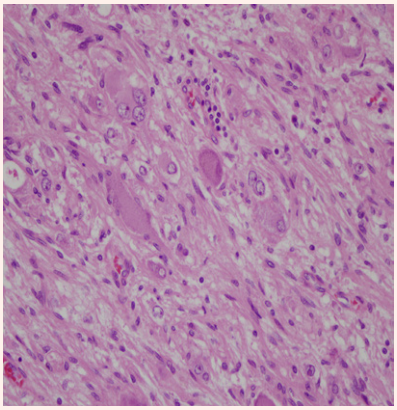
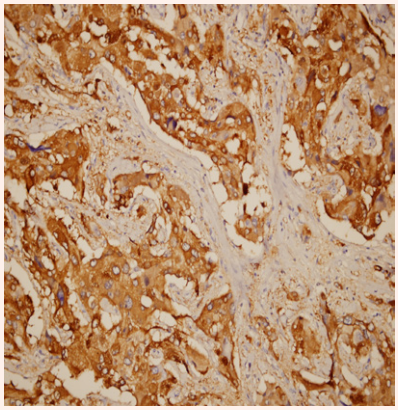
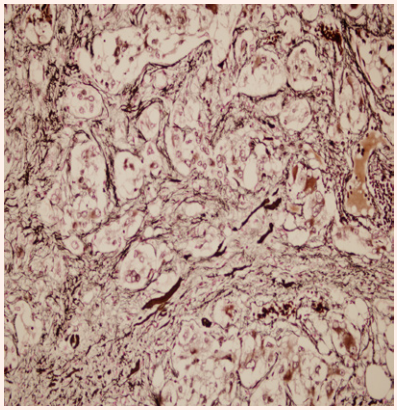
Journal of Experimental and Clinical Medicine

Vol: 35 • Issue: 2 • June: 2018

e-ISSN 1309-5129 JECM https://dergipark.org.tr/omujecm

Journal of Experimental and Clinical Medicine

e-ISSN 1309-5129

Vol: 35 Issue: 2 June 2018

e-ISSN 1309-5129

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Publish Type
Periodical

Press
HT MATBAA
Hamdi TANRIKULU
Hançerli Mah. Atatürk Bulvarı No:112/A İlkadım / SAMSUN
www.htmatbaa.com

Online Published Date
25.10.2019

Acid-free paper is used in this journal.

Indexed: CEPIEC, Crossref, DOAJ, EMBASE, EBSCOhost, Google Scholar, Index Copernicus, J-Gate, NLM Catalog (PubMed), Research Gate, Scopus, Turkiye Citation Index, World Cat.

Cover Art
Gün et al., Page 50; Figures 3, 4 and 5.

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https://dergipark.org.tr/omujecm

Clinical Research

J. Exp. Clin. Med., 2018; 35(2): 31-34
doi: 10.5835/jecm.omu.35.02.001

Premonitory awareness scale in children who stutter: PAIS-TR

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ARTICLE INFO

Article History
Received 10 / 05 / 2018
Accepted 04 / 01 / 2019
Online Published Date 25 / 10 / 2019

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Keywords:
Anticipation
Children
PAIS
Stuttering

ABSTRACT

Anticipation of stuttering is defined as the speaker's proprioceptive and/or cognitive sense that he or she is about to stutter and prevalent among people who stutter PWS. This research was motivated by the importance of the measurement of the anticipation effect in stuttering. Premonitory Awareness Scale in Stuttering (PAIS) was adapted to Turkish and psychometric properties of the scale in Turkish population was investigated. After the translation of the PAIS to Turkish, The PAIS-TR was administered to 60 children who stutter between 6-16 years of age and their age, gender, educational matched non-stutterer peers. Results showed that the PAIS-TR had a high level of internal consistency. The reliability and validity measurements demonstrate that the Turkish version of the PAIS is a psychometrically valid and reliable instrument that can be used both for research and clinical practices.

