



Revisión

Artículo inglés

Bioethics in the evaluation of the fetal central nervous system in third world countries: applying Rotary International's four way test

Bioética en la evaluación del sistema nervioso central fetal en países del tercer mundo: aplicando la prueba cuádruple de Rotary International

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Abstract

Evaluation of fetal central nervous system (CNS) can be performed with invasive and non-invasive tests but, the implementation of any of both present ethical dilemmas in the prenatal obstetrical management and perinatal therapy. Severely sick fetuses are usually aborted, and such practice is hazardous in third world countries, especially in current times with worldwide spread of Zika virus infection. Rotary International's four way test give the practitioners a guideline to perform a moral and ethical medical pattern in order to respect the woman and her fetus rights, beneficence and autonomy. Bioethical guidelines in case of an adverse fetal CNS diagnosis is proposed based in this Rotarian moral model.

KEYWORDS

Bioethics; Zika; Rotary International; Four way test; Fetal CNS

Resumen

La evaluación del sistema nervioso central (SNC) fetal puede realizarse con pruebas invasivas y no invasivas, y la implementación de cualquiera de las dos implica dilemas éticos presentes en el manejo prenatal obstétrico y la terapia perinatal. Los fetos gravemente enfermos suelen ser abortados, y tal práctica es peligrosa en los países del tercer mundo, especialmente en los tiempos actuales con la propagación mundial de la infección por el virus Zika. El correcto manejo bioético proporciona a los profesionales una guía para realizar un patrón médico moral con el fin de respetar a ambos mujer y feto valorando sus derechos, su beneficencia y su autonomía. Se proponen pautas bioéticas en caso de un diagnóstico adverso del SNC fetal.

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Palabras Clave

Bioética; SNC fetal; Ultrasonido

Introduction

Ethical approach is mandatory in clinical research and medical practice, and it allows us to answer questions that face us to the edge of science and technology. Due to recent emerging epidemical diseases as Zika infection and its risk to make structural changes in the fetal brain ⁽¹⁾, it is necessary to stop the quarrel and rethink what we are doing, what are the purposes of clinical research, and to start a correct way to face each particular affected pregnant, not only for Zika infection but also for all other cases of fetal CNS pathologies. Ethics gives us a reference to make such path, and it gives us a rational and hard reflection of our conceptions and values with solid basis. This ethical reflection is subjected to temporal revision, because it is under the scrutiny and reinterpretation by new science knowledge.

In third world countries such as Venezuela, fetal evaluation is commonly applied in public and private medical facilities, and obstetric ultrasound is performed by different skilled personal, such as ultrasonographers (usually general physicians), obstetricians and maternal-fetal specialists. In private medical practice, there is a first-world approach to diagnosis and management of pregnant women, and regrettably, it's not the same situation in public hospitals, where medical decisions are based on personal experience and office guidelines. Prenatal diagnosis is often applied to access early approach to fetal conditions such as common aneuploidies, structural body anomalies, diagnosis of fetal diseases and death, and to access ultrasound- based risk for preterm birth and preeclampsia, and when serological test are performed, also establishes the risk for gestational diabetes, fetal growth restriction and fetal macrosomy ⁽²⁾. State of the art technology is performed in patients who can afford serologic screening such as biochemical markers in first and second trimesters and new non-invasive tests as microarrays and DNA-tests, but these resources are not available to public medical services' patients.

Amniocentesis, chorionic villus sampling, cordocentesis and fetal surgery is highly expensive for the vast majority of pregnant women, but people are aware of its necessity when it is the occasion, and frequently avoid them as these techniques usually mean an implicit risk of losing their offspring ⁽³⁾.

As everywhere in the world, the obstetric purpose of prenatal diagnosis is whether to end the pregnancy in case of a non-viable fetal, or to obtain diagnosis orientation for the obstetrical management of the fetus in risk and to guide the parents for options to fetal and neonatal treatment, life expectance, neural function prognosis and setting of the proper conditions for birth ⁽⁴⁾.

Non-invasive prenatal testing has its main representation in ultrasound screening for fetal aneuploidies, fetal echocardiography and neurosonogram to best evaluate mayor life threatening diseases ⁽⁵⁾. As well as ultrasound techniques, fetal monitoring offers good standards for fetal health mainly in third trimester ⁽⁶⁾.

