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Novel synthesis of magnetic nanoparticles conjugation with perfluorocarbon nanobubbles for potential adjunct therapy of acute myocardial ischaemia

Synteza nowego koniugatu nanocząsteczek magnetycznych z nanopęcherzykami perfluorowęglowodoru jako potencjalnej terapii wspomagającej w ostrym niedokrwieniu mięśnia sercowego

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Abstract

Introduction. This study was performed in search of a novel adjunct agent for myocardial salvage in acute myocardial ischaemia.

Methods and results. This is a report of conjugation between perfluorocarbon nanobubbles with multifunctional biocompatible magnetic nanoparticles. It was possible to synthesise the conjugation of multifunctional biocompatible magnetic nanoparticles with perfluorocarbon nanobubbles. The potential nano-size magnetic product could cross the deranged endothelial borders in the ischaemic penumbra regions, and could help in myocardial salvage. Furthermore, the particles could be focused to the target region using the magnetic micromesh technique.

Conclusions. A conjugation between magnetic nanoparticles and PFC nano-bubbles is possible. Further studies need to be performed to explore the potential uses.

Key words: acute myocardial infarction, pharmacology, basic science research, hypoxia

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Introduction

Perfluorocarbons (PFC) are known to have a high affinity for oxygen, and they are useful as oxygen carriers. The combination of perfluorocarbons with magnetic nanoparticles would be useful to penetrate endothelium and supply oxygen because of their size. The potential aim of this study was to prepare this conjugate and analyse its basic characteristics. This could help in myocardial salvage or reduced infarct size, which is potentially very useful.

Methods and results

Perfluorocarbon nanobubbles were prepared using standard techniques [1]. PFC nanobubbles-magnetic nanoparticle conjugation was performed, and the final solution prepared had a pH of 8.0. The conjugation was performed to form covalent bonding and phosphate buffered saline (PBS) buffer was used. The final preparation was an emulsion with a PFC content of 25% and 40% concentration in each emulsion of 300 μL. The final volume achieved in the

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Figure 1. Photo image under microscope of the perfluorocarbons (PFC) nanobubble — magnetic nanoparticle conjugate emulsion

synthesis was 300 μL of each concentration, and the final compound was stable. The final sample when evaluated under microscope gave an image shown in Figure 1. The polydispersity index was < 0.25. The magnetic nanoparticle concentration was 15 mg/mL and the particle concentration in 300 μL was 4.5 mg. A drop of emulsion subjected to the magnetic field by a small magnet tends to polarise to one side due to the effect of the magnetic field. These particles are easy and respond quickly to the magnetic field. On a glass slide when allowed to dry the conjugate forms a thick film like a mountain, and when a small amount of water is added and a small magnet is applied nearby, the particles start moving towards the magnet.

A drop of the emulsion can be diluted with water or diluted podium dodecyl sulfate (SDS) solution, and the particle sizes can be measured by dynamic light scattering. The particle sizes were estimated by dynamic light scattering, and the magnetic nanoparticles were of 100 to 200 nm, and they were magnetically active, which has been proven in other studies [2–4]. These nanoparticles were multifunctional and highly biocompatible, again as demonstrated in other studies. A previous study showed the generation of high magnetic gradients using mesh, and through these remarkably high gradients, the magnetic nanoparticles movements could be controlled [4]. Using this, previous studies have shown that these particles can be activated on selected targets for effective drug delivery [1–4]. In ischaemic regions, oxygen could be delivered using the magnetic grid and magnetically conjugated particles. In myocardial infarction, the coronaries are like end arteries, and they are cutoff by the arterial occlusion. Hence, these nanoparticles can reach the penumbra of the infarct through their neighbouring blood vessels or branches, and they could deliver oxygen and thereby could have the potential to reduce infarct size [5]. Ultrasonication of these multifunctional particles is feasible, and they can be activated by ultrasound [6–8]. Potential further improvised conjugation with tripeptide Arg-Gly-Asp (RGD) and other bio-molecules is feasible. However, a simple oxygen gradient in ischaemic tissues is good enough to release oxygen from the nanodroplets. Perfluorocarbon nanobubbles have shown to prevent injury in ardiomyocytes subjected to hypoxia [9].

This is the first known synthesis of these magnetic nanoparticles with perfluorocarbon nanodroplets conjugation. However, further experiments are required to study its properties in greater detail. Also, physical evaluation with X-ray diffraction crystallography and scanning electron microscopy observations are required. This is the first preparation, and further evaluation with a large sample volume is required for the next phase. The samples could be estimated by tissue culture in Matrigel in various concentrations to evaluate their tissue penetration and oxygen delivery properties under magnetic fields.

Conclusions

A conjugation between magnetic nanoparticles and PFC nano-bubbles is possible. Further studies need to be performed to explore the potential uses.

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None.

Conflict(s) of interest

The author report no conflict of interest.

Streszczenie

Wstęp. Celem badania było poszukiwanie nowych leków wspomagających zachowanie żywotności miokardium po ostrym niedokrwieniu mięśnia sercowego.

Metody i wyniki. W niniejszej pracy opisano koniugację nanopęcherzyków perfluorowęglowodoru z biokompatybilnymi wielofunkcyjnymi nanocząsteczkami magnetycznymi. Okazało się, że możliwa jest synteza koniugatu wielofunkcyjnych biokompatybilnych cząstek magnetycznych z nanopęcherzykami perfluorowęglowodoru. Otrzymane w ten sposób nanocząsteczki magnetyczne mogą przenikać przez uszkodzony śródbłonek w regionie otaczającym obszar zawału i mogłyby zostać wykorzystane do ratowania mięśnia sercowego przed trwałym uszkodzeniem. Ponadto cząsteczki te można doprowadzić do docelowego miejsca, stosując technikę mikrosiatki magnetycznej.

Wnioski. Koniugacja między nanocząsteczkami magnetycznymi a nanopęcherzykami perfluorowęglowodoru jest możliwa. Należy przeprowadzić dalsze badania nad możliwościami ich wykorzystania.

Słowa kluczowe: ostry zawał serca, leczenie farmakologiczne, nauki podstawowe, hipoksja

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