Introduction

Non-invasive prenatal testing (NIPT) of cell-free fetal DNA has been entering and transforming prenatal care rapidly during the last three years, which led to a number of position statements in relation to practical standards for NIPT services from professional organisations [1–4]. At the moment, NIPT is recommended for high-risk pregnancies only, but recent studies tend to confirm good results also in low-risk populations, at least for trisomy 21 [5]. NIPT-related research in large part focuses on the testing methods, their accuracy, validity and implementation in general. However, studies and case reports with the aim to discover potential pitfalls for NIPT services regarding individual decision making and counselling in daily practice are still underrepresented. The existing studies are often hard to compare due to highly variable implementation processes and differing national regulative frameworks for prenatal testing [6]. While, for example, the UK or the Netherlands proactively have established national boards and research programs [7,8] in order to shape and monitor the implementation of the emerging technology, no such action has been taken in the majority of countries – among them Germany, where the first provider entered the market in 2012. This is particularly noteworthy, since NIPT has been defined as a genetic examination in accordance with the German Genetic Diagnostics Act (GenDG), which means among other things that a special training in genetic counselling issues is required from the offering gynecologists. The qualitative and quantitative specifications of this training are still a matter of inter- and intra-professional debate and in the meantime NIPT is being offered also by non-specialists. It is reasonable to assume that many gynecologists yet are not sufficiently prepared for offering NIPT to pregnant women. Apart from other NIPT-related aspects like the validity of the test, this is a serious problem for the implementation process in almost all countries. Studies from several countries are indicating that there are substantial educational gaps with regard to the limitations of NIPT also among maternal-fetal medicine (MFM) spe-

Abstract

While NIPT is being implemented rapidly, the implementation of a corresponding specialized counselling process in many respects lags behind. As a consequence, legal requirements and other testing conditions sometimes are not fulfilled adequately. The reported case illustrates the importance of trained personnel in the counselling and NIPT process and shows so far neglected risks for the pregnant woman and her reproductive autonomy.

Zusammenfassung

Während der nicht invasive pränatale Bluttest (NIPT) unaufhaltsam Einzug in die Praxis hält, hinkt die Implementierung eines darauf abgestimmten Beratungsprozesses in vielen Bereichen noch hinterher, sodass gesetzliche Regelungen und andere Testvoraussetzungen nicht immer eingehalten werden. Der hier beschriebene Fall eines Spätabbruchs nach missglücktem NIPT-Einsatz zeigt die Notwendigkeit von aktuellem Fortbildungsstand und Expertise bei den Anbietenden sowie die Risiken für die reproduktive Autonomie, wenn diese Bedingungen nicht erfüllt sind.

The Case of a Late Detected Trisomy 13 Reveals Structural Problems in NIPT Counselling and Highlights Substantial Risks for the Reproductive Autonomy

Nicht invasiver pränataler Bluttest (NIPT): Experten gefragt!
Der Fall einer spät entdeckten Trisomie 13 offenbart bezüglich der Beratung und bei der Implementierung des neuen Tests strukturelle Probleme, die Risiken für die reproductive Autonomie der Frau bergen

Authors

T. Ohnhaeuser, D. Schmitz

Affiliation

Institute for History, Theory and Ethics in Medicine, RWTH University, Aachen

Key words

- NIPT
- prenatal diagnosis
- counselling
- trisomy 13
- abortion

Schlüsselwörter

- NIPT
- Pränataldiagnostik
- Beratung
- Trisomie 13
- Spätabbruch

Bibliography

DOI http://dx.doi.org/10.1055/s-0042-100209
Geburtsh Frauenheilk 2016; 76: 277–279 © Georg Thieme Verlag KG Stuttgart - New York - ISSN 0016-5751

Correspondence

Tim Ohnhaeuser
RWTH University
Institute for History, Theory and Ethics in Medicine
Wendlingweg 2
52074 Aachen
tohnhaeuser@ukaachen.de

received 31.8.2015
revised 7.12.2015
accepted 3.1.2016
cialists [9], and these gaps are likely to be even more significant among non MFM. The following case may show this assumption in an unsettling clarity.

**Case**

B., a 36-year-old healthy woman (with an 11-year-old child) got pregnant in a new partnership. Her gynecologist – she knew him as being generally reluctant to do prenatal diagnosis beyond basic ultrasound (as a part of standard maternal care) – at her second visit during pregnancy (8th week of gestation) advised her not to do any further testing. Everything would go well with the baby and the maternal age would not be that important until she would be 37 years old. B., however, who had already heard about the new blood test from friends and through the media, together with her 52-year old partner decided to undergo NIPT. In Germany, NIPT is not generally covered by statutory health insurances yet (expected soon to be covered), so they would have to pay for it by themselves. She received no further counselling related to NIPT from her gynecologist, but he agreed to take the blood sample in the 11th week of pregnancy and to send it to an US provider, although he did not support this idea from his professional point of view and had no experience with the test procedure, too. When she came for her third visit in the 11th week, he had forgotten to arrange everything for the test, so that she had to wait another week and then came back. When the blood sample was taken, she was in the 12th week of pregnancy. A long time of waiting followed: after two weeks, when results should have been available at the latest, B. asked for results, but was told by the doctor’s receptionist that they had received nothing so far and that she had to wait longer. During the following days and weeks B. repeated her inquiries, but still got no information about any results. In the 18th week of gestation, the physician finally called her to let her know that the blood sample obviously had been lost in the US (according to his account). He advised her to check the bank account in order to see if any costs for the test had been debited (which had not).

