

CASE REPORT

Cerebral blood flow velocity during chest compressions in cardiac arrest

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Keywords - resuscitation, cerebral blood flow velocity, arterial blood pressure

Abstract

This report describes a single clinical observation in which arterial blood pressure and cerebral blood flow velocity were concomitantly measured during manual chest compressions in cardiac arrest. During basic life support in human cardiac arrest we observed that cerebral blood flow velocity in the brain is quickly restored to normal levels even when no relevant systemic arterial blood pressure can be detected concurrently. This observation illustrates that even in the absence of relevant arterial blood pressure, cerebral blood flow velocities may be quickly restored during basic life support.

Case report

Maintenance of cerebral blood flow during resuscitation is critical to neurological function and cognitive outcome. In this brief report, we describe a clinical observation regarding the relationship between the cerebral blood flow velocity (CBFV) in the middle cerebral artery and concomitant arterial blood pressure (ABP) in a patient while being resuscitated from cardiac arrest.

A 74-year-old male was admitted to the intensive care unit (ICU) after scheduled and uncomplicated coronary artery bypass grafting. After written informed consent, the patient was included in a study protocol (trialregister.nl, NTR5064), and monitored continuously for haemodynamic parameters, including ABP (radial artery catheter), central venous pressure (venous catheter inserted in right jugular vein), airway pressure (at the T-tube of the breathing circuit) and CBFV of the right middle cerebral artery with transcranial Doppler (TCD, insonation depth of 50 mm, Pioneer TC4040, Uberlingen, Germany) using different fractions of inspired oxygen. The TCD 2MHz-probe was fixated in a Marc 500 TCD head frame (Spencer Technologies Inc. USA). Cardiac output was monitored with arterial pulse power analysis using the LiDCOplus haemodynamic monitoring system (LiDCO Ltd, Cambridge,

UK). The parameters of ABP, central venous pressure, CBFV and airway pressure were recorded simultaneously at a frequency of 100 Hz and stored on a computer for further analysis.

The patient was mechanically ventilated (Evita-4, Dräger, Lübeck, Germany) and sedated using continuous infusion of propofol and sufentanil in the ICU.

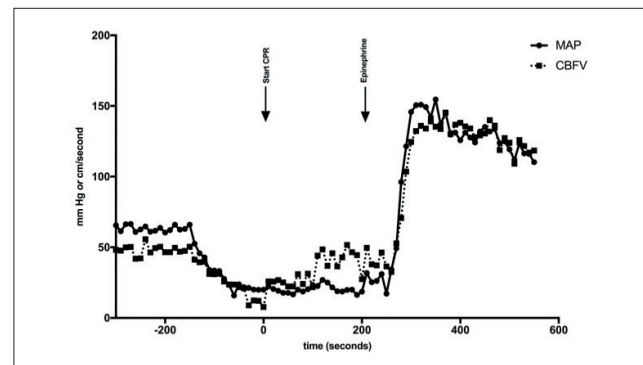


Figure 1. Showing values of mean arterial blood pressure (MAP) and cerebral blood flow velocity (CBFV) before, during and after cardiopulmonary resuscitation (CPR). Time points where CPR was initiated and time point of administration epinephrine are indicated.

All vital signs were normal on physical examination at the time of ICU admission. The ABP and cardiac output dropped significantly within the first hour after admission. Shortly thereafter, a pulseless electrical activity was observed and resuscitation was initiated immediately. At that time, the mean arterial pressure dropped to 22 mmHg and cardiac output was 0.0 l.min⁻¹. During manual chest compressions, a large discrepancy was observed between peak systolic CBFV (51 cm.sec⁻¹) and peak systolic ABP (33 mmHg). CBFV increased sharply to 60% of pre-circulatory collapse levels after the institution of chest compressions and was completely restored to baseline

