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REVIEW ARTICLE

KANET Test: Experience of Zagreb Group

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ABSTRACT

A new scoring system for the assessment of fetal neurological status, Kurjak antenatal neurodevelopmental test (KANET), has been recently published in several journals. Test is based on prenatal assessment of fetal behavior by three-dimensional/four-dimensional (3D/4D) sonography. Assessment of fetal behavior gave a promising opportunity to understand the hidden function of the developmental pathway of the fetal central nervous system. This new test has been proposed by the Zagreb group based on the several years of research. In this review we present the most significant results of the Zagreb group which led to construction of KANET test, basic presumptions of the KANET, and our published results on KANET.

Keywords: Fetal behavior, Four-dimensional ultrasound Prenatal assessment, Fetal central nervous system.

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INTRODUCTION

A new scoring system for the assessment of fetal neurological status has been recently published in several journals.[1-7] Test is based on prenatal assessment of fetal behavior by three-dimensional/four-dimensional (3D/4D) sonography. This promising new test has been proposed by the Zagreb group based on the several years of research. One of the first goals of Zagreb research group was assessment of normal neurobehavioral development by four-dimensional ultrasound, followed by attempts to identify functional characteristics of the fetus that predict a range of subsequent developmental dysfunctions. After summing own experiences and experiences of the leading authors in the field of fetal and neonatal neurology, new prenatal screening test for assessment of fetal behavior has been suggested. The test was named after the first author, Kurjak antenatal neurodevelopmental test (KANET). In this review, we present the most important results of the Zagreb group which led to construction of KANET test, basic presumptions of the KANET and finally or results on KANET.

THE ASSESSMENT OF FETAL BEHAVIOR USING FOUR-DIMENSIONAL ULTRASOUND BY THE ZAGREB GROUP

During the last decade, 4D sonography has stimulated studies on fetal and embryonic behavior with more convincing imaging and data than those obtained by conventional ultrasonic and nonultrasonic methods.[8] In addition, fetal behavior can be defined as fetal activities observed or recorded with ultrasonic equipment. It is obvious that fetal behavioral patterns directly reflect developmental and maturational processes of the fetal central nervous system (CNS).[9] The findings indicate that a good understanding of the relationship between fetal behavior and developmental processes in different periods of gestation might provide an important distinction between normal and abnormal brain development, as well as the tool for early diagnosis of structural or functional abnormalities.[10] The development of 4D ultrasound has significantly improved the assessment of quality of fetal spontaneous movements, and enabled a better evaluation of fetal behavior in comparison with 2D ultrasound.[8,11] Zagreb group has great experience using 4D ultrasound in the assessment of fetal behavior.[1-8, 12-23]

In one of the first studies, the aim was to determine the accuracy of 4D sonography in the assessment of embryonic and early fetal motor activity in the first trimester of normal pregnancies, in comparison to 2D sonography.[18] The observed body movements consisted of changing of the position of the head toward the body. With four-dimensional transvaginal sonography body movements were found at 7 weeks of pregnancy. Therefore, this technology enables the visualization of the moving phenomenon 1 week earlier than two-dimensional ultrasound. Using 4D US, quantitative assessment of fetal motility can be performed almost equally precisely as by conventional 2D US even at the very early period of gestation and at the onset of fetal motility. The qualitative assessment might be even more informative because this method allows the simultaneous visualization of the whole fetal body.[18]

Using 4D sonography, Kurjak et al have found that from 13 gestational weeks onward, a 'goal orientation' of hand movements appears and a target point can be recognized for each hand movement.[13] According to the spatial orientation, they classified the hand movements into several subtypes: Hand to head, hand to mouth, hand near mouth, hand to face, hand near face, hand to eye and hand to ear.

One of the most important studies of Zagreb group was longitudinal assessment of normal neurobehavioral development by 4D ultrasound.[22] The aim of this study was to construct normal standards for fetal neurobehavioral development using longitudinal observations through all trimesters by four-dimensional sonography. This longitudinal study established reference ranges for gestational ages. Standard of movement pattern and facial expression pattern curves were constructed through all trimesters of pregnancy. A group of 100 healthy normal singleton pregnancies were recruited for longitudinal 4D ultrasound examinations to evaluate fetal neurodevelopmental parameters between 7 to 40 weeks gestation. Variables of maternal and fetal characteristics including gestational age, eight fetal movements patterns in the first trimester and 14 parameters of fetal movement and fetal facial expression patterns recorded thereafter for the construction of fetal neurological charts. Measurement of seven parameters in the first trimester and 11 parameters in the second and third trimesters correlated with gestational age. Those parameters have been followed longitudinally through all trimesters and showed increasing frequency of fetal movements during the first trimester. A tendency toward decreased frequency of facial expressions and movement patterns with increasing gestational age from second to third trimesters has been noticed.