She then, together with her partner and again without any further counselling, opted for a special ultrasound scan for fetal anomalies in her 20th week of gestation and thus arranged an appointment with a prenatal diagnostics specialist by herself. At her next regular visit in the 19th week, her gynecologist suspected a cardiac anomaly of the fetus during ultrasound scan. With regard to the consequences of this finding he told B., who wanted to check the bank account in order to see if any costs for the test had been debited (which had not).

As B. told us, one main reason for her to do the blood test was being able to terminate at an early gestational age in case of a serious disorder in the fetus. With his skeptical attitude towards prenatal testing, the lacking knowledge about NIPT and the resulting inactivity in his interaction with B. and the provider, the physician therefore ultimately restricted B.’s reproductive autonomy.

Since this case was not persecuted legally, we are finally not able to clarify what happened to the blood sample. The situation for German physicians regarding liability aspects has been improved since NIPT’s market launch in 2012: Lifecodexx (“PraeTest”) and Ariosa (“Harmony”) laboratories analyse blood samples in Germany CE-certified, Natera (“Panorama”) still in the United States, the German provider declares to take liability risks. However, the solution of liability questions of course does not guarantee an absence of process- and communication related risks, especially for unexperienced providers. Besides, B.’s case had been discovered accidentally during our search for pregnant women as interview partners for our research. This leads us to assume a larger estimated number of unreported cases of a failed NIPT usage, hopefully not many with similar consequences as reported here.

So, regarding this case of medical malpractice only as a physician’s individual failure, and therefore as an unfortunate exceptional event, would be shortsighted. Deficits in the regulative framework promote such potential misconduct and must be taken into consideration as well. The problem here is that regulations not only need to be improved and adjusted with regard to the new NIPT technologies. At least in Germany they have already shown to be insufficient for the regulation of established procedures of prenatal (genetic) diagnosis at all. Many well-known ethical difficulties and practical problems now simply are transferred to the new technology. It is no secret that there is often a gap between legal framework requirements such as from the GenDG and actual consultations. This gap could be re-

**Discussion**

Several insufficiencies in the medical and counselling process are obvious in this case. For a deeper understanding we focus on two levels: individual failure as well as the structural, regulative setting. On the individual level this case illustrates impressively how influential personal attitudes and knowledge of clinicians in prenatal testing are. Apart from NIPT, physicians must be aware of their individual skills and honestly scrutinize their attitudes towards prenatal testing in order to enable autonomous reproductive choices. There is a broad agreement – not only in the opinions and statements mentioned above – that NIPT in practice needs a profound pre- and post-test counselling [10, 11]. B.’s gynecologist from the beginning did not hide his personal aversion towards advanced prenatal testing. Furthermore, he had not the additional, legally required training for offering NIPT and no practical experience with the test at all. In this constellation, adequate pre-test counselling is hardly possible and the resulting shared decision making (SDM) can only be deficient. While a physician’s personal aversion to NIPT of course is a general problem for the decision making process, the lacking knowledge leads to a concrete deficit: information sharing, one of SDM main pillars, cannot be conducted. It would have been the physician’s liability in this case to recognize his lack in knowledge as a potential risk, not only for the SDM. He then should have recommended that B. should see a colleague with more specific expertise.

Ohnhaeuser T and Schmitz D. Non-invasive Prenatal Testing... Geburtsh Frauenheilk 2016; 76: 277–279
duced, for example, by sharpening the counselling requirements for gynaecologists in prenatal testing together with an improve-
ment of the existing advanced trainings. Basic requirements
should become more standardized in order to ensure sufficient
skills levels. At this point, the professional organisations bear re-
 sponsibility for their members’ qualification status in order to be
less volatile than today.

Structural safeguards in prenatal care with regard to necessary
professional skills are indispensable, if cases as described above
shall be prevented henceforth. Thus, it is not enough to limit the
 provision of NIPT to MFM specialists. The question here is not
only who now should be allowed to provide NIPT [12]. In one
study several clinicians and also MFM specialists (13%) declared
to offer NIPT as a diagnostic test [9]. Another study showed 6% of
women terminating pregnancy without karyotype confirmation
after getting pathological findings from NIPT [5].

Therefore it has to be ensured effectively that the providing cli-
nician has a sufficient training in prenatal care counselling which
allows her to reflect upon and professionally dissociate herself
from own personal attitudes towards prenatal testing. Again, professional organisations have to make sure that physicians are
well informed and, thus, are able to inform women thoroughly in
turn.