1. Introduction

Stuttering is a multidimensional disorder characterised by involuntary prolongations, repetitions, pauses and blocks which interrupt the flow of speech and effect the person's quality of life in a negative way (Craig et al., 2002; Yairi and Ambrose, 2013).

One of the characteristics of stuttering is the anticipation of the stuttering moment and can be defined as the speaker's proprioceptive and / or cognitive sense that he or she is about to stutter. Anticipation of stuttering in early childhood is reported to be lower than in adolescence and adulthood and correlated with stuttering awareness (Alm, 2004; Jackson et al., 2015). Recent research suggest that children who stutter (CWS) become aware of stuttering as early as after 2 years of the onset but having difficulty describing avoidance behaviors. Although it is apparent that awareness increases with age, life experiences and cognitive development, the cause and effect relationship between these variables has been difficult to establish. In other words, it is not clear whether avoidance behaviors appears later in development or, alternately, with adulthood, awareness of avoidance behaviors increases due to cognitive development (Boey et al., 2009).

Premonitory awareness is one of the awareness types seen in stuttering. It refers to an uneasy sensation inside the body or feelings of physical discomfort, pressure before a stuttering comes (Cholin et al., 2016).

Palms, shoulders and throat are reported to be the most common localisations of premonitory urges (Rajagopal et al., 2013). Given the central role of awareness in stuttering therapies, especially the ones focusing on avoidance reduction techniques (desensitisation) like in Fluency Modification therapies, additional studies of this phenomenon are needed.

Cholin et al. (2016) adapted Premonitory Awareness in Stuttering Scale (PAIS) which is derived from a questionnaire assessing premonitory awareness in people with Tourette syndrome in a detailed way (Premonitory Urge for Tics Scale (PUTS) (Woods et al, 2005). Stuttering and Tourette Syndrome share many similarities like the onset age of the disorders, sex ratio of the incidence and prevalence or the abnormal dopamine utilization in speech motor control areas of the brain. One of the other similarities is that both groups report that most of their stutterings / tics are preceded by a premonitory urge. But while PWS can stop a stuttering event by entirely refraining from any speech action, it is not possible to refrain a tic in Tourette syndrome (Leckman and Cohen, 2003).

The current study was motivated by the theoretical and clinical importance of the evaluation of premonitory awareness in children and adolescents. So, the aim of this study is to adapt PAIS to Turkish as PAIS-TR and to investigate the psychometric properties of the scale in Turkish population between the ages of 6-16.

2. Materials and methods

Participants

Participants were recruited from consecutive patients with stuttering at the Samsun Ondokuz Mayıs University Hospital, Speech and Language Therapy clinic. All the participants were diagnosed by a speech and language therapist. Diagnoses of the participants were based on a detailed clinical interview and Stuttering Severity Instrument IV (SSI-IV). Approval of the Ethical Committee of Ondokuz Mayıs University is obtained to conduct the study and based on the committee requirements, written informed consents of all the participants were collected.

The sample consisted of 60 children who stutter (CWS) (48 male and 12 female) and their age, gender and educational status matched non stutterer peers. The mean age of the first group was 10.5 years (SD.= 3.1 years, range = 6-16 years). The age of the second group ranged from 6 to 16 (M = 10.3 years, SD= 33 years). None of the participants had a comorbid diagnosis of any neurological, psychiatric, hearing, visual or any speech and language disorder other than stuttering.

None of the participants have received any kind of treatment related to stuttering nor had any experience of stuttering self-help or support groups during the measurements were administered. Demographics of the participants can be seen in Table 1.

Table 1. Demographics and mean (variance scores) of the participants on all tasks.