Ethical dilemmas facing an adverse fetal diagnosis

Science itself gives ethical and social links to honesty, to the needs of cooperation and social exchange. Usual scientific practice in the health field involves a big vocational behavior, and it turns to be a very gratifying work. Being a professional in the health area becomes an inner attitude of creativity, honesty and humility, and these values are formed in early stages of the individual from home education and by social standards. But when it comes to face the truth of an adverse fetal diagnosis many questions are made to give the proper information to the patient and to explain her offspring's outcome on an evidence-based medicine ⁽⁷⁾. Explaining such details to patients need professional practice, and giving bad news must come together with a good medical management. These issues are always on topic when it comes to fetal diagnosis of a malformation in the CNS:

a. Applying invasive versus non-invasive prenatal tests (NIPT).

There should always be enough choices for prenatal diagnosis. On first trimester, NIPT are the first options as proposed by Nicolaides in his OSCAR plan (One Stop Clinics for Assessment of Risk) ⁽⁸⁾, where basal risks for aneuploidies by maternal age are modified by some ultrasound and serological findings, which can be made at her first visit on prenatal consult before week 14. On this visit, a simple blood sample should seek specific biochemical markers such as β -CGH, PAPP-A and others, and in junction to some ultrasound markers such as nuchal translucency, nasal bone, ductus venous, intracranial translucency, plexus choroid cysts, mayor cardiac anomalies, and others. These findings should change the basal risk to propose or not an invasive test. The same situation occurs in second trimester of pregnancy which is in the present a usual practice performed worldwide. Ethically speaking, to recommend an invasive test there should already be a NIPT and a patient with a fetus in risk. Amniocentesis, cordocentesis, and chorionic villus sampling are nowadays less indicated as long as NIPT have become more efficient, with the improvement of ultrasound techniques and clinical research specially oriented to determine risks ⁽³⁾. In some specific cases, such as fetal infections, amniocentesis can be mandatory to study fluid markers of inflammation and to seek by culture for bacteria, fungi, virus or parasite ⁽⁹⁾. The help of obstetric ultrasound in NIPT offers a good prenatal and risk-free test.

b. Risk/benefit when performing invasive tests.

Invasive procedures as amniocentesis and chorionic villus sampling (CVS) should deserve specific orientation as well as its implicit risk of fetal loss.

CVS is performed taking a small sample of placental tissue, and it is obtained either transabdominal or transcervically, always with direct vision by ultrasound. It should be performed just after first trimester ultrasound screening to those fetuses with markers of aneuploidy, during weeks 10 to 14 of gestation. The test itself has a risk of fetal loss of 2.9% compared to amniocentesis, 2.0, similar to late-second trimester amniocentesis. Even though, when compared to maternal death after a pregnancy termination (7-10/100.000), there can be a clear advantage for this invasive procedure ⁽¹⁰⁾. CVS should be done by maternal fetal medicine (MFM) specialists, and these professionals are not enough in number in underdeveloped countries, additionally, there are few hospitals (at least in Venezuela), with those MFM services or units. The information to the patient must satisfy her questions, and a written informed consent must be done. Pregnancy loss rates for CVS vs amniocentesis is 0.7 vs 0.6% within 2 weeks post procedure, 1.3 vs 0.9% to 24 weeks and 2.0 vs 1.9% for the entire pregnancy, suggesting similar risks ⁽¹¹⁾. These data should be given to patients for their informed consent.

Amniocentesis is usually performed before week 20 for diagnosis of aneuploidy, amniotic infection, DNA tests and some electrolytes into amniotic fluid, though its main indication is to access genetic and chromosomal status with high specificity and sensibility ⁽⁶⁾. Fetal loss related to this technique depends on each center and practitioner, and ranges from 1:100 to 1:1600. Amniocentesis also carries risk for amniotic band syndrome and alloimmunization, as well as amniotic infection, cervical bleeding and cervical fluid leakage, and also to a theoretical vertical infection risk with HIV and Hepatitis B/C ⁽³⁾.

c. How to explain statistical certainty on each diagnostic test.

