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SHORT COMMUNICATIONS OPEN ACCESS

A model for upstream signalling in the control of capillary blood flow

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Abstract

Blood supply to tissues is controlled through vasoconstriction and vasodilation activated by components of the vascular wall and smooth muscle cells. Local oxygen saturation and wall shear stress play an important role in this process and wall shear stress has a role in capillary and venular flow as well as flow in arterioles and arteries. Local capillary networks can dilate to increase flow but there is little clear evidence of how local capillary networks act to increase arteriolar blood flow when needed. Pulsatile flow plays an important part in signalling wall shear stress within the vascular system and it has recently been shown that pulse pressure changes can be efficiently transmitted along soft walled fluid filled tubes such as blood vessels. This confirms that pulse pressure within the system can maintain downstream flow; it also raises the question of whether pulse pressure changes can signal upstream from local capillary beds to the supplying arteriole.

Keywords: blood supply; capillary blood flow; pulse pressure

Introduction

Blood vessels are soft walled fluid filled tubes; recent physics research has demonstrated efficient propagation of pressure pulses along the length of soft walled fluid filled tubes [1]. Research has also shown that maintenance of pulsatile flow improves microcirculatory perfusion during extracorporeal membrane oxygenation; the pulsatile shear stress and endothelial glycocalyx maintaining microcirculatory function and integrity [2]. These findings would support other research that suggests control of blood flow in tissues is mediated by oxygen saturation in the venules. In this model reduced oxygen saturation combined with oxidation products in the draining venule cause the venule to dilate; this will allow more capillary blood to flow into the venule. Within the existing model of blood flow control there is little ability for the tissues to signal the need for an increase in supply to the capillary bed. However, with an intact glycocalyx combined with pulsatile flow, the increase of flow in the draining venule would cause a small pressure pulse to propagate back up the soft walled fluid filled microvascular tubes to the capillaries and from there to the arterioles. With an intact glycocalyx within the venules, capillaries, and arterioles this pulse could signal to the arterioles the need to dilate. Whilst there is no direct evidence of the pressure pulse propagating signals from the draining capillary to the supplying arteriole, recent research in rat brains has shown that the oxygen saturation in a venule draining a section of the brain will change by only a few percent whilst the oxygen consumption in the tissue and the blood flow to the tissues doubles over two seconds and returns to normal within three seconds; this level of change would require some form of signal passing from the tissues to the supplying arteriole [3].

We know the vascular system is structured to supply oxygenated blood to the tissues, and the control of vascular tone and arterial pressure in humans is fairly well understood, from the carotid baroreceptors to structural components of the vascular wall, endothelial

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cells and smooth muscle cells. However, there is no clearly described system for maintaining an appropriate supply of oxygenated blood to the capillaries. The model described above would integrate the previously proposed systems for control of blood flow within the tissues right up to the most recent research where oxygen saturation and metabolic compounds within the microvessels can mediate local vessel dilation [4-6]. The aim of this review is to describe our microvascular periodontal research over a fifteen year period and how unexpected results and incidental findings suggest that shear stress acting on the endothelial glycocalyx may act to control blood flow, from arteries to capillaries and venules, in humans.

Periodontal research

All pathogens known to cause periodontal disease in humans are obligate anaerobes which thrive in tissues with low oxygen tension [7]. In addition to this all individuals presenting with periodontal disease are found to have very low oxygen levels in their periodontal tissues [8]. The obvious conclusions were that: (a) lack of oxygen is promoting the growth of the pathogenic organisms, (b) investigating the low oxygen level in the periodontal tissues will find the cause of periodontal disease. With this aim our team have investigated the low oxygen level in the periodontal tissues over a period of fifteen years; starting with the development of a video probe to image the microvascular system in the periodontal tissues and then a baseline imaging study in healthy volunteers [9, 10]. This was followed by developing a method to analyse oxygen saturation within the imaged microvessels and then investigating the relationship between vascular fragility and the endothelial glycocalyx in the same tissues [11, 12]. This led to the conclusion that loss of the glycocalyx causes the development of venular capillaries in some individuals. These venular capillaries are very fragile and when they breakdown they cause the release of heme which essential for the growth of P gingivalis which is the primary pathogen in the development of periodontal disease [13]. All of the diseases which carry an increased risk of periodontitis are also associated with the development of fragile venular capilliaries; which has led us to conclude that periodontal disease is not caused by the low oxygen level but by the development of fragile venular capillaries linked to loss of the glycocalyx [14].

Incidental findings in periodontal research

The initial aim of our research was to investigate the increase volumes of deoxygenated blood found in periodontally inflamed tissues. However, we also found increased volumes of deoxygenated blood in patients with slight gingival inflammation but no periodontal disease. The plaque induced gingival inflammation led to vascular stasis with loss of the endothelial glycocalyx in some people whilst in others there was microvascular dilation with increased flow and an intact glycocalyx. As part of the research we also measured oxygen levels along the length of individual sublingual and labial capillaries imaged microscopically. This proved to be difficult as the pulsed blood flowing from the arteriole through the capillary and into the venule caused changes in individual vessel dimensions as well as optical density and oxygen saturation over the cardiac cycle, leading to different measurements at any given moment. We overcame this problem by simply averaging all measurements over a full cardiac cycle which gave clear results. Then in a final study we showed that plaque accumulation over three weeks led to reduced flow associated with development of venular capillaries in some people and maintenance of flow in participants who did not develop venular capillaries.