	PWS (N = 60) Mean (variance)	Control Group (N=60) Mean (variance)
Age (years)	10.5 (3.1)	10.3 (3.3)
Gender (boy/girl)	48/12	48/12
PAIS-TR	30.6 (7.6)	0.18 (.43)
SSI-IV		
Duration	11.8 (1)	0.2 (0.6)
Frequency	7.6 (0.8)	0.25(0.7)
Concomitant Disorders	1.5 (1.5)	0.0(0.0)
SSI-IV Total	21 (2.6)	0.45(1.2)
Percentage of Stuttered syllables	8.9 (4.7)	0.0 (0.0)
Subjective Stuttering Severity		
Instrument	4.9 (2.2)	0.0 (0.0)

Measures

Percentage of stuttered syllables

Spontaneous speech samples of CWS were collected by an experienced speech and language therapist. The duration of the recordings was of minimum 5 minutes in which children were suggested to talk about their daily routines, favorite movies, school, friends and such like topics. Percentage of stuttered syllables was obtained by taking the percentage of stuttered syllables to total syllables.

Stuttering severity instrument IV

In this study, the Turkish version of Stuttering Severity Instrument (SSI-4) (Mutlu, 2014) was administered to all participants in order to determine the frequency, duration and observed physical concomitants of the stuttering. The original version of SSI-IV was developed by Riley (2009) to determine the severity of overt features of stuttering. It provides a more comprehensive portrait of overt features of stuttering compared to measures including only the percentage of stuttered syllables alone. Another advantage of SSI-4 is using more than one speech sample since stuttering has been shown to vary from one time to other.

Subjective stuttering severity measurement

The Subjective Stuttering Severity Measurement was also evaluated because internal perceptions and dynamics of PWS like anxiety or being out of control could also contribute to premonitory awareness. This self-report measurement was based on a 9 item Likert type frequency scale (1= very mild to 9= very severe).

Translation of the PAIS-TR

Translation of the original English version of the PAIS into Turkish was based on a standard forward-backward translation process (Herdman et al., 2003). An additional question was added between 10 and 11 in the original one as suggested by the authors of the PAIS ("The anticipatory sensation allows me to avoid

the upcoming stutter by changing how I am talking") (Cholin et al., 2016).

A native Turkish linguist who is fluent in English translated the scale items to Turkish. The second examiner who is also a native Turkish speaker and fluent in English revised the translated version. Then the back translation process of the Turkish version of the scale to English was completed by a bilingual (Turkish-English) professional translator. The last comparisons between the original version and the back translation were made. Research team discussed the potential items that may lead to different meanings and the final version of the PAIS-TR was adapted.

Data analysis

Reliability

Test-retest reliability and internal consistency of the PAIS-TR was completed for the reliability analyses. For test-retest reliability, the PAIS-TR has completed by 20 CWS on two occasions 2 weeks apart. Mean age of the test-retest reliability group was 10.3 years (SD =36 ; range =6-182 years). PAIS-TR Total scores at Time 1 and Time 2 was calculated with the Spearman correlation and a paired t-test was conducted to test whether any differences in the scores existed between two-time points. For internal consistency of the PAIS-TR, inter-item correlations were evaluated by calculating Cronbach's alpha coefficient.

Validity

The validity of the scale was analyzed using Pearson's correlation analysis in order to investigate correlations between PAIS-TR, Self-Report Scale Score, Stuttering Severity Instrument IV (SSI-IV) and Percentage of Stuttered Syllables (SS%). Pearson's correlation coefficient over 0.6 was defined as strong correlation while values between 0.3 and 0.6 were defined as moderate correlations (Hinkle et al., 1998). Independent t-tests were conducted in order to compare gender and previous or current speech treatment experience. The data were analyzed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 22 package program.

3. Results

Descriptive statistics

The mean score of the PAIS-TR was 30.63 (SD=7.68) for the group of CWS and 0.18 (SD=0.43) for their age and gender-matched peers. The mean score of the Self Report Scale Score, Stuttering Severity Instrument IV (SSI-IV) and Percentage of Stuttered Syllables (SS%) was 4.9, 21, 8.9 respectively which implied mild to severe disfluency in the participants. The correlation between PAIS-TR total score and age was significant (r = , p <).

