Plan Overview

A Data Management Plan created using DMPTool-Stage

Title: A autofagia e a senescência celular na disfunção miccional e hiperplasia prostática benigna na obesidade

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Template: Digital Curation Centre (português)

Project abstract:

The worldwide incidence of obesity has increased dramatically in the past 25 years, and today is considered one of the most major public health problems. Clinical studies indicate a strong correlation between obesity and genitourinary tract diseases, such as voiding dysfunction and benign prostatic hyperplasia (BPH). Experimental studies demonstrated impaired voiding cycle and increased cell proliferation, resulting in prostate enlargement, in high-fat diet (HFD)-induced obese animals. Furthermore, obesity led to prostate and detrusor smooth muscle hypercontractility, which contributes to BPH and voiding dysfunction, respectively. However, the pathophysiology of the bladder and prostate impairments in obesity remains poorly understood and the available clinical treatments show low effectiveness. Recent and independent studies have been shown the reduction in autophagy process and the increase in oxidative stress levels and senescent cells accumulation in the genesis/maintenance of metabolic and tissue impairments, secondary to obesity. Nonetheless, little is known about the role of these alterations in the obesity-associated genitourinary tract dysfunctions. Preliminary studies evaluated the effects of obesity in the prostatic and bladder function. We demonstrated that the ventral prostatic weight, a parameter increased in BPH patients, was increased in obese mice. We also found ventral prostate and bladder smooth muscle hypercontractility induced by phenylephrine and carbacol in obese group, respectively. Obesity increased by 56% and 31% the basal levels of reactive oxygen species (ROS) in ventral prostatic and bladder tissues of obese group compared with control animals. *In vivo* protocols using cistometry assay revealed obesity-induced voiding impairments, characterized mainly by increase in voiding frequency in obese group. Our results also indicated increase in β-galactosidase positive cells (a marker for cellular senescence) and reduction in LC3 protein expression (protein involved in autophagy process) in ventral prostate of obese group. Therefore, we hypothesized that BPH and voiding dysfunction, secondary to obesity, have in common a reduction in local autophagy process with consequent unbalance in tissue oxidative state. The increased levels

of ROS levels lead to augmented senescent cells accumulation, which are responsible for inflammatory interleukins and growth factor release. The senescent-associated secretory phenotype (SASP) of senescent cells would exert a key role on smooth muscle hypercontractility and tissue growth and/or remodeling seen in obesity-associated BPH and LUTS. Thus, the aim of the present project is to evaluate functional, structural and molecular alterations by high-fat diet-induced obesity in ventral prostate and bladder from obese mice, focusing in the link between obesity, reduced autophagy process and senescent cells accumulation in the genesis of BPH and LUTS. We also intended to evaluate the effects of chronic treatment with drugs that modulate the autophagy process and senescent cells accumulation, aiming to restore the voiding and prostatic patterns in the obese group. If our hypothesis is right, the pathways involved in autophagy activation and consequently senescent cells reduction will represent new therapeutic target for the development of new drugs to treat obesity-related voiding and prostatic impairments.

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Copyright information:

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Serão avaliados dados relacionados à contratilidade da musculatura lisa prostática e vesical de camundongos controle e obeso. Curvas concentração-resposta à agonistas muscarínicos (ex: carbacol e acetilcolina) e alfa (fenilefrina) e beta adrenérgicos (isoproterenol) serão realizadas. Os resultados serão expressos como mN (unidade de força) e serão coletados utilizando o software Labchart 8.0 - AD Instruments (Austrália), tabulados utilizando o programa Microsoft Excel e analisados com o auxílio do programa GraphPad Prism 6.0.

Os dados de expressão proteica e análises histológicas serão obtidos por imagem de géis de eletroforese e armazenados como arquivos TIFF.

Os dados de expressão gênica serão obtidos e analisados pelo Software StepOne Plus da Applied Biosystems.

Os dados serão coletados a partir de experimentos realizados com animais de experimentação, mais especificamente camundongos controle e obeso.

Arquivos gerados pelo MS Office (xls), figuras (TIFF) e arquivos gerados pelo equipamento StepOne sistema qPCR (EDS).

O projeto já foi submetido e autorizado pelo Comissão de Ética no Uso de Animais (CEUA) da Unicamp (nº 5655-1/2020).

Os dados obtidos serão publicados em revista científica internacional, na qual será indicado o nome e filiação de todos os autores, assim como a agência de fomento e o número do auxílio obtido.

Os dados serão armazenados na nuvem, em drive criado exclusivamente para esse propósito.

O acesso aos dados armazenados na nuvem será restrito aos participantes do projeto e contará com toda segurança oferecida pela plataforma dropbox.

Os resultados obtidos em nosso projeto poderá indicar uma nova via terapêutica no tratamento das disfunções do trato geniturinário em condições de obesidade.

Os dados serão publicados em revista internacional, garantindo assim a preservação destes a longo prazo.

Os dados serão publicados em revista científica internacional.

não

O coordenador do projeto.

Recursos já contemplados pelo auxílio obtido junto à FAPESP, como banho pra órgão isolado e financiamento para bens de consumo.
