångsrik. Enbart det faktum att en person befinner sig i en svår situation behöver inte betyda att det föreligger ett behov av en specifik behandling. För detta krävs att det finns en genomförbar behandling med en rimligt förväntad positiv effekt. I den mån det finns en behandling med dokumenterad positiv effekt spelar patientens utgångsläge roll. Avseende HBO-behandling är den positiva effekten osäker.

Hälsoekonomisk bedömning
Kostnaden för att erbjuda HBO-behandling till personer i Region Skåne beror på flera faktorer såsom var behandling ges, kostnaden för att ha en anläggning för HBO-behandling och antal personer som erbjuds behandlingen. Den sammantagna bedömningen är att det är osannolikt att HBO kan minska andra sjukvårdskostnader vid förbättrad sårläkning i så stor utsträckning att det skulle göra tryckkammarbehandling kostnadsneutral.

Med hänsyn tagen till människovärdesprincipen, behovs- och solidaritetsprincipen samt kostnadseffektivitetsprincipen och att tillgänglig evidens för patientnytta är begränsad till otillräcklig anser rådet att tryckkammarbehandling för diabetesorsakade fot- och bensår, osteoradionekros i käkbenet och radiologiskt orsakad cystit och proktit inte bör erbjudas inom rutinsjukvård. I de fall enskilda patienter bedöms ha nytta av behandling bör detta kunna ske på plats utanför regionen. Det är också rådets uppfattning av det finns ett fortsatt behov av kontrollerade forskningsstudier med större patientunderlagför att få säkrare underlag för framtida bedömningar. I sådana studier bör alla nationella HBO-resurser användas.

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[2] SBU = Statens beredning för medicinsk utvärdering

Bakgrund och analys

Aktuella åtgärder för bedömning och jämförelsealternativ

A. HBO-behandling som tillägg till konventionell vård.
B. Konventionell vård

Hälsotillstånd

I Skåne uppskattas drygt 50 000 personer ha typ 2- diabetes och ca 6 000 individer typ 1- diabetes. Cirka 15% av dessa kommer någon gång i livet att behöva sjukvårdskrävande behandling av fotsår. Svårläkta fotsår är den dominerande icke-traumatiska orsaken till amputation i nedre extremiteten i Sverige och tillståndet är associerat med risk för förtida död. Incidensen av amputationer är mellan 6 och 8 per 1 000 personer med diabetes och år. Patienter med fotsår har nedsatt fysisk, emotionell och social funktion och är oftare deprimerade och har lägre livskvalitet. Social isolering, låg utbildningsnivå och låg socioekonomisk status ökar risken för att utveckla fotsår vid diabetes. Tillståndet bedöms ha måttlig svårighetsgrad.

Osteoradionekros innebär att vävnadsdöd och inflammation utvecklas i benvävnad som utsatts för strålning. Osteoradionekros i käkbenet uppkommer till följd av strålbehandling av olika cancerformer i huvud- och halsregionen och dessa cancerformer förväntas öka. Risken att drabbas av osteonekros i samband med strålningsbehandling ökar vid hög ålder. Incidensen varierar beroende på vilken strålningsteknik som används. Ju bättre precision desto färre skador. Incidensen har rapporterats till 35% för patienter med strålbehandlad huvud- och halscancer men med så kallad multifraktionerad teknik minskar risken till under 5%. Tillståndet bedöms ha stor svårighetsgrad.

Patienter som behandlats med strålning mot tumörer i lilla bäckenet kan utveckla kronisk inflammation i urinblåsan (cystit) eller ändtarmen (proktit). Symtomen från dessa inflammationer innefattar blödning, smärta, obehag samt minskad kapacitet eller oförmåga att hålla urin och/eller avföring. Dessa symtom är ofta så allvarliga att de begränsar patientens rörelsefrihet och leder till kraftigt nedsatt livskvalitet. Behovet av HBO-behandling för radiologiskt orsakad cystit och proktit har minskat kraftigt på senare år och 2015 återfinns enbart någon enstaka patient i den skånska statistiken, vilket troligtvis kan förklaras av en förbättrad precision på strålningstekniken. Tillståndet bedöms ha måttlig svårighetsgrad.

HBO-behandling

Vid behandling med HBO andas patienten 100% syrgas vid ett tryck som ungefär motsvarar 14–18 meters vattendjup. Det höga trycket gör att syrgas diffunderar cirka 4 gånger så långt som normalt, vilket medför att man bättre kan syresätta vävnad med kraftigt nedsatt blodcirkulation. HBO har använts som behandlingsmetod för sårbehandling sedan 1970-talet och ges med ett tryck på 2,0-2,5 bar under ca 90 minuter, vanligen i behandlingsserier om 30-40 behandlingar.

Genom tryckkammarbehandling stimuleras kärlnybildning vilket bedöms bidra till förbättrad sårläkning.

