MORE EFFECTIVE TREATMENT OF ALI BY THROMBOLYSIS WITH MICROBUBBLES AND ULTRASOUND

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DISCLOSURES

• MEDAC GMBH
• BTG, INTERVENTIONAL MEDICINE

THROMBOLYSIS

• ACUTE PERIPHERAL ARTERIAL OCCLUSIONS
• THERAPY: CATHETER DIRECTED THROMBOLYTIC INFUSION WITH UROKINASE, (R)TPA
• TREATMENT DURATION 12–96 H

HAEMORRHAGES ARE NOT RARE

<table>
<thead>
<tr>
<th>Major haemorrhage</th>
<th>Intracranial haemorrhage</th>
<th>Minor haemorrhage</th>
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<tbody>
<tr>
<td>6%</td>
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BETTER, SAFER AND FASTER THROMBOLYSIS IS NEEDED

ROLE FOR MICROBUBBLES, NANOPARTICLES AND NANOCARRIERS
MORE PRECISE, LOCAL DELIVERY AND TREATMENT OF VASCULAR DISEASES

MICROBUBBLES

OSCILLATE WHEN SUBJECTED TO LOW INTENSITY US AND CAN CAVITATE WHEN SUBJECTED TO HIGH INTENSITY US
MICROBUBBLES

- Initial for diagnostic use as intravascular contrast enhancers

ADVANTAGES OF MICROBUBBLES

Non-specific mechanical effects → thrombus breakdown due to mechanical force of microbubbles + ultrasound

IN VITRO EXPERIMENTS WITH A THROMBUS MODEL

TARGETED BUBBLES

Carry thrombolytics to the specific thrombus
NO CATHETER NEEDED

IN-VITRO STUDY WITH TARGETED BUBBLES

- FLUORESCENT LABELED UROKINASE

IN-CORPORATED IN THE BUBBLE
ON THE OUTER LIPID SHELL

MORE PRECISE DELIVERY AND NO NEED FOR A CATHETER

SUMMARY OF OUR ANIMAL STUDIES

<table>
<thead>
<tr>
<th>Control group</th>
<th>Microbubbles saline, in 1 hour</th>
<th>Microbubbles saline, in 1 hour</th>
<th>Targeted Microbubbles carrying UO 50,000 IU in 1 hour</th>
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<tbody>
<tr>
<td>Catheter</td>
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<tr>
<td>Urokinase</td>
<td>500,000 IU UO bolus 50,000 IU UO/ hour for 3 hours</td>
<td>50,000 IU UO/ in 1 hour</td>
<td>Urokinase 500,000 IU UO bolus 50,000 IU UO/ hour for 3 hours</td>
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<td>N=6</td>
<td>N=4</td>
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</tbody>
</table>
RESULTS OF OUR ANIMAL STUDIES

Thrombus weight (gr) at the end of the experiment

No haemorrhagic complications were observed during autopsy.

BMJ Open  Microbubbles and UltraSound-accelerated Thrombolysis (MUST) for peripheral arterial occlusions: protocol for a phase II single-arm trial

Harm P Wille,1,2 Johannes H Haverkamp,2 Roger J Up,2 Willem Ritsema,2 Kalhiko Young,2 on behalf of the MUST collaboration

NEW CONCEPT: NANOCARRIERS AND NANOPARTICLES FROM MICROBUBBLES TO NANOBUBBLES

Superior for imaging and drug delivery by:
- More penetration of the target tissue through the Endothelial barrier
- Less damage of the endothelial barrier cells
- Improve longevity in blood

NANOMEDICINE AS A STRATEGY TO FIGHT THROMBOTIC DISEASES

Urokinase-Conjugated Magnetic Nanoparticles as a Promising Drug Delivery System for Targeted Thrombolytic Synthesis and Preclinical Evaluation

Anna P. Rogozhnikova,2 Anna F. Paukab,2 Andrey S. Derevs,2 Villy V. Vinyagodes,2 Igor P. Palkov,2 Alexander A. Shtukova,2 Far F. Shtukov,2 Anna M. Shkol,2 Natasha M. Kabanova,2 Dmitry S. Shtukov,2,3 and Vladim V. Vinyagodes2,3

(TPA)-LOADED IRON OXIDE NANOPARTICLES + MAGNETIC GUIDANCE
FUTURE EXPERIMENTS INCLUDE LOCAL GENE DELIVERY FOR TREATMENT OF VASCULAR DISEASES: DIABETES

Bastarrachea RA et al. 2017. IUBMB Life

FROM MICROBUBBLES TO NANOBUBBLES TO NANOBOTS

Huynh E. et al. Nature Nanotechnology. 2015

NANOMEDICINE IS THE FUTURE FOR MORE PRECISE LOCAL TREATMENT OF VASCULAR DISEASES

http://boards.medscape.com/forums

http://english.varthabharati.in/health/nano-bubbles-filled-with-drug-may-kill-cancer-cells-study

Courtesy of Wei Deng. CNBP