ORIGINAL ARTICLE

Mini KANET: Simple Fetal Antenatal Neurodevelopmental Test

Toshiyuki Hata[1], Kenji Kanenishi[2], Nobuhiro Mori[3], Mohamed Ahmed Mostafa AboEllail[4], Uiko Hanaoka[5], Kosuke Koyano[6], Ikuko Kato[7], Takashi Kusaka[8], Asim Kurjak[9]

Abstract

Objective: The objective of this study is to develop a simple antenatal fetal neurodevelopmental test [Mini Kurjak's antenatal neurodevelopmental test (Mini KANET)] for the prediction of postnatal developmental disabilities.

Methods: Three hundred and fifty-three healthy fetuses between 28 and 38 weeks of gestation were examined using a four-dimensional ultrasound. Fetal behavior was assessed with the Mini KANET, which consists of three parameters (isolated eye blinking, facial alteration or mouth opening, and isolated leg movement). A score range of 0–1 was characterized as abnormal, and 2–6 was normal. Diagnostic indices for the prediction of postnatal developmental disabilities were compared between the modified and Mini KANET assessments.

Results: There were 334 normal (94.6%) and 19 abnormal (5.4%) cases among the 353 fetuses studied with the Mini KANET. Four cases of postnatal developmental disabilities were noted among the 334 normal fetuses (1.19%), whereas four cases of developmental disabilities were found among the 19 abnormal fetuses (21.05%) ($p < 0.0001$). There was a significant difference in sensitivity between the modified (37.5%) and Mini KANET (50%) assessments ($p = 0.001$), whereas no significant differences were noted for other diagnostic indices between the two assessments.

Conclusion: The Mini KANET may become a simple antenatal fetal neurodevelopmental test for the prediction of postnatal developmental disabilities in healthy fetuses. However, the data and their interpretation in the present study should be taken with some degree of caution because of the small number of subjects studied. Further studies involving a larger sample size are needed to assess the validity of the Mini KANET for the prediction of postnatal developmental disabilities, comparing with the results of modified KANET.

Keywords: 4D ultrasound, Antenatal fetal neurodevelopmental test, Developmental disability, Mini KANET, Modified KANET.

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Introduction

Our previous investigation showed that Kurjak's antenatal neurodevelopmental test (modified KANET) may be a useful diagnostic modality for the prediction of postnatal developmental disabilities in healthy fetuses.[1] Original KANET consists of 10 parameters.[2] The standardization of the test (modified KANET) was proposed in Osaka in 2010. In the modified KANET assessment,[3] a total of eight types of fetal movements (isolated head anteflexion, cranial sutures and head circumference, isolated eye blinking, facial alteration or mouth opening, isolated leg movement, isolated hand movement or hand-to-face movements, finger movements, and gestalt perception of general movements) are assessed using a four-dimensional (4D) ultrasound. Each ultrasound assessment is conducted for 15–20 minutes, while fetuses are awake.[3] The scoring system is as follows: 0–5 is abnormal, 6–9 is borderline, and 10–16 is normal.[4–7] However, it must be remembered that the modified KANET assessment still involves a learning curve, and it may be unfamiliar to beginners. Furthermore, this test necessitates high-level operator-dependent 4D reconstruction of fetal behaviors. In addition to technical familiarity, a detailed knowledge of fetal anatomy is essential for the application of this test, and extensive experience may shorten the learning curve. Therefore, in the present study, we aimed to develop a simple antenatal fetal neurodevelopmental test (Mini KANET) for the prediction of postnatal developmental disabilities.

Subjects and Methods

The design of the study, sample of patients, criteria for inclusion, and definitions of parameters of the modified KANET are described in detail in our previous publication.[1] A cross-sectional study of 353 pregnant Japanese women at 28–38 gestational weeks was conducted between June 2013 and March 2016, with the application of Voluson E8 (GE Healthcare Japan, Tokyo, Japan) and a curved array transabdominal transducer (4–8.5 MHz). During this period, all mothers were informed of the study, with their random recruitment. All fetuses with chromosomal and lethal structural abnormalities were excluded. The present study received approval from the Kagawa University Graduate School of Medicine Ethics Committee. Also, all participants provided standardized written informed consent.