Konventionell vård

Omhändertagandet av personer med diabetes med etablerade fotkomplikationer är komplext, vilket motiverar ett multidisciplinärt förhållningssätt. På diabetesfotmottagningarna i Skåne behandlas årligen cirka 2200 personer för diabetesrelaterade fotsår. Fyra av tio är i behov av vård som överstiger tre månader och en av fem mer än 6 månader. Ett multidisciplinärt angreppssätt som omfattar prevention, patientutbildning och multifaktoriell behandling av etablerade skador minskar amputationsrisken med mer än 50%.

Patienter med osteoradionekros behandlas inledningsvis med lokal infektionssanering och antibiotika. Flertalet patienter klarar tillfrisknande med dessa enklare behandlingsmetoder. I vissa fall används HBO-behandling inför lokal infektionssanering till exempel vid extraktion av tänder. I andra utvalda fall måste mer omfattande kirurgisk behandling tillgripas till exempel resektion av död vävnad samt rekonstruktion med lambåer.

Patientnytta och ogynnsamma effekter

HBO som behandlingsmetod har använts under fyra decennier och det har publicerats många små fallstudier och randomiserade, kontrollerade studier men med mycket varierande metodologi och kvalitet.

Det finns ett fåtal studier som återkommer i de systematiska översikter som är gjorda de senaste åren. Översikterna sammanfattar evidensläget för de olika HBO-indikationerna och evidensstyrkan bedöms enligt GRADE- systemet[3].

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[3] **GRADE Grades of evidence**

GRADE (⊕⊕⊕⊕) – starkt vetenskapligt underlag

GRADE (⊕⊕⊕o) – Måttligt starkt vetenskapligt underlag

GRADE (⊕⊕oo) – Begränsat vetenskapligt underlag

GRADE (⊕ooo) – Otillräckligt vetenskapligt underlag

Starkt vetenskapligt underlag: Vi har högt förtroende för att den sanna effekten ligger nära den den redovisade effekten. Det är mycket osannolikt att ytterligare forskning kommer att ändra vår säkerhet gällande den redovisade effekten.
Måttligt starkt vetenskapligt underlag: Vi har måttligt förtroende gällande den redovisade effekten. Den sanna effekten ligger sannolikt nära den redovisade, men det finns en möjlighet att den verkliga effekten är betydande annorlunda. Det är troligt att ytterligare forskning kommer ha en viktig påverkan på vårt förtroende gällande resultaten och kan också komma att förändra den redovisade effekten.
Begränsat vetenskapligt underlag: Vårt förtroende gällande redovisad effekt är begränsat. Den sanna effekten kan vara markant annorlunda än den redovisade effekten. Ytterligare forskning kommer med stor sannolikhet att ha en betydande påverkan på vår säkerhet gällande effekten och kommer sannolikt att ändra slutresultatet.
Otillräckligt vetenskapligt underlag: Vi är väldigt osäkra och har väldigt lågt förtroende gällande den redovisade effekten. Den sanna effekten är sannolikt betydande annorlunda än den redovisade.

Det finns begränsad evidens för att tilläggsbehandling med HBO vid diabetes och kroniska svårläkta fotsår i en öppenvårdspopulation ökar läkningsförekomsten efter ett år men evidensen för att amputationer minskar vid ett års uppföljning bedöms otillräcklig. Det finns enstaka mindre studier som tyder på att HBO som tillägg till kirurgi ökar andelen personer med läkta sår vid osteoradionekros och ett begränsat vetenskapligt stöd för att HBO kan ha positiva effekter på proktit, däremot saknas evidens för cystit. Det behövs fler och större studier av hög kvalitet, ett robust system för selektionskriterier inför behandling, optimering av behandlingsprotokoll och ett tydliggörande av indikationerna för att starta och avsluta behandling för att fullt ut kunna bedöma effekterna av HBO.

Tryckkammarbehandlingen är i sig inte förenad med några vetenskapligt belagda medicinska risker. Behandlingen är tidskrävande. Totalt kan en behandling innebära 30 pass om ca 1,5- 2 timmar åt gången vilket kan innebära att en patient måste bo på patienthotell i flera veckor för att kunna ta del av behandlingen. Vissa patienter kan ibland uppleva klaustrofobi i kammaren.