Reliability

In evaluating the test-retest reliability, high correlations were found between scores at Time 1 and Time 2 for the PAIS-TR (r = 0.99, p<.01). Cronbach's alpha value of the scale was 0.98, indicating a high level of internal consistency.

Validity

Table 2 shows the correlations between the PAIS - TR, Self Report Scale Score, Stuttering Severity Instrument IV (SSI-IV) and Percentage of Stuttered Syllables (SS%). All of the correlations between scales were significant. The highest correlation was observed between scales Stuttering Severity Instrument and PAIS-TR total score (r = 0.927, p < 0.01) while the lowest was between Subjective Stuttering Severity Measurement and PAIS-TR (r = 0.79, p < 0.01).

Table 2. Correlations (pearson product moment) between PAIS-TR Total score and SSI-IV, Subjective Stuttering Severity Measurement, and Percentage of Stuttered Syllables.

	TR-PAIS	SSI-IV	Subjective Stuttering Severity Measurement	Percentage of Stuttered Syllables
PAIS-TR	1	0.92(**)	79(**)	0.92(**)
SSI-IV	0.92(**)	1	0.86(**)	0.98(**)
Subjective Stuttering Severity Measurement	0.79(**)	0.86(**)	1	0.83(**)
Percentage of Stuttered Syllables				

** p < 0.01 level (2-tailed).

4. Discussion

The importance of detecting and monitoring premonitory awareness in children who stutter highlights the need for a valid and reliable instrument that can be used widely from clinic to research purposes. Although premonitory awareness has been proved to be a valuable clinical and research concept there are very few valid and reliable instruments that measure it in this way.

Recently, Cholin et al. (2016) developed the PAIS which contains items derived from the PUTS (Assessing Premonitory Awareness in Tic Disorders) (Woods et al., 2005). Most of the items were directly translated and the word "tic disorder" was changed with "stuttering" assuming that the two groups having some phenomenological similarities. Although initial psychometric properties of the PAIS were good, additional psychometric data are needed to replicate the study with an independent sample.

With regard to the reliability of the PAIS-TR, test-retest analyses and Cronbach alpha level were

measured. The correlatpon between PAIS-TR total score and each item showed also strong correlations as described and discussed below. Cronbach alpha level of the PAIS-TR was 0.97 which indicates a high internal consistency and also higher than the original one (Cholin et al., 2016).

The correlations between scales were high and similar to the original PAIS. Unlike, Cholin's et al.(2016)'s findings, correlations between PAIS-TR and Percentage of Stuttered Syllables and Subjective Stuttering Severity was positive. Although PAIS-TR appears to be less correlated with Subjective Stuttering Severity than the other measures correlational degree was still strong.

The correlation between PAIS-TR total score and age in CWS was also significant. A possible explanation of this can be the increase in the consistency of reporting of preliminary urges.

Anxiety disorders, obsessive-compulsive disorder (OCD) and Attentional Deficit and Hyperactivity Disorder (ADHD) are found to be strongly correlated with premonitory urges in Tourette Syndrome and other chronic tic disorders. A growing body of research has also demonstrated a high rate of ADHD (Riley and Riley, 2000; Ardnt and Healey, 2001; Conture, 2001), anxiety (Bloodstein and Bernstein Ratner, 2008) and obsessive-compulsive disorders (Murphy et al., 1989) among PWS. Given the comorbidity of all these disorders, it may be an interesting question to evaluate the relationship between anxiety-related physiologic or cognitive symptoms which can be an underlying phenomenon of all these disorders and premonitory urges in the future studies.