In the study of fetal behavior by 4D ultrasound, special attention is given to the fetal face. The fact that even in the embryonic period same inductive forces that cause the growth and reshaping of the neural tube influence the development of facial structures, and that many genetic disorders affecting the CNS are also characterized by dysmorphology and dysfunction of facial structures, emphasize the importance of structural and functional evaluation of the fetal face.[24,25]

The incorporation of three-dimensional (3D) ultrasound technology into clinical practice has resulted in remarkable progress in visualization and anatomic examination of the fetal face. 4D ultrasonography, in turn, provided for the first time an opportunity to evaluate subtle fetal facial expressions, which can be used to understand fetal behavior.[26] Because of its curvature and small anatomic details, the fetal face can be visualized and analyzed only to a limited extent with 2D ultrasound.[27] 3D ultrasound has the capability of demonstrating planes of section that cannot be obtained with 2D ultrasound and, thus, allows for a comprehensive evaluation of facial anatomy.[26-30] The standardized image display helps sonologists to understand fetal anatomy better and to communicate complex observations to both parents and less-experienced observers. The entire face cannot be seen on a single 2D ultrasound image. 3D ultrasound allows spatial reconstruction of the fetal face and simultaneous visualization of all facial structures, such as the fetal nose, eyebrows, mouth and eyelids. The application of 4D sonography in the examination of fetal facial movements has revealed the existence of a full range of facial expressions, including smiling, crying and eyelid movements,[22,26,31] similar to emotional expressions in adults, in the 2nd and 3rd trimesters. Other facial movements, such as yawning, suckling, swallowing and jaw opening can also be observed in this period by 4D ultrasound.

Beside fetal behavior in normal pregnancies, behavior of the fetuses from the pathological pregnancies was also followed.[23] Data on IUGR fetuses obtained by 4D sonography during the 3rd trimester of pregnancy have shown that IUGR fetuses have less behavioral activity than normal fetuses in hand to head, hand to face and head retroflexion movements. Statistically, significant differences could be shown in the five qualitative categories of head and hand movements.[23]

Further, several behavior patterns were observed in the anencephalic fetus and compared with the normal fetus at the same gestational age by 4D ultrasound.[16] Movement of the hand in the anencephalic fetus occurred only in one direction (hand to head) and it was abnormal, forceful and jerky. In the normal fetus, the movement patterns of the hand were continuous and variable in direction. Hand movement around the mouth and other movements of the hand to specific body parts can be observed in a normal fetus, but these characteristic patterns did not appear in the anencephalic fetus. Body movements in the anencephalic fetus showed lack of positional changes, and they appeared to be abnormal. They showed a waxing and waning in intensity, with a sequence of arm and leg movements attained by effort. They were monotonous and their onset was abrupt and jerky. In the normal fetus, body movements appeared to be continuously variable and occurred in any direction. There were overall differences in the frequency data between the anencephalic fetus and normal fetus. All of the frequency of the movement patterns in the anencephalic fetus seem to be decreased.[16]

KURJAK ANTENATAL NEURODEVELOPMENTAL TEST (KANET)

The starting point of this new test is the presumption that fetal behavior reflects the function of fetal brain. The parameters of the KANET were selected based on developmental approach to the neurological assessment and on the theory on emergence of general movements (GM) from central pattern generators.[18] The scoring system is a combination of some parameters from the fetal GM assessment and parameters from postnatal ATNAT assessment, which can be prenatally visualized by 4D US.[1]

Overlapping of sutures and neurological thumb are included in KANET on suggestion of Amiel Tison.[32] However, analytical criteria of typical passive and active tone in the neonate cannot be elicited in the fetus: Head anteflexion *vs* retroflexion, ventral *vs* dorsal incurvations in the axis,[33,34] both being of the utmost importance postnatally to confirm CNS optimality.[1] Still, optimality in the fetus should be reflected in typical GMs. GMs are part of the spontaneous movement repertoire and are present from early fetal life onward until the end of the first-half a year of life. They involve the whole body in a variable sequence of arm, leg, neck and trunk movements. They wax and wane in intensity, force and speed and they have a gradual beginning and end. If the nervous system is impaired, GMs loose their complex and variable character and become monotonous and poor.[35]

The main two advantages of the 4D ultrasound in comparison to 2D ultrasound, incorporated in KANET, are the possibility of evaluation of fetal face movements and better evaluation of the quality of fetal movements.

The following parameters have been incorporated in the KANET test: Isolated head anteflexion, overlapping cranial sutures and head circumference, isolated eye blinking, facial alteration, mouth opening (yawning or mouthing), isolated hand and leg movements, hand to face movements, finger movements and thumb position, Gestalt perception of general movements (overall perception of the body and limb movements with their qualitative assessment).