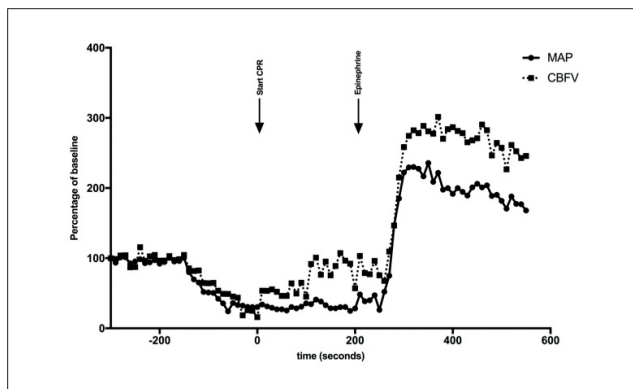


Figure 2. Mean arterial blood pressure (MAP) and cerebral blood flow velocity (CBFV) depicted as a percentage of baseline value before cardiopulmonary collapse during cardiopulmonary resuscitation (CPR). This figure shows a rapid normalisation of CBFV in contrast to the absence of an increase in MAP during CPR

levels within 100 seconds after the start of cardiopulmonary resuscitation (CPR), whereas peak ABP increased only after administering a 1 mg bolus of epinephrine (*figures 1 and 2*). Return of spontaneous circulation was achieved 255 seconds after the initiation of CPR (ABP was 83/35 mmHg and cardiac output 6.1 l.min⁻¹). Unfortunately the patient developed a second cardiac arrest in his clinical course and remained in cardiogenic shock. Despite maximal therapy the patient died in the ICU due to multi-organ failure.

During CPR we observed a notable difference between the course of ABP and CBFV in the middle cerebral artery. In contrast with the observed effects in the cerebral circulation, the systemic ABP did not initially respond to manual chest compressions and only returned after epinephrine was administered.

The human brain is exquisitely sensitive to changes in cerebral blood flow and harbours a complex mechanism by which cerebral blood flow is maintained at a constant level independent of ABP, which is known as cerebral autoregulation.^[1] However, it is widely assumed that the process of cerebral autoregulation does not function below a systolic systemic arterial pressure of about 50-70 mmHg.^[1,2] We observed a very rapid increase in CBFV during chest compressions whereas systemic ABP was still below this threshold. When cerebral autoregulation is intact, the cerebral vasculature responds to a lower blood pressure with vasodilatation. The resulting decrease in vascular resistance may induce an increase in cerebral blood volume, and a decrease in CBFV. However, no decrease in vascular resistance and CBFV may have been possible since the ABP fell below the range of cerebral autoregulation. The increased CBFV measured is therefore probably a direct consequence of the instituted chest compressions. As perfusion pressure remains essential to maintaining or restoring cerebral blood flow, the

increase in blood pressure was further warranted by administering epinephrine during CPR. There could also be a direct cerebral vascular effect of epinephrine although it is believed that cerebral vessels do not contain $\alpha 1$ -receptors.

It is conceivable that during chest compressions, the peak systolic pressure was sufficient to maintain or restore cerebral autoregulation and reinstitute preferential blood flow. In line with this, studies in humans have showed that peak systolic pressures over 60 mmHg can be observed during cardiopulmonary resuscitation.^[2,3] It is tempting to speculate that, directly after cardiac arrest, the discrepancy between peak ABP and CBFV may be explained by differences in vascular resistance or differences in vasomotor tone between the cerebral circulation and the systemic circulation, considering that blood output volume will primarily circulate to organs with less vascular resistance. Thus, blood flow generated by manual chest compressions may predominantly redistribute to the cerebral circulation. This effect may be more prominent after administration of epinephrine. In the later period after resuscitation, we noted a close relation between systemic ABP and CBFV after the administration of epinephrine (*figures 1 and 2*).