The main limitation of the study is the small sample size. Future studies with larger samples and longitudinal designs are needed to understand the dynamic properties of age and therapy on premonitory awareness abilities. Stuttering heterogeneity can also be investigated in relation to different responses to different items of the PAIS-TR. Responses of PWS with different etiologies (e.g., psychogenic stuttering, neurogenic stuttering etc.) is another interesting research question to be investigated.

In summary, the present study replicates the findings of Cholin's et al.(2016)'s findings among a Turkish sample. The reliability and validity measurements demonstrate that the Turkish version of the PAIS is, like the original one, a psychometrically valid and reliable instrument that can be used both for research purposes and in healthcare practice.

REFERENCES

Alm, P. A., 2004. Stuttering, emotions, and heart rate during anticipatory anxiety: A critical review. J. Fluency Dis. 29, 123–133.

Arndt, J., Healey, E.C., 2001. Concomitant disorders in school-age children who stutter. Lang Speech Hear Serv Sch. 32, 68–78.

Bloodstein, O., Bernstein Ratner, N., 2008. A handbook on stuttering (6. Ed.). Clifton Park, NY: Thomson Delmar, pp. 110-115.

Boey, R.A., Van de Heyning, P.H., Wuyts, F.L., Heylen, L., Stoop. R., De Bodt, M.S., 2009. Awareness and reactions of young stuttering children aged 2-7 years towards their speech disfluency. J. Comm. Dis. 42, 334–346.

Cholin, J., Heiler, S., Whiller, A., Sommer, M., 2016. Premonitory awareness in stuttering scale (PAIS). J. Fluency Dis. 49, 40-50.

Conture, E.G., 2001. Stuttering: Its nature, diagnosis, and treatment. Boston: Allyn and Bacon, pp. 255-257.

Craig, A., Hancock, K., Tran, Y., Craig, M., Peters, K., 2002. Epidemiology of stuttering in the community across the entire lifespan. J. Speech Lang. Hear. Res. 45, 1097-1105.

Elsabbagh, M., Johnson, M. H., 2007. Infancy and autism: Progress, prospects, and challenges. In From Action to Cognition. Progress in Brain Research, Vol. 164, C. von Hofsten and K. Rosander, eds. Elsevier, Amsterdam, pp. 355-383.

Herdman, M., Fox-Rushby, J., Rabin, R., Badia, X., Selai, C., 2003. Producing other language versions of the EQ-5D. In: Brooks R., Rabin R., de Charro F. (Eds) The measurement and valuation of health status using EQ-5D: A European perspective. Springer, Dordrecht, pp. 183-187.

Jackson, E., Yaruss, S., Quesal, R., Terranova, V., Whalen, D., 2015. Responses of adults who stutter to the anticipation of stuttering. J. Fluency Dis. 45, 38-51.

Leckman, J.F., Cohen, D.J., 2003. Tic disorders. In Rutter, M., Taylor, E. (Eds.), Child and adolescent psychiatry (4th Ed.). Oxford, Blackwell. pp. 593–611.

Murphy, D.L., Zohar, J., Benkelfat, C., Pato M.T., Pigott, T.A., Insel, T.R., 1989. Obsessive-compulsive disorder as a 5-HT subsystem-related behavioral disorder. Br. J. Psychiatry. 155, 15–24.

Mutlu, A. 2014. The Turkish application of stuttering severity instrument between 6-16-year-old school age children (Unpublished master's thesis). Gazi University, Ankara, Turkey.

Rajagopala, S., Serib, S., Cavanna, A. E., 2013. Premonitory urges and sensorimotor processing in Tourette syndrome. Behav. Neur. 27, 65–73.

Riley, G., 2009. The stuttering severity instrument for adults and children (SSI-4) (4th ed.). Austin, TX: PRO-ED, pp.1-13.

Riley, G. D., Riley, J., 2000. A revised component model for diagnosing and treating children who stutter. CICSD. 27, 188–199.

Woods, D.W., Piacentini, J., Himle, M.B., Chang, S., 2005. Premonitory urge for tic scale (PUTS): Initial psychometric results and examination of the premonitory urge phenomenon in youths with tic disorders. J. Dev. Behav. Pediatr. 26, 397–403.

