REVIEW ARTICLE

The KANET Test in Twin Pregnancies

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Abstract

The revolution of ultrasonography in obstetrics has enabled us to assess the neurological development of the fetus *in utero*. The KANET test has proven to be a useful tool in identifying neurological anomalies and might have the potential to early on diagnose pathologies that nowadays can be diagnosed only postpartum. Studies have shown a strong correlation between antepartum evaluation using four-dimensional ultrasonography for the assessment of the fetal behavior and postpartum neurodevelopment. Studying twin pregnancies can offer us even more insight into fetal development, as they are considered high-risk pregnancies with a higher incidence of lower-weight newborns predisposed to neurological disorders such as cerebral palsy. As neurological disorders are frequently identified in high-risk pregnancies, we reviewed the latest studies on twin pregnancies. We also studied KANET integration in a routine fetal assessment and observed its role in reducing the complications and even in treating neurological disorders prenatally. Along with our personal experience in applying the KANET test in the evaluation of twin pregnancies with a 2-year postnatal follow-up, we hope that a better understanding of fetal neurodevelopment should be reached.

Keywords: Behaviour, Cerebral palsy, Dichorionic twin, Fetal movements, Four-dimensional ultrasound, KANET test, Monochorionic twin, Neurodevelopment, Neurological disorders, Review, Twin pregnancies, Ultrasonography.

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Background

Obstetric ultrasonography has been a great tool when dealing with the challenge of studying the fetal nervous system. The way fetuses behave *in utero* directly reflects the development and maturation process of the fetal nervous system, while ultrasound technology offers us the direct means to visualize and assess the fetal anatomy and activity. Prechtl et al. were the first to study fetal behavior *in utero* using two-dimensional ultrasonography (2D-US), thus laying the foundation for fetal neurosonography.[1] Since 2D-US offers poor-quality images and can be subjective, the introduction of three- (3D-US) and four-dimensional ultrasound (4D-US) answered the need for better technology, being bound to become a routine part of the fetal assessment.

The assessment of fetal behavior using 4D-US indirectly monitors the maturation and staged development of the central nervous system (CNS).[2] The behavior is the attribute of a functional CNS. Fetal expressions may offer an insight into the function and development of the fetal brain in the second half of pregnancy.[3,4] These expressions reflect the maturation and development of different parts of the CNS controlling these actions.[4]

Four-dimensional ultrasonography assessment of fetal behavior and facial expressions as well as studying the usefulness of the KANET represent a diagnostic criterion for prenatal brain injury and may be a useful diagnostic method when predicting postnatal developmental disabilities.[5,6]

The revolution of ultrasonography has enabled obstetricians to identify more neurological disorders with an intrauterine onset. Every day we see more evidence that some disorders formerly thought to be a consequence of perinatal and postnatal factors could also have prenatal factors. Antenatal and perinatal complications are more common in multiple pregnancies, these pregnancies being at a significantly higher risk than a singleton pregnancy. The main problems regarding the fetal outcome in multiple pregnancies are due to preterm delivery, low-birth-weight, intrauterine growth restriction (IUGR), and cerebral palsy (CP).[7] Cerebral palsy is 5–10 times more frequent in twin pregnancies than in singletons.[8,9] The incidence of cerebral palsy, considered the most common lifelong neurological disability, increases with decreasing gestational age at delivery and birth weight.[10–12] The prevalence of CP among twins is 7.4%, as opposed to 2–3 per 1,000 in singletons, increasing exponentially with the number of fetuses.[13]

The diagnosis of CP is usually based on the clinical picture, being rarely diagnosed before 6 months of age. Frequently, the older the child, the bigger the disability, thus a positive diagnosis being possible.[3] The large majority of children diagnosed with CP present severe forms that need special attention, such as institutional help, rehabilitation, and special health care.[14]

Early identification of CP, as well as prevention, is of great public health importance. Therefore, ultrasonographic studies on twin neurobehavior and neurological development are important to evaluate the possible mechanisms of these neurological disorders.

Aim of the Study

The aim of this paper was to review the main results of the studies conducted so far on neurodevelopment and neurobehavior in twin pregnancies. The studies included mono- or dichorionic pregnancies. Antenatal assessments were performed at different

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gestational ages, using either the KANET test or ultrasound assessments of certain fetal movements or expressions.[15–17] We also analyzed the assessment method and the postnatal follow-up of children up to various ages.

Review Results

Multiple Pregnancies and Ultrasonographic Assessment

Historically, the ultrasound evaluation of the fetal neurodevelopment in twin pregnancies was initially performed by 2D-US. In 1996, Arabin et al. investigated intertwin contacts until the 16th week of pregnancy, using 2D-US. The first contact observed in monochorionic twins was at 8 weeks. In early pregnancy, they reported more frequent intertwin contacts in monochorionic than dichorionic twins.[18] They demonstrated that the first contacts between twin fetuses are always initiated by the extremities: the arms or legs.

