LS18-059 - Improvement of taste perception by homoeriodictyol in cancer patients after chemotherapy

Abstract

Chemotherapeutic agents such as platinum (Pt)-based drugs play a crucial role in the treatment of cancer, but also have side effects. One of the most common side effects is taste alteration, such as increased sensitivity for bitter taste and a persistent bitter taste (phantogeusia). The resulting negative effects on appetite, nutrition and quality of life are risk factors limiting the positive outcome of therapy. Despite these far-reaching consequences, the underlying mechanisms are still unclear and an effective treatment is missing.

In our WWTF-funded project titled “Improving taste perception by homoeriodictyol (HED) in cancer patients after chemotherapy”, we therefore wanted to identify the mechanisms that lead to an enhanced bitter taste induced by Pt-based chemotherapy. We also aimed to find out whether HED, a compound that can mask bitter taste, counteracts the bitter taste caused by Pt-based chemotherapy.

When evaluating taste scientifically, study participants are required to taste the studied compound in their mouth. Since such classical sensory evaluations of chemotherapeutic drugs are obviously not possible, we used a cellular model to investigate the bitter-tasting capability of Pt-based drugs in the laboratory. Our results showed that both cis- and carboplatin induced a cellular bitterness response, with cisplatin showing stronger effects. HED effectively counteracted these cellular bitterness responses caused by the Pt-based chemotherapeutics, which supports its potential as therapeutic agent for bitter taste alterations. On a molecular level, we were able to proof that out of the 25 bitter taste receptors (TAS2Rs), which are responsible for eliciting bitter taste in humans in general, at least two are functionally involved in the Pt-based chemotherapy-induced bitterness response. Consequently, TAS2Rs can be used as molecular targets for potential therapeutics against bitter taste alterations, like HED.

Pt-based drugs are administered intravenously to patients and then distribute across the body reaching the site of cancer, but also other areas like the saliva and the oral cavity. Since Pt-based drugs present in saliva could directly interact with oral taste cells, we investigated their transport from blood to saliva to identify potential new targets for the therapy of bitter taste alterations. Using a cellular model mimicking the blood-saliva barrier, we were able to demonstrate a rapid transport of Pt-based drugs. In line with this, in our clinical pilot study on gynaecological cancer patients, Pt was also quantitated in saliva after administration of carboplatin-based chemotherapy.

Within the clinical pilot study, we showed that the sensitivity to bitter taste was increased in gynaecological cancer patients after chemotherapy with carboplatin, while rinsing the mouth with an HED solution reduced the bitterness perception. These findings underline the potential of HED as therapeutic agent in the context of carboplatin-based chemotherapy. However, HED might also be useful in other settings, since alterations of bitter taste are also reported as side effect of other chemotherapeutics.

The extent to which the use of HED in cancer patients with bitter taste changes can contribute to improve the therapy-associated side effects, such as loss of appetite, inadequate nutrition and reduced quality of life, needs to be clarified in a clinical trial.

Scientific disciplines:
Oncology (70%) | Molecular biology (25%) | Nutritional sciences (5%)

Keywords:
taste dysfunction, platin based chemotherapy, homoeriodictyol

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Further links to the persons involved and to the project can be found under
https://wwtf.at/funding/programmes/ls/LS18-059/