Yairi, E., Ambrose, N., 2013. Epidemiology of stuttering: 21st century advances. J. Fluency Dis. 38, 66-87.

Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Clinical Research

J. Exp. Clin. Med., 2018; 35(2): 35-39
doi: 10.5835/jecm.omu.35.02.002

Alternative method in experimental ERG for retinal toxicity

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ARTICLE INFO

Article History
Received 04 / 12 / 2018
Accepted 09 / 01 / 2019
Online Published Date 25 / 10 / 2019

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Keywords:
Electroencephelography
Electroretinography
Photic stimulator
Retinal toxicity

ABSTRACT

We aimed to define a cost-effective and alternative method for experimental electroretinography (ERG) in rabbits. The trigger input port of data acquisition device was connected to output port of an unemployed EEG device. The exposure area of photic stimulator was firmly covered by Wratten neutral density filters with variable optical densities (ODs). Different optical transmissions were obtained by putting more than one filter over the other one. The illumination of the area at the level of rabbit eye was measured by a luminometer in photic stimulations. ERG was performed to the both eyes of three albino rabbits in scotopic and photopic conditions at the baseline. Intravitreal saline injections were performed in right eyes of the rabbits. ERG and ophthalmologic examination were repeated one week later. ERG responses were obtained by short-duration light stimuli with different strengths in scotopic (-2.69; -1.69; 0.00; 0.30; 0.69; 0.90; 1.10; 1.30; 1.69; 2.00 log stimulus energy (log cd.s/m^2)) and in photopic conditions (1.3; 1.69; 2.0; 2.10; 2.30 log stimulus energy (log cd.s/m^2)). Although minimal decays in amplitudes of a- and b- waves were detected after saline injection, there was no significant difference between baseline and after injection for the stimulus-response time of a- and b- waves ($p>0.05$). An unemployed EEG device can be effectively used for photic stimulation in experimental ERG in the studies of retinal toxicity.

1. Introduction

Electroretinography (ERG) is a test that measures the physiological response of retina to light exposure in light and dark adapted state of the subject. ERG is generally needed for detecting of retinal toxicity or retinal function loss in experimental study (Huang et al., 2015).

Assessing retinal drug toxicity is becoming increasingly important and routine as different molecules are now developed for the treatment of retinal diseases and vascular disorders. In pharmacology and toxicology, ERG can be used to quantify the possible side effects of any systemic drugs or intraocular administrated agents (Huang et al., 2015).

When performing ERG for retinal toxicity, the ERG recording should include a subjective assessment of the waveforms as well as a report of the more objective parameters. In order to analysis the response, two parameters are considered: implicit time (or the stimulus-response time, or peak time) and the amplitude. Delayed implicit time and/or decay in amplitude of the waves show an impairment in retinal integrity and function. So, researcher should obtain precise and reliable measurements to detect the change in amplitude and the stimulus - response time. In order to determine the implicit time, the moment of the stimulus should be determined and photic stimulator should be synchronized with ERG recorder. In our method, we

used an unemployed electroencephalography (EEG) device for photic stimulation. EEG is electrophysiologic test that is used for diagnosis of some neurological disease, particularly for epilepsy and flash EEG is technically similar to ERG. It has photic stimulator and it amplifies weak electrical signals to analysis, and it is performed by light flashes with different frequencies and these frequencies can be adjusted by control panel over the device (Fylan et al., 1999).

Compact experimental set of ERG may not be easily available, especially for laboratory studies because of high cost. We combined and synchronized the photic stimulator of an unemployed EEG machine with a basic data acquisition device and we defined a cost-effective method to measure electrical response of retina for investigating the retinal toxicity in animals.