Physicians make most clinical decisions with evidence-based medicine and personal experience. A screening test is done for diagnosis of a disease, injury and medical conditions, and in obstetric ultrasound, to assess risk status of the patient and her fetus. Each exam is also evaluated through some statistical test to know its sensitivity, specificity, negative and positive predictive value, false negative and positive cases.

To explain these mathematical issues is not an easy task, and the correct information should be given without statistical details, but in understandable way ⁽¹²⁾. In some cases, a lack of adequate education about the meaning of test results may cause an unsuitable decision of pregnancy termination or continuation. At this respect, it should be carefully evaluated the bias effects on patient decisions induced by the physician during the notification ⁽⁷⁾.

d. Choosing the right time for birth and its obstetric method based on an adverse fetal neurological disease.

Some ultrasound parameters can be observed to access fetal maturation, but lungs evolution is hardly recognized. Researchers have identified some NIPT such as ultrasound Doppler evaluation of pulmonary artery and some other data such as placental calcifications, bowel hypoechogenity, bones ossification cores in femur, tibia and humerus, echogenic particles in amniotic fluid, and some biometric measures: biparietal diameter, cephalic perimeter and length of long bones. Invasive tests to access fetal maturation include phosphatidyl inositol, Clement's and lecithin/sphingomyelin indexes ⁽¹³⁾.

When a fetus is neurologically compromised, these exams are usually not made because of some technical difficulties due to associated anomalies and oligohydramnios. Choosing the right time for birth can be difficult, especially due to cephalic diameters in ventriculomegaly and hydrocephaly, cranial malformations like macro and microcephaly, dolichocephalic or brachycephalic and early closure of fetal fontanelles ⁽⁵⁾. These malformations can confuse the correct diagnosis of fetal maturity. Cephalic perimeter and biparietal diameter should always be measured to compare with maternal pelvis diameters, and cephalopelvic disproportion is a formal indication of caesarean section. In fetus with incompatible with life brain malformations in preterm period, vaginal birth is usually recommended.

e. Fetal therapy surgery such as fetoscopy and amnioscopy.

Fetal therapy might be justifiable when: 1) there is reasonable certainty that the fetus will suffer irrevocable and substantial harm without the intervention, 2) the intervention has been shown to be effective, 3) the risk to the health and well-being of the pregnant woman is negligible and 4) the pregnant woman can give appropriate informed consent to the intervention. In addition, the therapy should bring together a team of consulting professionals in a collaborative and multidisciplinary approach to care during and after the pregnancy, with clear strategies on communication, diagnostic, therapeutic and care needs ⁽¹⁴⁾.

f. Elective abortion.

A diagnosis of an anatomical neurological disease faces the pregnant woman and her family to the hard decision of having a child with mental, behavioral and motor problems for life or to finish the pregnancy and face all the psychological, economical and legal consequences. In countries like Venezuela, abortion is forbidden by law, and termination of the pregnancy is always illegal and usually performed by unexperienced personal, increasing the risks of hemorrhage, infections and maternal deaths. Ethical dilemmas about abortion is a worldwide problem, and its discussion includes social, religious, legal, economical and medical concerns ⁽¹⁵⁾.

Mainly, the option of an elective abortion after a diagnosis of a fetal brain or neurological problem will depend on: 1) the date of pregnancy when the diagnosis is done, 2) the presence of chromosomopathies 3) the association with abnormalities in other organs and systems 4) the severity of the disorders diagnosed ⁽¹⁶⁾.

In countries where abortion is permitted, it should be done with informed consent, guided by an ethical committee and in a medical facility oriented to this procedure, followed by psychological and often psychiatry consultation ⁽¹⁶⁾.

Autonomy of women reproduction's rights against the fetus is always an ethical problem for obstetricians. In cases of fetal risk for CNS malformations such as ZIKV infection, abortion is not accepted in all medical fields until real plausible association are made, and until a fetal brain anomaly is observed ⁽¹⁷⁾. In Brazil, with the increased incidence of microcephaly after October 2015, its link to Zika virus infection was evident, and some direction in neighbor countries have suggested women on reproductive age to avoid pregnancies during different periods of time. This reality has pledged the right to reproductive freedom, which is a human right ⁽¹⁸⁾.

g. Doing the right diagnosis: professional skills.

