The oral cavity as a source of febrile neutropenia, an observational study in cancer patients treated with myelosuppressive chemotherapy

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Overall aimThe overall aim is to assess whether associations can be identified between the presence of oral/dental foci, the composition of the oral microbiome, the incidence and severity of OM, and the risk to develop FN in cancer patients treated…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ancillary infectious topics
Study type	Observational non invasive

Summary

ID

NL-OMON50743

Source
ToetsingOnline

Brief title
ORA-FEBRIS

Condition

- Ancillary infectious topics
- Miscellaneous and site unspecified neoplasms benign

Synonym
fever

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: febrile neutropenia, myelosuppressive chemotherapy, oral cavity

Outcome measures

Primary outcome

Primary study parameters/endpoints

- The presence of oral/dental foci prior to the start of chemotherapy

- The development of FN, bacteremia and/or or SIRS/sepsis

Secondary outcome

Secondary study parameters/endpoints:

- The presence of oral/dental foci and the incidence and severity of OM

- The presence of ulcerative OM and its relative contribution to FN, bacteremia and SIRS/sepsis

- The oral microbiome (bacteria/fungi) assessed by open-end sequencing in rinsing samples taken prior to chemotherapy and during routine visits for a period of 100 days following the first administration of chemotherapy

- Microorganisms identified in diagnostic blood samples from patients presenting with FN compared retrospectively with oral cavity microorganisms using DNA finger printing techniques and Q-PCR.

- To explore whether genetic polymorphisms in candidate genes demonstrate an increased risk for the development of severe OM, FN, and SIRS/sepsis

- Differences in inflammation parameters in peripheral blood at baseline and

when presenting with fever and/or mucositis.

Study description

Background summary

Febrile neutropenia (FN) is a clinically important adverse effect of myelosuppressive chemotherapy. If patients present with FN, attention is focused on well-recognized sites of origin of infection: the airways, urinary tracts, and skin. However, infections can be only documented clinically in about two-third of febrile episodes, whereas a causative microbial pathogen cannot be identified in the majority (>70%) of cases.
Pre-treatment oral evaluation aimed to identify and eliminate oral/dental foci is only routinely used in patients at high risk for oral complications (i.e. head and neck cancer patients and stem cell transplantation recipients). However, any patient treated with myelosuppressive chemotherapy, be it for cure or palliation, is at risk of developing infection in and/or originating from the oral cavity. Nevertheless, in these patients dental screening is somewhat randomly employed at the oncologist*s discretion.
More insight into the pre-treatment oral condition and its potential role in FN is mandatory, particularly considering the growing numbers of older patients retaining their natural dentition and the increase of dental diseases and cancer incidence with age.
In addition, oral diseases may aggravate chemotherapy-induced oral mucositis (OM). OM is associated with an inflammatory response, which together with ulcerations providing a portal of entry for bacteria, can result in FN and systemic inflammatory syndrome (SIRS) and/or sepsis. Evidence suggests that microorganisms are involved in the pathobiology of OM, but no longitudinal studies using open-end sequencing are available.
Furthermore, comparing bacteria identified in blood cultures in febrile patients with those of the oral cavity will expand our knowledge on the role of the oral cavity as a potential source of bacteremia.
We expect that our results will provide a scientific base for subsequent intervention studies on the efficacy of dental screening and elimination of foci, and other interventions aimed at modifying the oral environment before and during chemotherapy.

Study objective

Overall aim
The overall aim is to assess whether associations can be identified between the presence of oral/dental foci, the composition of the oral microbiome, the incidence and severity of OM, and the risk to develop FN in cancer patients treated with myelosuppressive chemotherapy.

Primary objective:
- To identify oral/dental foci prior to the start of chemotherapy and to determine whether these are associated with the development of FN, bacteremia and/or SIRS/sepsis

Secondary objectives:
- To assess whether oral/dental foci are associated with the incidence and severity of OM
- To assess whether OM is associated with FN, bacteremia and SIRS/sepsis
- To document microbiological shifts (bacteria/fungi) in oral rinsing samples taken prior to chemotherapy and during standard care visits thereafter using an open-end technique and to investigate potential associations with the development of OM
- To assess retrospectively whether any microorganisms found in blood samples from patients with FN are (likely) derived from the oral cavity using DNA finger printing techniques and Q-PCR.
- To explore whether genetic polymorphisms in candidate genes demonstrate an increased risk for the development of severe OM, FN, and SIRS/sepsis
- Differences in inflammation parameters in peripheral blood at baseline and when presenting with fever and/or mucositis.

Study design

A single-center prospective observational study.

Study burden and risks

The burden for patients is minimal, as the study is observational. It involves a non-invasive pre-chemotherapy oral examination, and collecting of oral rinsing samples (during standard care visits). In patients presenting with FN, blood samples are taken routinely as part of standard care. There are no risks or benefits for participating subjects. The anticipated knowledge gained from this study will help to improve future supportive care protocols.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Diagnosed with a solid cancer, lymphoma or multiple myeloma
- Planned treatment with myelosuppressive chemotherapy with FN risk of 10%-20% (with or without targeted therapies or hormonal therapy)
- Willing and able to give written Informed consent
- Age 18 or older
- Presence of (partial) natural dentition and/or dental implants

Exclusion criteria

- Unable to give written informed consent
- Age under 18 years
- Prior irradiation to the head and neck
- Edentulous patients

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2015
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	23-09-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28600

Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL53440.018.15
OMON	NL-OMON28600