For the assessment using the modified KANET, pregnant women were examined only once. According to the first day of the

[1–5]Department of Perinatology and Gynecology, Kagawa University Graduate School of Medicine, Kagawa, Japan

[6–8]Department of Pediatrics, Kagawa University Graduate School of Medicine, Kagawa, Japan

[9]Department of Obstetrics and Gynecology, Medical School University Zagreb, Zagreb, Croatia

Corresponding Author: Toshiyuki Hata, Department of Perinatology and Gynecology, Kagawa University Graduate School of Medicine, Kagawa, Japan, Phone: +81-(0)87-891-2174, e-mail: toshi28@med.kagawa-u.ac.jp

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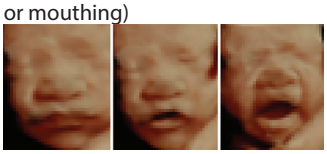
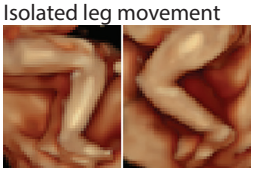
Table 1: Modified and Mini KANT scores in each fetus with developmental disorder

Case	*Developmental disorder*	*Gestational age at examination (weeks)*	*Isolated head anteflexion*	*Cranial sutures and head circumference*	*Isolated eye blinking*	*Facial alteration or mouth opening*	*Isolated leg movement*	*Isolated hand movement or hand-to-face movements*	*Finger movements*	*Gestalt perception of general movements*	*KANET total score*	*Mini KANET total score*
1	Werdnig–Hoffmann disease	35 w	2	2	0	0	0	2	2	2	10	0
2	Developmental disorder	36 w 6 d	2	2	2	2	2	2	2	2	16	6
3	Autism spectrum disorder	31 w 2 d	2	2	1	1	2	2	0	2	12	4
4	Developmental disorder	29 w 6 d	2	2	0	2	2	2	2	2	14	4
5	Ullrich congenital muscular dystrophy	29 w 4 d	2	1	2	0	1	2	2	2	12	3
6	Duchenne muscular dystrophy	34 w 1 d	2	2	0	1	0	1	1	2	9	1
7	Motor developmental delay	34 w	1	2	0	1	0	1	2	2	9	1
8	Autism spectrum disorder	29 w 6 d	2	2	0	1	0	0	0	2	7	1

Table 2: Mini KANET assessment

	Score			
Sign	*0*	*1*	*2*	*Sign score*
Isolated eye blinking 	Not present	Not fluent (blinking 1–5 times)	Fluency (blinking >5 times)	
Facial alteration (grimace or tongue expulsion)  Or mouth and opening (yawning or mouthing) 	Not present	Not fluent (alteration 1–5 times)	Fluency (alteration >5 times)	
Isolated leg movement 	Cramped	Poor repertoire or small in range movement 0–5 times)	Variable in full range, many alterations (movement >5 times)	
			Total score	

last menstrual period, gestational ages were estimated, and these were confirmed by the first-trimester or early second-trimester ultrasound. Based on the scans taken in the 20th week of pregnancy, there were no abnormalities in either group. All neonates received a detailed pediatric assessment within first 24 hours postdelivery, revealing no neurological abnormalities excluding one with the Werdnig–Hoffmann disease. After discharge, the neonates were followed-up for at least 2 years.

There were 8 fetuses with postnatal developmental disabilities out of the 353 cases (2.27%) (Table 1). After examining the score of each parameter in these eight fetuses, we chose three parameters (isolated eye blinking, facial alteration or mouth opening, and isolated leg movement) for the Mini KANET (Table 2). A score range of 0–1 was characterized as abnormal, and 2–6 was normal (Table 3). Diagnostic indices for the prediction of postnatal developmental disabilities were compared between modified and Mini KANET assessments.

IBM SPSS statistical software version 22 for Windows (IBM SPSS Inc., Chicago, IL, USA) was used in all cases. Differences between the two groups regarding the maternal age, gestational age at examination, gestational age at birth, birth weight, umbilical artery blood pH, and prevalence of postnatal developmental disorder were examined using the unpaired t test, whereas the Mini KANET score and Apgar score differences were assessed with the Mann–Whitney U test. Comparisons of diagnostic indices between modified and Mini KANET assessments were conducted with the X^2 test. A value of $p < 0.05$ was considered significant.

Table 3: Interpretation of Mini KANET score

Total score	*Interpretation*
0–1	Abnormal
2–6	Normal

Results

Clinical characteristics of the subjects are shown in Table 4. There were 334 normal (94.6%) and 19 abnormal (5.4%) fetuses among the 353 studied with the Mini KANET. The gestational age at the Mini KANET examination in the abnormal group (34.4 ± 2.07 weeks) was slightly older than that (33 ± 2.73 weeks) in the normal group ($p < 0.05$). The total Mini KANET score in the abnormal group (median, 1; range, 0–1) was significantly lower than that in the normal group (median, 5; range, 2–6) ($p < 0.001$). There was a significant difference in the prevalence of postnatal developmental disabilities between the normal (1.19%) and abnormal (21.05%) Mini KANET groups ($p < 0.001$). However, there were no significant differences in the maternal age, gestational age at birth, birth weight, Apgar scores at 1 and 5 minutes, or umbilical artery blood pH between the two groups. Four cases of postnatal developmental disabilities were noted among the 334 normal fetuses (1.19%), whereas four cases of developmental disabilities were found among the 19 abnormal fetuses (21.05%) ($p < 0.0001$).