In a study of fetal behavior in the first half of pregnancy, Piontelli et al. showed that the incidence of spontaneous movement patterns in twins was similar to that in singletons, representing 88% of overall activity at 13 weeks of gestation and 71% at 20–22 weeks.[19]

The 4D-US enables us to observe the fetal activity, identifying patterns of behavior and later on interpreting them in order to detect anomalies.

In terms of general movements, in more recent studies, it has been shown that twins have a lower incidence of general movements than singletons.[20] The patterns of fetal movements seem to be independent of zygosity, sex combination, position, presentation, or chorionicity.[21]

While observing the fetal behavior in a multiple pregnancy, an interesting fact comes forward in many studies—the motor activity induced by the intertwin contact.[21–23]

Using 4D-US, Sasaki et al. reported monochorionic twins having significantly more contacts than dichorionic twins at the end of the first trimester. However, in late pregnancy, the behavioral differences between monochorionic and dichorionic twin pairs seemed to decrease.[24]

In 2011, Hata et al. reported no significantly difference between monochorionic and dichorionic twins regarding fetal movements at 12–13 weeks of gestation in the 14 cases studied. Moreover, when evaluating the reaction to touch, they reported a higher median rate of 33.9% than previously reported in other studies using 2D-US.[25]

Kurjak, and later on Degani, tried to prove the existence of fetal behavior in intrauterine life using 4D-US, early in pregnancy.[26,27] They observed fetal movements such as isolated eye blinking movements, mouth and eyelid opening, yawning, tongue expulsion, smiling, scowling, and hand movements directed to other parts of the face. These motor parameters correlate with the type of intrauterine behavior and differ between twins. Intrauterine behavior seems to correlate with the type of temperament in the postnatal period. The child's temperament is strongly determined by genetic factors and influenced by environmental factors. The usual term "temperament" refers to variations in behavioral predispositions, caused by distinct neurophysiological substrates.[27]

The earliest assessments of fetal movements in twin pregnancies were made by Hata et al., at 10–13 weeks of gestation. They investigated the frequencies of each of the 10 intertwin contact types between monochorionic and dichorionic twins using 4D-US at 10–13 weeks of gestation. The total frequency of all contacts in dichorionic twins at 10–11 weeks of gestation was very low because of the thicker intertwin membranes and the larger intertwin distance. The follow-up assessment, at 12–13 weeks, showed that the frequencies of head to arm contact in monochorionic pregnancies were significantly higher than those in dichorionic pregnancies. The variable position of the twins *in utero* did not affect the frequency of intertwin contact at 10–13 weeks gestational age.[17]

AboEllail et al. performed a comparative analysis on eight fetal movements (head anteflexion, head retroflexion, body rotation, hand-to-face movement, general movement, arm movement, leg movement, and mouthing) in twin pregnancies vs. singleton pregnancies before 20 weeks of gestation, using 4D-US. They reported that the general movements were significantly more frequent in twin fetuses at 12–13 weeks. Later on, at 14–19 weeks of gestation, they noticed an increased frequency of arm movements. A possible explanation would be that the small space they share affects the frequency of general movements, allowing only arm and leg movements. It cannot be proved that the decrease in the frequency of general fetal movements before 20 weeks of gestation in twin pregnancies might be linked to low neurodevelopment and maturation before and after birth.[28]

Assessing the fetal behavior by analyzing fetal movements in the three trimesters of pregnancy, Kurjak et al. reported that twins had a lower motor activity and different behavioral patterns than singleton pregnancies in the third trimester of pregnancy.[29]

In very recent studies, Mori et al. did not report statistically significant differences in general movements between the active twin and the cotwin until 12–13 weeks of gestation or between 14 and 19 weeks of gestation. Using 4D-US assessment, eight fetal movements were observed for 15 minutes.[20]

The interaction between twin fetuses provides us with clues regarding sensitivity that cannot be assessed in a singleton fetus. As twins are exposed to stimuli from one another, we can investigate the reactions to touch and different types of intertwin contact that may occur.[18]

The 4D-US antenatal assessment can also offer an insight into the social behavior between the twins. Castiello et al. tried to demonstrate in a small study (five cases) that twins interact from intrauterine life, when they share the same space—the maternal uterus.[30] If social interaction is not just a form of evolution and development in postnatal life, starting to develop from intrauterine life, then ultrasound evaluation of their behavior *in utero* can demonstrate this hypothesis.[24] The traditional description of the interaction between twins is that the movements are only a reflex.[25] The evaluation was performed by 4D-US at 14 and 18 weeks of amenorrhea, for 20 minutes. The researcher assessed three types of movements: directed toward the fetus' own body, toward the uterine wall, and toward the co-twin. His recent results show that twins plan and perform movements addressed to each other, aiming at social interaction.[24]

Fetal behavior directly reflects the process of neurodevelopment.[31,32] Starting from this theory, we could advance the idea that social adjustment disorders might be early diagnosed by analyzing the intrauterine behavior.[31,33]

Very recently, Nitta et al. studied twin fetal facial expressions at 30–33 + 6 weeks of gestation by 4D-US, in order to assess the age-appropriate neurodevelopment and maturation by comparison with singleton pregnancies. They reported that the most common facial expressions were mouthing and blinking, both in singleton pregnancies and in twin pregnancies.[34,35] Nevertheless, in twin