Reports on the effects of resuscitation on cerebral perfusion and circulation in humans are scarce. Our observation is unique in the sense that we were able to continuously measure cerebral blood flow velocities in the middle cerebral artery during an unexpected cardiopulmonary resuscitation. To the best of our knowledge, only one previous report has demonstrated a similar effect during cardiac arrest since a direct effect of immediate

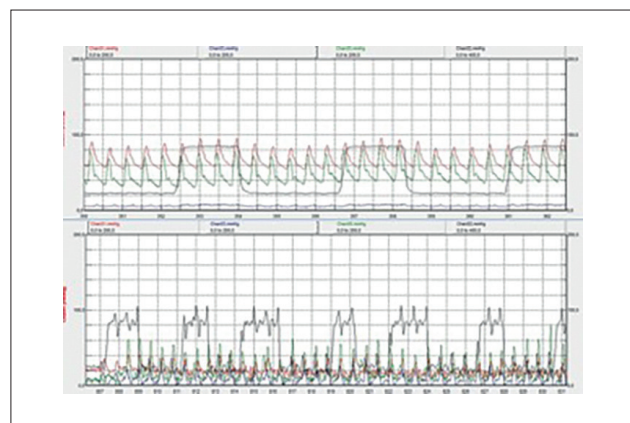


Figure 3. Two screenshots of the original data recording

Channel 1: arterial blood pressure in red; Channel 3: central venous pressure in blue; Channel 5: cerebral blood flow velocity of right middle cerebral artery in green; Channel 2: airway pressure in black. X-axis is time in seconds; Y-axis is pressure in mmHg or CBFV in cm/sec. Screenshots are produced during off-line analysis of measurements using Beatscope 1.1a (Finapres Medical Systems, Enschede, the Netherlands).

Upper panel: An original data recording, of a randomly chosen period, before cardiac arrest; Lower panel: original data recording at start of resuscitation.

institution of CPR on cerebral tissue oxygen tension in a patient with traumatic brain injury was shown.^[4] While we acknowledge that CBFV in the middle cerebral artery is not a direct equivalent to general cerebral blood flow, the use of transcranial Doppler for assessing changes in the cerebral circulation has previously been evaluated in an experimental setting of cardiopulmonary resuscitation.^[5] Based on earlier animal studies, it is advised to start CPR as soon as possible after a witnessed cardiac arrest because of the observed relation between the height of restored cerebral blood flow and the moment resuscitation is started.^[6,7] In our patient, CPR started immediately after the cardiac arrest was observed at the bedside.

A preclinical study in pigs measured continuous cerebral cortical blood flow during cardiac arrest and showed that standardised manual compressions during cardiac arrest resulted in a mean cortical blood flow of only 40% in relation to baseline blood flow.^[8] In this and another study, chest compressions with the Lund University Cardiac Assist System (LUCAS) device resulted in much improved cerebral blood flow and it was noted that even brief interruptions of compressions resulted in significantly decreased cerebral perfusion.^[8,9] In line with this preclinical evidence, we conclude that during basic life support in human cardiac arrest, CBFV in the brain is quickly restored even when no relevant systemic blood pressure can be detected.

Disclosures

All authors declare no conflict of interest. No funding or financial support was received.