There was a significant difference in sensitivity between modified (37.5%) and Mini KANET (50%) assessments ($p = 0.001$),

Table 4: Clinical characteristics of subjects

		Maternal age (yo)	*Gestational age at examination (weeks)*	*Mini KANET total score*	*Gestational age at birth (weeks)*	*Birth weight (g)*	*Apgar score*		*UApH*	*Developmental disability*
							1 min	*5 min*		
Subject	*n*	*Mean (SD)*	*Mean (SD)*	*Median (range)*	*Mean (SD)*	*Mean (SD)*	*Median (range)*	*Median (range)*	*Mean (SD)*	*n (%)*
Normal	334	32.2 (5.03)	33 (2.73)	5 (2–6)	39.5 (1.33)	3055.1 (444.1)	8 (1–9)	9 (5–10)	7.29 (0.08)	4 (1.19)
Abnormal	19	32.3 (5.36)	34.4 (2.07)	1 (0–1)	39.5 (1.22)	2997.8 (436)	8 (7–9)	9 (9–10)	7.27 (0.07)	4 (21.05)
Significance		NS	$p < 0.05$	$p < 0.0001$	NS	NS	NS	NS	NS	$p < 0.0001$

KANET, Kurjak antenatal neurodevelopmental test; min, minute: NS, not significant; SD, standard deviation; UApH, umbilical artery blood pH; yo, years old

Table 5: Comparison of diagnostic indices between modified and Mini KANET assessments

	Sensitivity	*Specificity*	*Positive predictive value*	*Negative predictive value*	*Accuracy*
Subject	*(%)*	*(%)*	*(%)*	*(%)*	*(%)*
KANET	37.5	96.23	18.75	98.52	94.4
Mini KANET	50	95.65	21.05	98.8	94.62
Significance	$p = 0.001$	NS	NS	NS	NS

KANET, Kurjak antenatal neurodevelopmental test; NS, not significant

whereas no significant differences were noted for other diagnostic indices between the two assessments (Table 5).

Discussion

In the present study, the Mini KANET used only three parameters (isolated eye blinking, facial alteration or mouth opening, and isolated leg movement) instead of the eight parameters in the modified KANET. However, the rate of detecting postnatal developmental disabilities (21.05%) was the same as that by the modified KANET (18.75%).[1] Moreover, the sensitivity of the Mini KANET assessment (50%) was significantly higher than that of the modified KANET assessment (37.5%). These results suggest that the Mini KANET may be superior to the modified KANET for the prediction of postnatal developmental disabilities. However, fetuses with chromosomal abnormalities and lethal structural anomalies were excluded from the present study. Moreover, there were no abnormalities noted on anomaly scan in the 20th week of pregnancy. Therefore, the Mini KANET may be applicable only for healthy fetuses without any structural abnormalities.

In the modified KANET, some parameters such as cranial sutures/head circumference and finger movements, which are used in postnatal neurological assessment, are incorporated into the antenatal fetal neurodevelopmental test.[7] However, the score of cranial sutures/head circumference in fetuses with postnatal developmental disabilities except for one case (Ullrich congenital muscular dystrophy: case 5) was always 2 in the present study. So, we decided to exclude this parameter from the Mini KANET. With respect to finger movements, rates of predicting postnatal developmental disabilities were not improved using this parameter. So, we also decided to exclude this parameter from the Mini KANET.

The overall impression of general movement such as "Gestalt perception" is also a part of modified KANET assessment. Stanojevic et al.[7] stated that the incorporation of this parameter facilitates a more accurate and reliable functional assessment of young and immature central nervous systems. In the present study, however, the score of "Gestalt perception" in fetuses with postnatal developmental disabilities was always 2. The reason for this result on the assessment of "Gestalt perception" using 4D ultrasound is unknown. One possible explanation is the slow frame rates (1–3 frame rates/second) of the 4D ultrasound used in the present study. This image speed yields a dynamic image, not a real-time one. So, the examiner has to assess very wooden fetal movements, and it may be impossible to differentiate normal fetal movements from abnormal ones. Such limitations of fetal behavioral assessment by 4D ultrasound will be overcome by future technical advances, such as the advent of high-frame rate 4D ultrasound devices.[8]

In the present study, the score of isolated head anteflexion in fetuses with postnatal developmental disabilities excluding one case (motor developmental delay: case 7) was always 2. So, we also decided to exclude this parameter from the Mini KANET.

With regard to isolated hand movement/hand-to-face movements, rates of predicting postnatal developmental disabilities were not improved using this parameter. So, we also decided to exclude it from the Mini KANET.

In conclusion, the Mini KANET may become a simple antenatal fetal neurodevelopmental test for the prediction of postnatal developmental disabilities in healthy fetuses. However, the data and their interpretation in the present study should be taken with some degree of caution because of the small number of subjects studied. Further studies involving a larger sample size are needed to clarify the validity of the Mini KANET for the prediction of postnatal

developmental disabilities, comparing with the results of modified KANET in healthy and abnormal fetuses.

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