Table 1: Comparisons between average values of the KANET score in MC twins at the three visits

	Average	*SD*	*t test*	*95% CI*	*p*
Visit 1					
MC sIUGR	17.30	1.55	6.9	1.58–2.88	<0.0001
MC normal growth	19.53	0.61			
Visit 2					
MC sIUGR	17.63	1.41	6.45	1.35 –2.57	<0.0001
MC normal growth	19.59	0.55			
Visit 3					
MC sIUGR	15.00	3.11	7.42	3.36–5.88	<0.0001
MC normal growth	19.62	0.59			

Table 2: Comparison between KANET scores of MC and DC twins

	DC		*MC*			
	Mean KANET	*Standard deviation*	*Mean KANET*	*Standard deviation*	*t test*	*p*
Visit 1	19.47	0.87	18.79	0.005	2.39	2.7901
Visit 2	19.62	0.73	18.97	0.005	2.35	2.8263
Visit 3	19.55	1.40	18.92	0.02	2.11	2.2622

pregnancies, the mouthing was less frequent compared to the singleton pregnancies. They reported a decrease in the frequency of mouth movements as the pregnancy progressed. The mechanism is not yet entirely understood, but the accelerated maturation of the twins' brain caused by stress might be one of the causes.[23]

The cause of stress could be the progressive limitation of the uterine space. Regarding scowling, this facial expression is also less common in twin pregnancies. It is the expression of pain or discomfort in the womb. The twins are familiar with intertwin contact, thus repetitive reciprocal stimulation leads to advanced functional brain development.[34]

Our Experience with KANET in Assessing Multiple Pregnancies

In our study, we assessed the original KANET score in two populations of pregnant women: 67 dichorionic twin pregnancies and 24 monochorionic twin pregnancies. We included in the two groups pregnancies with normal fetal growth and pregnancies with abnormal fetal growth: discordant fetal growth (dichorionic twin group) and selective intrauterine restriction (monochorionic twin group). For both groups, we assessed the antenatal KANET score during three visits and compared the results with the neurodevelopment immediately after birth up to 2-year-old children, using neurological test Amiel-Tison.[16,36,37]

Regarding the distribution of the KANET score in the group of dichorionic twin pregnancies complicated with discordant growth, we found normal values of the KANET score in all cases, during all three visits, for both fetuses, and normal postnatal neurological assessment. Follow-up visits were also normal, which demonstrates and strengthens the correlation between the normal values of this score and the normal postnatal neurological status in infants and children up to 2 years.[38]

The same correlation was found in normal growth monochorionic pregnancies, for pregnancies with normal growth, as well as for the pregnancies with selective intrauterine growth restriction. The analysis of the average values of the KANET score in the group of monochorionic twin pregnancies revealed statistically significant differences between the monochorionic twins with abnormal growth vs. twins with normal growth at all three visits ($p = 0.0001$), with average values between 17.30 and 19.62, deemed as normal[38,39] (Table 1).

There is a statistically significant difference between the mean KANET scores of dichorionic and monochorionic twins (Table 2). Dichorionic twins have a higher score at all three visits ($p = 0.005$ at the first and second visit and $p = 0.02$ at the third visit).[39]

We also reported a rising trend of the KANET score from one visit to another, for both monochorionic and dichorionic twins.[38]

The study of fetal behavior and the clinical integration of the KANET neurological score are extremely important considering the possible correlations between the abnormal values of this score and certain postpartum impairments in monochorionic pregnancies complicated with selective IUGR. In hindsight, even if we found abnormal KANET scores, the association with postpartum neurological anomalies is still unclear. Although the antenatal KANET score was borderline or abnormal for selective IUGR fetuses (monochorionic twin pregnancies group), the postnatal neurological evolution of the children was favourable.[38]

An abnormal KANET score seems to be largely associated with the occurrence of CP at 2 years' postpartum. We did not find any cases of CP in our study. Our results were obviously limited by the small number of subjects and the subjectivity involved in the ultrasound examination performed by several operators. Therefore, we definitely need more studies focusing on the neurological assessment of twin pregnancies as they are scarce and many questions remain unanswered.[38,39]

Conclusion and Clinical Significance

One of the biggest challenges that healthcare obstetricians and neonatologists face nowadays is detecting and diagnosing neurological impairments, both in the prenatal and postnatal period. For the past 10 years, the KANET scoring system has proven to be a great tool in assessing the neurological status of the fetus and is now being used in many centers for evaluating not only high-risk pregnancies but also low-risk cases.[40] KANET is now an

important diagnostic tool for the identification of neurological impairment and abnormal fetal neurobehavior.

In the future, maybe KANET will offer a better diagnostic approach and a thoroughgoing neurobehavioral assessment of the fetus, hence increasing the chances of an intrauterine or early postpartum intervention with the aim of treating or improving the neurological conditions of some of these neonates.[22]

Given the fact that this test is more and more widely used, new medical data and approaches are bound to emerge and early detection will result in an early medical intervention for more neurological syndromes.

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