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Posaconazol remt het enzym lanosterol 14 α -demethylase (CYP51), dat een essentiële stap in de biosynthese van ergosterol katalyseert. **THERAPEUTISCHE INDICATIES** **Behandeling van: invasieve aspergillose** die ongevoelig is voor amfotericine B of itraconazol of als deze geneesmiddelen niet verdragen worden; **fungosie** die ongevoelig is voor amfotericine B of als amfotericine B niet verdragen wordt; **chromoblastomycose** en **mycetoom** die ongevoelig is voor itraconazol of als itraconazol niet verdragen wordt; **coccidioidomycose** die ongevoelig is voor amfotericine B, itraconazol of fluconazol of als deze geneesmiddelen niet verdragen worden. Noxafil is eveneens geïndiceerd voor **Prophylaxe van: invasieve schimmelinfecties** bij: 1. Patiënten die remissie-inductiechemotherapie krijgen voor acute myeloïde leukemie (AML) of myelodysplastische syndroom (MDS) waarbij aanhoudende neutropenie verwacht wordt en bij wie een hoog risico bestaat op ontwikkeling van invasieve schimmelinfecties; 2. Ontvangers van hematopoëtische stamceltransplantaten (HSCT) die immunosuppressieve therapie met hoge dosering ondergaan voor graft-versus-host ziekte en bij wie hoog risico bestaat op ontwikkeling van invasieve schimmelinfecties. **Alleen voor Noxafil suspensie voor oraal gebruik; Behandeling van orofaryngeale candidiasis:** eerstelijnsbehandeling bij patiënten die een ernstige ziekte hebben of die immungecompromiteerd zijn, bij wie verwacht wordt dat de respons op lokale therapie zwak is. **CONTRA-INDICATIES** Overgevoeligheid voor de ingrediënten; co-administratie van ergotalkaloiden; co-administratie van CYP3A4-substraten terfenadine, astemizol, cisapride, pimozide, halofantrine of kinidine, omdat verhoogde plasmaconcentraties van deze middelen kunnen leiden tot QTc-verlenging en zelden tot torsades de pointes; co-administratie van de HMG-CoA-reductaseremmers simvastatine, lovastatine en atorvastatine. **BELANGRIJKSTE WAARSCHUWINGEN EN VOORZORGEN BIJ GEBRUIK** Voorzichtigheid is geboden bij overgevoeligheid voor andere azolen. Met voorzichtigheid gebruiken bij leverfunctiestoornis i.v.m. beperkte klinische ervaring en mogelijke verhoogde posaconazolplasmaconcentraties. Leverreacties (verhoging ALAT, ASAT, alkalische fosfatase, totale bilirubine en/of klinische hepatitis) zijn gemeld; leverfunctiestoornissen waren meestal reversibel bij staken. Zelden zijn fatale leverreacties gezien. Het therapeutisch beleid moet laboratoriumbeoordeling van de leverfunctie omvatten, m.n. leverfunctietesten en bilirubine, bij starten en tijdens de behandeling. Bij abnormale functiestwaarden regelmatig controleren op ontwikkeling van ernstigere leverbeschadiging. Staken moet overwogen worden bij klinische tekenen van het ontstaan van een leveraandoening. Sommige azolen zijn geassocieerd met QTc-verlenging. Noxafil mag niet worden gegeven met CYP3A4-substraten die QTc-verlenging geven. Met voorzichtigheid toedienen bij pro-arritmische aandoeningen, zoals congenitale verworven QTc-verlenging, cardiomyopathie m.n. met hartfalen, sinusbradycardie, bestaande symptomatische aritmieën, gelijktijdig gebruik van andere middelen die QTc-interval verlengen. Electrolytstoornissen, m.n. kalium, magnesium of calcium, moeten gecontroleerd en gecorrigeerd worden zolang als nodig vóór en tijdens behandeling. Noxafil remt CYP3A4 en mag alleen gebruikt worden onder specifieke omstandigheden met andere CYP3A4 substraten. I.v.m. risico op verlengde sedatie en respiratoire depressie mag co-administratie van posaconazol met benzodiazepinen die door CYP3A4 gemetaboliseerd worden (bijv. mid- tria-, alprazolam) alleen indien strikt noodzakelijk. Overweeg dosisaanpassing van door CYP3A4 gemetaboliseerde benzodiazepinen. Gelijktijdige toediening van azole antimycotici, waaronder posaconazol, met vincristine is in verband gebracht met neurotoxiciteit en andere ernstige bijwerkingen, waaronder convulsies, perifere neuropathie, anti-duretisch