Short communication

Interventional Cardiology

Efficacy of Rheocarna® in no-option chronic limb-threatening ischemia

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Abstract

In 2021, a new low-density lipoprotein apheresis device (Rheocarna®; Kaneka Corporation, Osaka, Japan) was developed in Japan for treating Chronic Limb-Threatening Ischemia (CLTI) with refractory ulcers (Rutherford classification score, 5 or 6), referred to as no-option CLTI. This device eliminates key contributors to CLTI such as Low-Density Lipoprotein Cholesterol (LDL-C) and fibrinogen. Rheocarna® therapy might enhance skin perfusion pressure, reduce LDL-C, fibrinogen, and C-reactive protein levels, and improve acute-phase angiography findings, leading to better microcirculation and wound healing and help maintain chronic-phase blood microcirculation and wound healing. This study demonstrates that Rheocarna® may be a viable treatment option for no-option CLTI.

Keywords: Rheocarna® • Low-density lipoprotein apheresis • Chronic limb-threatening ischemia

Abbreviations: CLTI: Chronic Limb-Threatening Ischemia; LDL-A: Low-Density Lipoprotein Apheresis; LDL-C: Low-Density Lipoprotein Cholesterol; SPP: Skin Perfusion Pressure; CRP: C-Reactive Protein; ACE: Angiotensin-Converting Enzyme

Description

Chronic Limb-Threatening Ischemia (CLTI) represents the final stage of lower-extremity artery disease, defined as the presence of peripheral artery disease combined with pain at rest, gangrene, or lower-limb ulceration for over 2 weeks, is associated with a poor prognosis for the affected limb [1]. Arterial revascularization *via* bypass surgery or endovascular therapy is the most effective treatment for wound healing in CLTI [2]. However, clinicians often encounter challenging cases in which revascularization may fail or be impractical that are referred to as no-option CLTI [3-5]. Below-the-knee disease can be challenging because of its anatomical and lesional characteristics [6]. In such cases, adjunct therapies such as apheresis, vascular regenerative therapy, hyperbaric oxygen therapy, and spinal cord stimulation therapy play an important role. Appropriate wound management by wound specialists and multidisciplinary teams is necessary to avoid major amputations.

Rheocarna® device, uses porous cellulose beads containing negatively charged dextran sulfate and hydrophobic tryptophan, eliminates key contributors to CLTI, such as LDL-C and fibrinogen, unlike conventional LDL-A (Liposorber®; Kaneka Corporation, Osaka, Japan), which removes only LDL-C [7]. In addition, unlike conventional LDL-A (Liposorber®; Kaneka Corporation, Osaka, Japan), the Rheocarna® is not required in cases of treatment-resistant hyperlipidemia. Additionally, up to 24 sessions over a 3-month period are covered by insurance. Rheocarna® therapy might enhance SPP, reduce LDL-C, fibrinogen, and CRP levels, and improve acute-phase angiography

findings, leading to better microcirculation and wound healing [8,9]. Furthermore, we recently reported that Rheocarna® therapy might help maintain chronic-phase blood microcirculation and wound healing [10].

Two other reports in Japan showed that wound healing was achieved with Rheocarna® treatment in 45.9% and 68.4% of patients with no-option CLTI. The efficacy of Rheocarna® includes improved microcirculation and wound healing in no-option CLTI. Moreover, Rheocarna® is believed to enhance inflammation and reduce tissue edema, leading to improved microcirculation. The most common complication is hypotension, possibly due to bradykinin production. Thus, an ACE inhibitor should be withheld before the initial Rheocarna® therapy.

Fibrinogen is a key determinant of whole-blood viscosity, a critical factor in blood flow rheology that influences the microcirculation in lower-extremity arterial diseases. CLTI comprises microcirculatory diseases involving impaired blood flow rheology. A reduction in fibrinogen levels seems to influence whole-blood viscosity by decreasing erythrocyte aggregation, potentially through increased electrical repulsion between erythrocytes, which may enhance the microcirculation and wound healing [11]. Therefore, modulating fibrinogen levels is an important therapeutic target. For these reasons, Rheocarna® can be considered a viable treatment for no-option CLTI.

Similar to fibrinogen, LDL-C and CRP are viscosity-related factors. Reports have shown that hyperlipidemia leads to hemorheological impairments and that a decrease in LDL-C levels may reduce blood viscosity and enhance blood supply to wounds [12]. Guidelines strongly recommend statin therapy to prevent all-cause and cardiovascular mortality in patients with CLTI. Elevated CRP levels are related to major amputations, suggesting that a decrease in CRP levels may enhance wound healing [13]. Therefore, the modulation of LDL-C and CRP levels is also an important therapeutic target. Rheocarna® can be considered a viable treatment option for no-option CLTI for these reasons as well.

SPP measurement, a reliable method for evaluating the microcirculation, is unaffected by arterial calcification, unlike other physiological tests such as ankle-brachial pressure index and toe pressure [14]. Therefore, SPP measurement is the standard evaluation method for patients with CLTI in daily practice [15]. SPP measurement is also an accurate predictor of wound healing, and an SPP ≥40 mmHg can indicate successful wound healing [16,17]. The Rheocarna® may reduce fibrinogen levels and improve SPP, improving microcirculation and wound healing in no-option CLTI.

Hemodialysis is a known risk factor for CLTI, and patients with CLTI on hemodialysis have a poorer limb prognosis than those with CLTI but not on hemodialysis. The number of patients with CLTI on hemodialysis is higher inside than outside Japan [18,19]. Therefore, patients with CLTI and on hemodialysis are the main therapeutic targets. Vascular access for Rheocarna® therapy is achieved through a regular dialysis access puncture site. In patients not on hemodialysis, catheters are commonly inserted into the cervical veins. However, such catheters carry the risk of infection and discomfort. Therefore, Rheocarna® therapy is relatively easy to introduce for patients with CLTI on hemodialysis.

Conclusion

Rheocarna® may be a viable treatment for no-option CLTI and may enhance SPP, reduce LDL-C, fibrinogen, and CRP levels, and improve angiography findings with effects that potentially persist from the acute to chronic phase, leading to better microcirculation and wound healing. Rheocarna® is particularly well-suited for patients with no-option CLTI on hemodialysis. Further prospective studies with larger sample sizes are warranted to validate these findings.

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Competing and Conflicting Interests

The authors declare that they have no conflicts of interest.

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