Influences of antibiotics on biodiversity of intestinal microbiota in newborns

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1.) Is the gut flora of the healthy infant on day 3, day 7 and day 28 originally from the mother or the environment?2.) Is the process of colonizing in healthy term infants dependent on the mode of delivery?3.) Does breast milk contain bacteria and...

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal infections
Study type	Observational non invasive

Summary

ID

NL-OMON33555

Source
ToetsingOnline

Brief title
Biodiversity of Intestinal Microbiota & Antibiotics (BIMA)

Condition

- Gastrointestinal infections
- Bacterial infectious disorders

Synonym
intestinal flora, Microbiota

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Stichting Beatrix Kinderziekenhuis

Intervention

Keyword: Antibiotics, colonization, Microbiota, microflora

Outcome measures

Primary outcome

Biodiversity of intestinal microbiota in newborns.

Secondary outcome

The quantity of the specific bacteria in the intestinal microbiota of the

newborn infant.

Study description

Background summary

Introduction
The neonatal period is crucial for intestinal colonization. It is assumed that the gastrointestinal tract of newborns becomes colonized immediately after birth with organisms from mainly the mother, the role of the environment is unknown. Maternal vaginal and fecal flora provides the natural first source of colonising organisms for the neonatal gut. After this first inoculation the flora changes rapidly, presumably under the influence of diet. Some authors have suggested that the composition of the first human microbiota could have long lasting effects, up to months (Grönlund 1999) or even years (Salminen 2004).
The composition of enteric microbiota in early days of life seems therefore an important factor for achieving good health in later life.

Antibiotics and micro flora
A particularly potent means of disturbing early-colonisation patterns is by using antibiotics with a broad and unselective spectrum in the postnatal period and in the first days of life. Antibiotics are very commonly used when a neonatal sepsis is suspected without considering their impact on gut microbiota. Most studies of normal microbiota have been done in volunteers or in patients undergoing decontamination of procedures for intestinal surgery. These have reported a decrease in anaerobes, aerobes, and gram negative bacilli and an increase in yeast and E.coli after the administration of antibiotics to adults (McFarland 2000). Less is known of the impact of antibiotics on the gut flora of the newborn infant and the long term effects.

Immune system
There is evidence that intestinal bacteria play an important role in the postnatal development of the immune system (Heavey 1999, Björksten 2001). Alterations in the development of the intestinal microbiota might increase atopic disease and early wheezing (Isolauri 2008, Alm 2008). Murine studies have also demonstrated that changed early-life gut flora may promote the development of autoimmunity in genetically predisposed animals (Bach 2002).

Human milk
Human milk is a factor in the initiation and development of neonatal gut microbiota, not only because it contains prebiotic substances that promote the growth of selected bacterial groups in the infant gut (Boehm 2005), but also because this substrate represents a continuous source of micro-organisms to the infant gut during several weeks after birth (Martín 2003, Heikkilä 2003). The presence of a few predominant bacterial species in breast milk (Martin 2007) may explain why gut microbiota of breast-fed infants is composed of a narrow spectrum of species, and a more diverse microbiota develops only after weaning.

Route of delivery
Route of delivery is a major confounder for the intestinal microbiota development (Biasucci 2008). The studies about the route of delivery could not be corrected for antibiotic usage of the mothers.

It is unclear at this stage what the effects of antenatal and/or postnatal antibiotics are on the short and long term colonization with intestinal microbiota. And if this is influenced by the micro flora and breast milk of the mother.

Study objective

1.) Is the gut flora of the healthy infant on day 3, day 7 and day 28 originally from the mother or the environment?
2.) Is the process of colonizing in healthy term infants dependent on the mode of delivery?
3.) Does breast milk contain bacteria and are the equal to the flora of the mother or the infant?
4.) Does the administration of antenatal antibiotic influence the colonization of the infant?
5.) Does the administration of postnatal antibiotic influence the colonization of the infant?

Study design

- Non-therapeutic observational study in Groningen, The Netherlands and Jakarta, Indonesia.
- Only term infants (37-42 wks).

- Mother and infant will be included in one of the five groups. Five groups will be formed based on route of delivery, prescription of antenatal antibiotics and prescription on postnatal antibiotics. For more information see the flowchart and the inclusion criteria.

For all groups:
- Stool of the infants will be collected on three different moments:
1.) 3 days after birth
2.) 7 days after birth
3.) 28 days after birth
- Stool of the mothers will be collected within 3 days after birth.

For group 1 and group 5 only:
- Breast milk of the mothers will be collected on day 1 (< 24hrs), day 3, day 7 and day 28.

Study burden and risks

None

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria Group 1
• Newborn infants born by vaginal delivery
• Without any complications during both intrauterine and intra partum period
• No antenatal/postnatal antibiotics
• Normal healthy infant
• Breastfed;Inclusion criteria Group 2
• Newborn infants born by vaginal delivery
• Without complications during both intrauterine and intra partum period except minor risk factors (GBS colonisation, unknown GBS status, Temp < 39°C) to prescribe antenatal antibiotics to the mother
• Antenatal antibiotics I.V. (2-8 hours before delivery)
• No postnatal antibiotics
• Normal healthy infant
• Breastfed;Inclusion criteria Group 3
• Newborn infants born by vaginal delivery
• Without any complications during both intrauterine and intra partum period
• No antenatal antibiotics
• Postnatal antibiotic therapy started within first 12 hours after birth and discontinued within 48-72 hours (discontinued course of antibiotics).
• Normal healthy infant with low risk for early onset sepsis
• Breastfed;Inclusion criteria Group 4
• Newborn infants born by vaginal delivery
• Without any complications during both intrauterine and intra partum period
• No antenatal antibiotics
• Postnatal antibiotic therapy started within first 12 hours after birth and discontinued after one week (full course of antibiotics).
• Normal healthy infant in whom an early onset sepsis could not be excluded.
• Breastfed;Inclusion criteria Group 5
• Newborn infants born by cesarean section
• Without any complications during both intrauterine and intra partum period
• No antenatal/postnatal antibiotics
• Normal healthy infant
• Breastfed

Exclusion criteria

- APGAR Score after 5 minutes < 6
- Major congenital abnormality
- Congenital abnormonality of gastro intestinal tract

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2009
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	05-01-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL26110.042.09