hormoon-secretie-deficiëntiesyndroom en paralytisch ileus. Reserveer azole antimycotici, waaronder posaconazol, voor patiënten die een vinca-alkaloïd ontvangen, waaronder vincristine, die geen andere mogelijkheden hebben voor behandeling met antimycotici. Rifampicine antibiotica (rifampicine, rifabutine), sommige anticonvulsiva (fenytoïne, carbamazepine, fenobarbital, primidon), efavirenz en cimetidine (niet voor Noxafil i.v.) kunnen posaconazolconcentraties significant verlagen. Vermijd gelijktijdig gebruik tenzij het voordeel opweegt tegen het risico. Farmacokinetische gegevens bij ernstige gastro-intestinale stoornissen zijn beperkt. Bij ernstige diarree of braken is zorgvuldige controle nodig i.v.m. eventuele doorbraak van schimmelinfecties (waarschuwing GI-stoornissen n.v.t. voor Noxafil i.v.). Noxafil tabletten en Noxafil iv bieden over het algemeen een hogere blootstelling aan het geneesmiddel in het plasma dan de Noxafil orale suspensie. Veiligheidsgegevens over hogere blootstellingspiegels bij tabletten en iv zijn beperkt. Raadpleeg SPC voor alle interacties. Noxafil orale suspensie bevat 1,75% w/v glucose, daarom niet gebruiken bij glucose-galactose malabsorptie. **Alleen voor Noxafil i.v.:** 1) ivm effect op QTc-interval bijzondere voorzichtigheid betrachten bij perifere toediening omdat bij aanbevolen infusietijd van 30 min. C_{max} verder kan stijgen. 2) wegens variabiliteit in blootstelling, patiënten met ernstige nierfunctiestoornis monitoren voor doorbraak van schimmelinfecties. 3) trombo-embolische voorvallen zijn een potentieel risico, maar zijn niet waargenomen tijdens klinische studies; voorzichtigheid is geboden bij trombofobes. Elke injectieflacon Noxafil bevat 462 mg (20 mmol) natrium. Hiermee rekening houden bij natriumarm dieet. **BIJWERKINGEN** Zeldzaam: misselijkheid/jaak; neutropenie, versterking van elektrolytenbalans, anorexie, verminderde eetlust, hypokaliëmie, hypomagnesiëmie, paresthesie, duizeligheid, slaperigheid, hoofdpijn, dysgeusie, hypertensie, braken, abdominale pijn, diarree, dyspepsie, droge mond, flatulentie, constipatie, anorectaal ongemak, verhoogde leverfunctiestwaarden (ALAT, ASAT, bilirubine, alkalische fosfatase, GGT), rash, pruritus, pyrexie (koorts), asthenie en vermoeidheid. **Soms:** trombocytopenie, leukopenie, anemie, eosinofilie, lymfadenopathie, miltrinfarct, allergische reactie, hyperglykemie, hypoglykemie, abnormaal dromen, verwarde toestand, slaapproblemen, convulsies, neuropathie, hypo-esthesie, tremor, afasie, slapeloosheid, wazig zien, fotofobie, verminderde gezichtsscherpte, lange QT-syndroom, abnormaal ECG, palpaties, bradycardie, supraventriculaire extrasystolen, tachycardie, hypotensie, vasculitis, hoesten, bloedneus, de hik, verstopte neus, pijnlijke pleuritis, tachypneu, pancreatitis, abdominale distensie, enteritis, epigastrisch ongemak, oprisping, gastro-oesofageale refluxziekte, maandoeseem, hepatocellulaire schade, hepatitis, gezichts, hepatomegalie, cholestase, leverfunctiestoornis, abnormale leverfunctie, monoduratie, alopecia, dermatitis, erythem, petechiae, rugpijn, nekpijn, musculoskeletale pijn, pijn in extremiteit, (acuut) nierfalen, verhoogd bloedcristalin, mensstratiestoornis, oedeem, pijn, koude rillingen, malaise, pijn op de borst, geneesmiddelenintolerantie, zich zenuwachtig voelen, mucosale ontsteking, veranderende geneesmiddelenpiegels, verlaagd bloedtoeflow en afwijkende thoraxvoflow. Post-marketing is ernstige leverbeschadiging met fatale afloop gemeld bij Noxafil orale suspensie. Bijkomende bijwerkingen voor Noxafil iv (soms): tromboflebitis; pijn, flebitis of trombose op infusieplaats en slijmvliesontsteking. Zie SPC voor alle bekende bijwerkingen. **REGISTRATIEHOUDER** MSD Ltd, Hertford Road, Hoddesdon, Hertfordshire EN11 9BU, UK **LOKALE VERTEGENWOORDIGER** MSD BV, tel. 0800 9999 000, medicalinfo.nl@merck.com. **REGISTRATIENUMMERS** EU/1/05/320/001, 002, 004 **VERGODENING** Voldoelig vergoed. **AFLEVERSTATUS** UR Datum April 2017