More NIPT specific questions include: Is there a sufficient failure
management on the commercial providers’ side? The significant
difference between shipping a blood sample thousands of miles
for doing a genetic testing and an on-site blood test result must be
internalized by all agents involved. There should be standard-
dized procedures in the prenatal care pathway for occurring pro-
cess-related problems in order to minimize time loss – little delay
might not be an obvious risk for providers and physicians but in
total can become essential for the pregnant woman as the re-
ported case shows.

Furthermore, it can be argued that NIPT at least in the short run
should not replace the first-trimester screening (FTS), although
it has significantly lower false-positive rates and a significantly
higher positive predictive value [13, 14]. As long as NIPT is not im-
plemented together with an adequate quality management, a
parallel testing procedure even can be seen as a clinical utility. In
B.’s case NIPT alone, if performed accurately, most likely would
have shown a trisomy 13. A FTS would have shown signs of varia-
tion as well. Since NIPT for trisomy is superior to the combined
test, the role of high-quality first-trimester ultrasound scan
should be emphasized [15]. Still too expensive for most pregnant
women, NIPT with its limited diagnostic scope should be seen as
an additional screening test rather than an alternative to high-
quality ultrasound-scan, which is able to detect a much wider
range of potential anomalies. This is an important difference that
should be communicated more clearly – to pregnant women as
well as within the professional community. With a combination
of both non-invasive testing procedures, process-related vulner-
abilities of each procedure could be moderated more effectively.

Returning to B.’s case, a well performed FTS ultrasound scan could
have compensated the time loss caused by the failed NIPT usage.
Many questions of how to include NIPT responsively into every
day practice have not been answered adequately yet in many
countries and become more urgent in light of the forthcoming
coverage by health insurances and increasing numbers of tests.
Clinicians report insecurities with regard to the adequate provi-
sion of NIPT services and ask for specific legal regulations [10], as
also expert interviews from our project confirm (unpublished
data). If cases like the reported example shall be avoided in the
future, it is inevitable to install effective safeguards for the shared
decision making process in prenatal testing against individual
and structural inadequacies related to the increasing use and sig-
nificance of NIPT.

Acknowledgements

We are much obliged to B. We had heard from the case during the
recruiting of pregnant women for an interview study and con-
tacted her several weeks after this event. B. read the manuscript
and gave us written informed consent for publication. Our re-
search project “Indication or Information? The physician’s role
in the context of non-invasive prenatal diagnosis” is funded by the
Federal Ministry of Education and Research (BMBF, funding
number 01GP1201).

Conflict of Interest

None.

References

1. American College of Obstetricians and Gynecologists (ACOG). Committee
opinion no. 640: Cell-free DNA screening for fetal aneuploidy. Pub-
www.acog.org/Resources-And-Publications/Committee-Opinions/
Committee-on-Genetics/Cell-free-DNA-Screening-for-Fetal-
Aneuploidy; last access: 06.12.2015
2. Devers PL, Cronister A, Ormond KE et al. Noninvasive prenatal testing/
noninvasive prenatal diagnosis: the position of the National Society of
3. The Royal College of Obstetricians & Gynecologists (RCOG). Non-invasive
prenatal testing for chromosomal abnormality using maternal plasma
www.rcog.org.uk/en/guidelines-research-services/guidelines/sip15/;
last access: 06.12.2015
for aneuploidy and beyond: challenges of responsible innovation in prenatal
5. Dar P, Carnow KJ, Gross SJ et al. Clinical experience and follow-up with
large scale single-nucleotide polymorphism-based noninvasive pre-
natal aneuploidy testing. Am J Obstet Gynecol 2014; 211: 527
6. Warsow SL, Larion S, Abuhamad AZ. Overview of the impact of noninva-
sive prenatal testing on diagnostic procedures. Prenat Diagn 2015; 35:
972–979
7. NHS RAPID project. Online: http://www.rapid.nhs.uk/; last access:
06.12.2015
8. NIPT consortium. TRIDENT and ESPRiT studies. Online: http://niptcon-
sortium.nl/studies/; last access: 06.12.2015
9. Haymon L, Simi E, Moyer K et al. Clinical implementation of non-inva-
sive prenatal testing among maternal fetal medicine specialists. Prenat
Diagn 2014; 34: 416–423
10. Benn P, Chapman AR, Erickson K et al. Obstetricians and gynecologists’
practice and opinions of expanded carrier testing and noninvasive pre-
natal testing. Prenat Diagn 2014; 34: 145–152
11. Vonstone M, King C, de Vrije B et al. Non-invasive prenatal testing:
526
12. Schmitz D. Terminating pregnancy after prenatal diagnosis – with a lit-
13. Bianchi DW, Parker RL, Wentworth J et al. DNA sequencing versus stan-
abnormalities by first trimester combined screening and noninvasive
prenatal testing. Ultraschall Med 2015; 36: 40–46
15. Quezada MS, Gil MM, Francisco C et al. Screening for trisomies 21, 18
and 13 by cell-free DNA analysis of maternal blood at 10–11 weeks’
gestation and the combined test at 11–13 weeks. Ultrasound Obstet
Gynecol 2015; 45: 36–41