We did not include the individual variations in vessel dimensions in the research findings as they were not part of the aims and objectives. However, we noted that as the arterial blood flowed into the healthy capillary there was a reduction in the measured diameter of the capillary; then as the pulse of blood flowed into the associated venule there was an increase in diameter and increase in speed of flow. Once the pulse had passed then the microvessels and the speed of flow returned to the initial value.

These changes in capillary and venular dimensions imaged in healthy well oxygenated tissues would reduce the size of any pulse pressure propagating back up the arteriolar system. If on the other hand the venule and capillary had dilated due to low oxygen saturation then this could in turn increase the size of any pulse pressure propagating back up the arteriolar system. This model would support the possibility of the pulse pressure propagation acting on the upstream glycocalyx to control the supply of blood to the tissues. Our final study with loss of glycocalyx leading to vascular stasis and development of venular capillaries during plaque accumulation in some subjects would also suggest the loss of the ability to signal upstream to increase blood flow.

Upstream signalling

Accumulation of dental plaque leads to gingivitis along with increased blood flow, and dilated blood vessels; but in those who subsequently develop periodontal disease there is then a significant reduction in blood flow and oxygen supply to these dilated vessels [14, 15]. However,

the vascular resistance measured by mechanically infusing the supplying arteriole shows that the passive vascular resistance in periodontally inflamed tissues is significantly reduced [16]. How can the blood flow to periodontally inflamed tissues be reduced when the vascular resistance is also reduced?

This would support the theory of upstream signalling to the arterial tree and loss of the glycocalyx causing loss of the upstream signalling. There is little evidence to confirm this model of upstream signalling, however the model would integrate nearly all published microvascular research findings. This is particularly evident in cerebral blood flow described by Bouchard; arteriolar flow in a 1mm region can increase by 100% over three seconds and return to normal over four seconds and yet the venular oxygen saturation draining the area remains stable with no change beyond a few percentage points, and no change at all in neighbouring regions [17]. This model would integrate with the dynamic wall signalling described by Chen and Li, and recent research supporting the role of capillaries in regulation of skeletal muscle oxygen supply [4, 5]. It would also integrate the role of red blood cell and wall derived mechanisms for metabolic blood flow regulation [18].

Conclusion

This report describes only incidental research findings. However, the model described integrates with existing research and provides a simple mechanism to explain control of microvascular blood flow in humans.

Conflicts of interest

Author declares no conflicts of interest.

References

[1] Levitsky S, Bergman R. Pressure pulse propagation in a double-layered elastic tube with viscoelastic liquid. J Phys Conf Ser. 2018; 1141:012080.

[2] Zhang Y, Zeng J, He X, Cao W, Peng X, et al. Pulsatility protects the endothelial glycocalyx during extracorporeal membrane oxygenation. Microcirculation. 2021; 28:e12722.

[3] Yaseen MA, Srinivasan VJ, Sakadia S, Radhakrishnan H, Gorczynska I, et al. Microvascular oxygen tension and flow measurements in rodent cerebral cortex during baseline conditions and functional activation, J Cereb Blood Flow Metab. 2011; 31:1051–1063.

[4] Chen M, Li X. Role of TRPV4 channel in vasodilation and neovascularization. Microcirculation. 2021; 28:e12703.

[5] Ghonaim NW, Fraser GM, Goldman D, Milkovich S, Yang J, et al. Evidence for role of capillaries in regulation of skeletal muscle oxygen supply. Microcirculation. 2021; 28:e12699.

[6] Ribatti D, Tamma R. Epigenetic control of tumor angiogenesis. Microcirculation. 2020; 27:e12602.

[7] Loesche W, Gusberti F, Mettraux G, Higgins T, Syed S. Relationship between oxygen tension and sublingual bacterial flora in untreated human periodontal pockets. Infect Immun. 1983; 42:659-667.

[8] Llu K, Xiang X, Man A, Sowa M, Cholakis A, et al. In vivo determination of multiple indices of periodontal inflammation by optical spectroscopy, J Perodontal Res. 2009; 44:117–124.

[9] Townsend D, D'Aiuto F. Periodontal capillary imaging in vivo by endoscopic capillaroscopy. J Med Biol Eng. 2010; 30:119–123.

[10] Townsend D, D'Aiuto F, Deanfield J. Preliminary study of video imaging of blood vessels in tissues lining the gingival sulcus in periodontally healthy individuals. J Periodontal Res. 2014; 49:670–679.

[11] Townsend D, D'Aiuto F, Deanfield J. Vascular fragility and the endothelial glycocalyx in the tissues lining the healthy gingival crevice. J Periodontology. 2016; 87:1–16.

[12] Townsend D, D'Aiuto F, Deanfield J. In vivo capillary loop hemoglobin spectroscopy in labial, sublingual and periodontal tissues, Microcirc. 2015; 12:475–484.

[13] Olczak T, Simpson W, Liu X, Genco C. Iron and heme utilization in Porphyromonas gingivalis, FEMS Microbiological Review. 2005; 29:119–144.

[14] Townsend D. Identification of venular capillary remodelling: a possible link to the development of periodontitis? J Periodontal Implant Sci. 2021; 51:e40.

[15] Zhang C, Xiang X, Xu M, Fan C, Sowa M, et al. Assessment of tissue oxygenation of periodontal inflammation in patients with coronary artery disease using optical spectroscopy. BMC Oral Health. 2014; 14:25.