There should exist different levels of medical attention in prenatal diagnosis. From the simple use of clinical parameters to high-tech, state of the art medical approaches, all of them are operator-skill-dependent. There must be a reference system in each hospital to access the accurate diagnosis in a multidisciplinary management ⁽¹⁹⁾.

In Venezuela, the patient is referred to a MFM specialist (III level specialists) at least three times during pregnancy (first and second trimester screening and morphogenetic screening), though most ultrasound scans in low risk pregnancies are performed by obstetricians or radiologists (II level specialists) or by ultrasonographers (I level). Usually, obstetric management is performed by the obstetrician with a junction with other reference colleagues.

h. 3D and 4D ultrasound screening as fun photography, as a test without clinical indication.

The diagnosis of a malformation in the CNS is done by 2D ultrasound, but 3D ultrasound give important information on location of the anomaly, phenotypic characteristics and volume acquisitions can be used to better access the anomalies. Also, 4D can be used to see neural function and fetal behavior, in real life scanning⁽²⁰⁾.

Some professionals tend to use 3D-4D technology in order to obtain images of the fetal face and genitals and this situation is ethically criticized, because it is considered as a physician response to patient pressure asking for these pictures, but not as a medical indication. We recommend to make them after discarding fetal abnormalities and with previous information of pros and cons of such practice.

i. Controversies during diagnosis of a malformation associated to Zika virus infection.

Beside the previously items explained above, there are some other issues related such as the lack of privacy of infected patients from the media, science journals and government policies. Each infected pregnant woman is wrapped with fear due to media information about the risk of brain abnormalities after confirmation of ZIKV infection, but with little advice of true risk of having such malformations. Indeed, not all infected pregnant patient will actually develop a brain problem evidenciable during fetal life, and obstetrical management and monitoring should be performed in serial echographic evaluations.

Although notices of public authorities speak of risks, it is difficult to understand to most patients specially in third world countries, and here is where media images humanize and contextualize these risks into the face of a baby severely ill, and these pictures reflect an invasion to that patient's autonomy, even though they consent that publication⁽²¹⁾. Bioethics in journalism tends to respect the patient's privacy and autonomy, but in cases such as this ZIKV outbreak the coverage and scientific research should go further than a simple informed consent, with special considerations to the patients who will eventually find themselves under public scrutiny, and their decisions on whether continue the pregnancy or end it, undergo on medical research, offer her products of conception to laboratory analysis and manage such data to scientists around the world to help understand this disease and help other mothers in similar situations.

In Venezuela, most infected women do not perform confirmation tests even if they have a prenatal diagnosis of a CNS malformation associated to ZIKV. The causes are many, specially based on government policies on publication of the real number of positive serology for this disease. This lack of information denies medical practitioners and health institutions to the real advance of the disease and the verification on the real prevalence of ZIKV in every case of an affected fetus. Also, this bioethical governmental misinformation problem affect neighbor countries in their incidence. Cases of CNS affected fetuses and newborns could have appeared at the same time than in Brazil, but the information is uncertain. Also, legal abortion is not permitted in any case, so complications related to non-medical abortions sums risks to Venezuelan poor pregnant women with less opportunities to expensive underground medical treatment. In every case, bioethical postulates of autonomy, beneficence and justice mirrors an affected society from its legal origins, and a change of political paradigm in health services is necessary to improve diagnosis, obstetrical and neonatal management of every case.

By the time, each case with a CNS malformation, associated or not to ZIKV infection is treated the same, with sufficient information on the baby's prognosis and treatment options depending on each cerebral problem found.

Rotary international's four way test

"The four-way test of the things we think, say or do" is an ethical test used by rotarians all over the world as a moral code for personal and professional relationships. These four questions can be applied to almost all situations where an ethical problem appears, and its practice guides Rotary International members ⁽²²⁾.

In case of an ethical dilemma, such as decisions facing an adverse fetal diagnosis, this can lead to help to figure out the best road to take in challenging situations. When applied, the physician's path can be clearer. If practitioners take their medical conducts according to these four questions, they can decide their options based on honesty, compassion and courage. Positive moral values are important to all medical standards.