Etiska aspekter

- En central fråga är kopplingen mellan behandlingen, vårdbehovet och evidensläget.
- Bland de som kommer ifråga för tryckkammarbehandlingen finns det patienter vars sammantagna sjukdomsbörda är stor. Även en begränsad, men gynnsam, effekt på deras livskvalitet kan anses högt prioriterad. Avseende HBO-behandling är den positiva effekten osäker.
- *Om* tryckkammarbehandlingen förebygger allvarliga komplikationer, såsom behov av amputation eller rekonstruktiv kirurgi, följer det ur Behovs- och solidaritetsprincipen att behandlingen kan ges hög prioritet.
- Hälso- och sjukvård ska vila på frivillig grund. Respekt för patientens självbestämmande förutsätter adekvat, saklig och mottagaranpassad information om behandlingen, genomförandet och vad man vet om utsikterna om framgångsrik behandling. I det aktuella fallet kan det handla om att erbjuda en behandling som är baserad på ett svagt vetenskapligt stöd.
- Ett avsteg från principen att hälso- och sjukvård ska vila på vetenskap och beprövad erfarenhet är inte bara problematisk ur ett samhällsperspektiv – då den förväntade nyttan är oviss – utan även problematisk i mötet med patienten, där det gäller att göra gott och inte skada. I den mån det finns en behandling med dokumenterad positiv effekt (sårläkning, färre amputationer, ökad livskvalitet mm) spelar patientens utgångsläge roll. Som tidigare framgått följer det ur den svenska prioriteringsplattformen att det är de största vårdbehoven som ska tillgodoses först.
- Behandlingen är inte förenad med kända medicinska risker. Enskilda patienter kan dock uppleva obehag inför att vistas i en tryckkammare.
- Avståndet till behandlingsorten gör att vissa personer sannolikt inte kommer att utnyttja behandlingen. Detta skulle kunna utgöra ett hot mot principen om vård på lika villkor under förutsättning att det finns säkerställd patientnytta av HBO.

Hälsoekonomisk bedömning

Det saknas underlag för att med säkerhet fastslå förväntade kostnader för att kunna erbjuda HBO till personer i Region Skåne.

Den första osäkerheten rör hur infrastrukturen ser ut framöver och därmed de totala budgetkostnaderna för verksamheten. Region Skåne kan investera i en ny tryckkammare vilket förutsätter en noggrann bygg- och anläggningsingenjörsberedning av de infrastrukturella förutsättningarna inklusive lämplig placering, byggnationsbehov, anpassning och, vid behov, utbyggnad av försörjning av syrgassystem med mera. Den totala investeringskostnaden är i nuläget oklar. De hälsoekonomiska beräkningarna beskriver därför beräknad kostnad per behandlad person utifrån scenarier för olika nivåer på den totala investeringskostnaden (30 Mkr, 60 Mkr samt 90 Mkr) i syfte att illustrera hur detta kan påverka förväntade behandlingskostnader.

Den andra osäkerheten avser hur många personer som kan få nytta av behandlingen och därmed storleken på patientpopulationen där HBO-behandling bedöms vara ett aktuellt behandlingsalternativ. Kostnadsscenarierna redogör för hur antalet behandlade personer påverkar skattad kostnad per person.

Antaganden om storlek på investeringskostnader och driftskostnader samt förväntade patientvolymer påverkar kostnaden per behandlad person om Region Skåne gör en nyinvestering i en tryckkammare för HBO-behandling. Dessa kostnader bör jämföras med en förväntad kostnad per person vid remittering till annat landsting (alternativt Köpenhamn) för HBO-behandling inklusive reskostnader, kost och logi som blir nödvändigt på grund av HBO-behandlingens karaktär med dagliga sessioner under minst 6 veckor.

En nyinvestering i en tryckkammare för HBO-behandling *kan* vara billigare än att remittera personer till annat landsting om åtminstone 150 personer behandlas årligen. Detta gäller även vid en investeringskostnad på 90 miljoner kronor och årliga driftskostnader på 8 miljoner kronor. Om antalet behandlade personer däremot motsvarar genomsnittligt behandlat antal personer vid tryckkammarverksamheten i Helsingborg under 2011-2015 (70 personer) blir det billigare att remittera till Göteborg om investeringskostnaden är större än 30 miljoner kronor och driftskostnaderna överstiger 6 miljoner kronor.

En kompletterande analys visar att det är osannolikt att HBO kan minska andra sjukvårdskostnader till följd av en förbättrad sårläkning i så stor utsträckning att det skulle göra tryckkammarbehandling kostnadsneutral. **Resultaten för genomgången av kostnader per person för behandling med HBO bör vägas tillsammans med förväntad patientnytta.**

Konsekvensanalys organisation

Tryckkammarverksamhet har bedrivits vid Helsingborgs lasarett sedan 1984. På grund av ombyggnaden av Helsingborgs sjukhus är det beslutat att tryckkammarverksamheten i Helsingborg måste avvecklas. En förflyttning av verksamheten till SUS Lund har föreslagits. Om en ny tryckkammare ska placeras på sjukhusområdet i Lund, krävs bland annat en ny byggnad, nya gasledningar, kompressorer och lufttankar. Ytterligare utredningar av de tekniska, byggnadsmässiga och ekonomiska förutsättningarna krävs. Behov av personalrekrytering med särskild kompetens och särskilda utbildningskostnader har inte bedömts.

Referenslista kan erhållas via prioriteringsrådets sekretariat.

För Prioriteringsrådet

Kjell Asplund
Ordförande