The KANET should be performed in the 3rd trimester from 28th to 38th weeks of gestation. The assessment should last from 15 to 20 minutes, and the fetuses should be examined when awake. If the fetus is sleeping, the assessment should be postponed for 30 minutes or for the next day between 14 and 16 hours. In cases of definitely abnormal or borderline score, the test should be repeated every 2 weeks till delivery. New modified KANET test should be used with eight instead of 10 parameters: Facial and mouth movements are combined in one category, isolated hand movements and hand to face movements are combined in one category.[7] The score should be the same for abnormal fetuses 0 to 5, borderline score is from 6 to 13 and normal score is 14 or above. After 4D US assessment of behavioral patterns in the fetuses from high-risk pregnancies, it is very important to continue with follow-up after delivery in infants who were borderline or abnormal as fetuses. Infants should be followed until the age of at least 24 months when diagnosis of disabling or nondisabling cerebral palsy can be ultimately made.[7]

KANET: OUR RESULTS

The new scoring system was first retrospectively applied in a group of 100 low-risk pregnancies.[1] After delivery, postnatal neurological assessment was performed, and all neonates assessed as normal reached a score between 14 and 20, which we assumed to be a score of optimal neurological development. Subsequently, the same scoring system was applied in the group of 120 high-risk pregnancies in which, based on postnatal neurological findings, three subgroups of newborns were found: Normal, mildly or moderately abnormal and abnormal. Normal neonates had a prenatal score between 14 and 20, mildly or moderately abnormal neonates had a prenatal score of 5 to 13, whereas those infants who were assigned as neurologically abnormal had a prenatal score from 0 to 5. Ten fetuses who were postnatally, according to neurological assessment, described as mildly or moderately abnormal, achieved prenatal score of 5 to 13, while another 10 fetuses postnatally assigned as neurologically abnormal had a prenatal score from 0 to 5. Among this group four fetuses had alobar holoprosencephaly, one had severe hypertensive hydrocephaly, one had tanatophoric dysplasia and four fetuses had multiple malformations. These preliminary results demonstrated ability of KANET to identify abnormal behavior in severely neurologically damaged fetuses.[1]

To verify the new scoring test, study has been continued in several collaborative centers (Zagreb, Istanbul, Bucharest, and Doha).[2] This multicentric research included 228 fetuses from high-risk pregnancies, of whom 18 had definite abnormal KANET score. Of these 18 pregnancies, five pregnancies were terminated, and six fetuses died *in utero*. Of seven fetuses with abnormal KANET, postnatal neurological assessment by Amiel Tison's method revealed three newborns out of seven fetuses to be abnormal (arthrogryposis, vermis aplasia and neonate of the mother with the previous child with CP), while four were considered normal (ventriculomegaly, preeclampsia, thrombophilia, oligohydramnios). The three very illustrative cases with abnormal KANET scoring were arthrogryposis, vermis aplasia, and the fetus whose previous sibling had verified cerebral palsy. The fetuses in these three cases had especially reduced facial movements, the faces were like mask during repeated scans. Fetuses with vermis aplasia and arthrogryposis had normal cranial sutures but the isolated head flexion was small in range for both cases. Isolated hand movements, hand to face and leg movements were poor in repertoire for all three cases. The finger movements were cramped and invariable in all three cases. The Gestalt perception of GMs was also abnormal in these cases. In this study, the behavior of a fetus with acranius was also longitudinally followed.[2] It has been observed that the fetus at 20 weeks of gestation had hypertonic movements with high amplitude and high speed. The movements emerged abruptly with burst-paused patterns, the variability of head movements was missing, without changes of facial expressions. As the gestational age advanced and the motor control was shifting from lower to upper control center the movement patterns changed as well. At the gestational age of 32 weeks the fetus had no facial expressions (mask-like face) and hand movement repertoire was very poor. At 36 weeks the absence of both the facial expressions and limb movements was observed. In this fetus abnormal behavior patterns, as a result of lack of the appropriate control of the upper cortical centers on the motor activity, was clearly documented. The objective of this multicentric study was to apply the KANET to the fetuses from high-risk pregnancies for neurological disorders and to verify the results of the test by neonatal neurological assessment. The primary outcome was the usefulness of new antenatal screening test to identify the fetuses from high-risk pregnancies at neurological risk.[2]

Another study confirmed statistically significant difference in fetal behavioral patterns between the fetuses from low-risk and high-risk pregnancies.[3] Statistically significant difference for eight out of 10 parameters of KANET has been showed: Isolated anteflection of the head, eye blinking, facial expressions (grimacing, tongue expulsion), mouth movements (mouthing, jawing, swallowing), isolated hand movement, hand to face movement fist and finger movements and GMs. Statistically significant, moderate correlation of KANET and ATNAT tests was also confirmed. In practical sense, it means that the neuropediatricians who examined the newborns with ATNAT test confirmed the results of KANET.[3]

Further, in recently published case report KANET indicated normal early neurological development of the child, confirmed by postnatal tests, despite unfavorable intrauterine conditions, diagnosed IUGR and fetal hypoxemia.[5]

CONCLUSION

Assessment of fetal behavior gave a promising opportunity to understand the hidden function of the developmental pathway of the fetal central nervous system. The idea of diagnosis *in utero* of some functional neurological disorders was very intriguing. As a result of years of reaserch of Zagreb group on fetal behavior KANET test was introduced. By now the KANET has been shown to be useful in standardization of behavioral assessment with the potential for antenatal detection of fetuses with severe neurobehavioral impairment. Further, studies have been initiated in several centers, including Zagerb, with similar objectives: To assess practical clinical application of the test in both, normal and high-risk pregnancies.

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