To prove what was said, we invite our colleagues to rethink each prenatal diagnosis test, prognosis and fetal treatment based on this code of conduct.

a. Is it the truth?

Each diagnostic test has its own validation test, and based on sensibility, specificity and predictive values, NIPT are performed with knowledge of their implicit statistic errors. Even gold standard tests are not always 100% reliable. When reading research literature, some bias are simply given and mostly hardly understood by medical audience.

This statement establishes a dispute between tests, where the more adequate is the one chosen for each particular case. For instance, some practitioners tend to like Doppler ultrasound better than fetal electronic monitoring, and as far as we know, each test has its particular use in each particular case.

Maternal serological test are indeed nonhazardous, but their clinical application can be limited by maternal age, risk of false negative cases, and that is the main reason an invasive test is often offered, with all its risk, though small, with special consideration that we are speaking of human lives in formation.

Even amniocentesis and chorionic villus sampling are not 100% accurate because of probable mosaicisms that can result in a false negative result, rare, but feasible.

So we must say what is real in fetal diagnosis, with specific information of statistic truth if demanded, and always informed in written consent.

b. Is it fair to all concerned?

The point of this question is to ask whether everyone received what they truly deserved. Diagnostic test can be unsafe if performed by inexperienced staff, and risk/benefits questions should be informed to all concerned patient and their families.

In this question we can also speak about women's right to decide over their bodies when having a severely ill fetus, and the particular rights of this unborn child of having the opportunity of living and let nature take its path when it comes to finish a fetal life.

Also, fairness comes along with medical and surgical costs, fetal and neonatal interventions and fetal survival in each particular CNS malformation. When there is a decision on fetal therapy, the competence of each health center in terms of surgical experience, surgical success rate and survival truth helps to think on the best place to make the treatment, to choose the surgical team and neonatal facility in case of any complication.

Before viability, most therapies are non-invasive and their purpose is to diagnose malformations, and in few cases, continue the pregnancy with fetal therapy. All fetal surgical interventions are considered experimental, and the learning curve for each perinatal center is far from perfection, and fetal demises are still very much. This situation offers the woman small counseling options, and she has to decide in a short period of time whether to continue pregnancy or to finish it. Even offering fetal therapy must always be based on strict ethical standards, including institutional review board approval ⁽²³⁾.

Being fare usually does not involve fetal rights, and such question is mostly undone. Also, another person involved in a drastic decision is the physician. A doctor will help the woman make her own path based on the fetus outcome, but also his own medical behavior can be influenced on his religious, familiar and ethical judgement. If the doctor denies pregnancy termination based on his ethical belief, this practitioner must respect the patient's autonomy and beneficence, and for that reason the doctor should offer her treatment options with a colleague whose values should allow medical assistance in case of an abortion. Legal considerations forbid abortions in countries like Venezuela, and many women perform this procedures with unexperienced and non-medical personnel, increasing the risks for a complicated surgery. Also, not every hospital has a bioethical committee, and when it exists, pregnancies termination are not always presented to such instance. In private practice, practitioners assume all legal responsibilities, and it is mandatory to perform a written consent to avoid legal medical problems.

c. Will it build goodwill and better friendships?

Current medical practice demands to respect the patient's human rights based on her values and preferences. It begins with understanding the relationship between patients and doctors and the way it influences the authentic defense of her autonomy and fundamental rights. The models of medical decisions are these four: a) Paternalist: traditional. The doctor uses his skills and knowledge and decides diagnostic and therapeutic path for the sake of the patient, giving minimal information and without considering the patient's values or preferences. b) Informed decision: opposed to paternalist, the patient makes the final decision once all the information is offered to her. c) The doctor as a perfect agent: it incorporates preferences of patients, but only assumes that the doctor has enough knowledge to make the decision. c) Shared decision making: patients and doctors face uncertainty situations, in where there is not a superior treatment, and the medical decision is based on multiple options with uncertain benefits, side effects and economical cost ⁽²⁴⁾.

This model strengthens the doctor-patient relationship, and provides benefits to both parts and to the health system, also, it increases the number of reported adherence to treatment and decreases unjustified expenses, and it impacts positively the quality of life of patients, safeguarding and promoting the patient's fundamental rights. Furthermore, in situations of uncertainty, medical decisions will be taken to ensure full understanding of procedure's risks and how such risks are reduced with appropriate medical intervention, based on understandable medical evidence.

d. Will it be beneficial to all concerned?

The people involved in prenatal diagnosis are the pregnant woman, her partner and family, the medical team and the fetus or fetuses (in multiple pregnancies). Most patients after the diagnosis of a malformation in the CNS of her fetus choose elective abortion as therapeutic option to avoid the fetus suffering a life with mental and motor disease. Some others reject elective abortion based on moral, ethical or religious issues. To apply diagnostic procedures can be beneficial to both mother and fetus because it can define diagnostic approach the child's outcome, to choose the ideal hospital for the birth, to prepare pediatric team when receiving a high risk newborn, to prepare a path for the child's treatment or even to prepare the mother and her family for the child's eventual death.

Also, genetic counselling can be done as soon as an accurate diagnose is performed, and the risk of recurrence must be informed to the patient for future pregnancies.

Conclusions

Ethical guidelines in case of a fetal CNS malformation should be performed in each center. We suggest the following path as a base to perform guidelines in each medical center, in order to respect the patient and the fetus integrity, autonomy and beneficence in case of diagnose of a CNS malformation:

1. All patients should be encouraged to perform first and second trimester ultrasound for screening of aneuploidies, as well as neurosonogram between 18-24 weeks of gestation.

2. In cases with suspicion of a malformation in CNS, refer to a maternal-fetal specialist (MFMs) to confirm the diagnosis, with a syndromic approach.
3. MFMs should work in a bigger team to verify such diagnosis and should refer the case to a medical meeting to access different medical points of view to better treat the mother and her fetus.
4. The geneticist opinion is mandatory in order to know his opinion on recurrence risk of the disease.
5. Non-invasive as well as invasive prenatal tests should be performed in order to verify ultrasound findings, with accurate informed consent to the patient to detail all aspects related to her offspring's medical condition. There should always be information about their outcome in a short and long term, as well as her son's capability to integrate to the society and to be independent in a future.
6. After a medical board meeting, the information and conclusions related to each particular case should be immediately informed to the family, with the support of psychologists and social workers.
7. Hospital administrative and economic conditions must be notified clearly and detailed, with options for financial support when necessary.
8. Conditions for pregnancy termination should be informed if the legislation doesn't forbid it, and the ethical concerns about such practice should be listened from the patient with respect, offering the best options in each particular case. All elective abortions should be approved by the hospital's bioethical board, and the pregnancy products obtained must be directed to genetic and pathologist studies, handled with maximum respect.
9. Post abortion psychological therapy must be performed to all the patient's family, dealing with perinatal bereavement.
10. When the results of the pathologist and genetic test arrive, the obstetrician should inform them in a respectful and professional way.
11. If the patient chooses to continue the pregnancy, the medical board must decide treatment options for each particular CNS syndrome, future surgery corrections and whether the possibility or not to perform resuscitation maneuvers.
12. All medical data concerning the fetal CNS malformation is material for clinical research, so there must be enough information to the patient about such obtained details to best know this fetus condition, and help other similar cases in a future. Written consent should be performed related to her case data, and bioethical board should give assistance if needed.
13. Epidemiological guidelines should be offered by the local authorities in case of a suspected case of Zika virus infection, test should be available locally in each city to confirm the infection by serum samples, as well as available high risk obstetric services in public hospitals. In case of a fetal malformation linked to Zika, there must be an honest management with respect to the patient and her future son or daughter. Preventive sanitary measures against viral infections such as Zika should be performed by the governments, and specific information to both patients and clinicians should be updated in regular bases, especially in association with medical boards with responsibility in fetal and pediatric diagnosis and management.

Infant with CNS disease must be followed by a team of specialists, and the initial treatments should be performed with neonatologists in an appropriate birth center. Each medical step should be informed to the patient and her family, in order to respect her personal case and future decisions.

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