2. Experimental procedure

The Ondokuz Mayıs University Animal Care and Use Committee, Samsun, Turkey, approved all aspects of this investigation, and all experiments were carried out in accordance with the Association for Research in Vision and Ophthalmology and European Union guidelines for the use of animals in research. Healthy female New Zealand white rabbits, weighing between 2.0 and 3.0 kg, were housed in separate cages. Three rabbits were maintained in a controlled environment with a 12-hour on/off light cycle, and food and water were administered ad libitum. All procedures were performed with these rabbits under anesthesia induced with an intramuscular injection of ketamine hydrochloride (35 mg/kg body weight; Ketalar 50 mg/ml; Pfizer; İstanbul, Turkey) and xylazine hydrochloride (5mg/kg bodyweight; Rompun 2%; Bayer, Germany).

Pupils were fully dilated by phenylephrine hydrochloride 2.5% (Mydfrine; Alcon Lab., Inc.; Texas, USA) and cyclopentolate hydrochloride 1% (Siklopleji n; Abdi İbrahim; İstanbul, Turkey) throughout the entire procedure in order to achieve a maximal retinal illumination. Pupil size was measured at the beginning and at the end of testing procedure. Eyelids were kept open by speculum during the examination and both corneas protected with a viscoelastic substance solution such as 1% methylcellulose in order to prevent corneal dehydration as well as to maintain a stable corneal potential. Electroretinographic waveforms were obtained from the eye simultaneously by positioning the active electrode (ERG-jet monopolar contact lens electrodes; Universo Plastique SA; Le Cret-Du-Locle, Switzerland) on the cornea. Reference electrode was placed at the junction of the ear and the temple whereas ground electrode was inserted subcutaneaously in the interscapular zone. Rabbits were kept in fully dark room for dark adaptation at least 30 minutes and the duration for light adaptation of the rabbits was at least 15 minutes in the study.

Device set up

Corneal electrode was inserted to the port of negative pole and reference electrode was inserted to the port of positive pole and ground electrode to ground port on the bio-amplifier connector. The exposure area of photic stimulator was firmly covered by 15.3 cm x 3.8 cm Wratten neutral density filters (Wrattten 96; Eastman Kodak; Rochester, NY) with variable optical densities (ODs). Different optical transmissions were obtained by putting more than one filter over the other one (Table 1). The distance between the photic stimulator and the eye of rabbit was kept in 15 cm and the illumination at the level of rabbit eye was measured by a luminometer (TES digital luminometer; TES Electronic Corp.; Taipei, Taiwan) in every photic stimulations. The trigger input port of data acquisition device (DAQ) (PowerLab 26T; ADInstruments Pty Ltd; New South Wales, Australia) was connected to output port of an unemployed EEG device (Nihon Kohden; EEG 4318) by BNC cable (Fig. 1). The PowerLab traces were automatically synchronized with the flash by the synchronizing trigger output of the flash unit. In order to see a marker on ERG trace for every light stimulus, we have adjusted the triger marker settings as 'on' in Scopus software (ADInstruments Pty Ltd; New South Wales, Australia). The signals were filtered with a pass-band of 1–300 Hz. The trace began 10 s prior to the flash in order to provide a pre-flash baseline of the bioelectric signal recorded from the eye. In order to keep the inter-stimulus interval at least 5 seconds for getting stronger responses, we have used 0.1Hz temporal frequency in photic stimulation for scotopic ERG. Low (1 Hz) and high (10 Hz and 30 Hz) temporal frequencies have been used in light stimulation to test cone system function (for photopic ERG). All frequencies were manually adjusted and managed by the control button over the EEG device (Fig. 2).

Table 1. Optical densities and transmissions of neutral density filters used in the study and stimulus strength obtained by the filters are shown.

ERG Condition	Optical Density	Transmission (%)	Stimulus Strength (log cd.s/m²)
Scotopic	4 + 1	0.001	-2.69
	4	0.01	-1.69
	2 + 0.3	0.5	0.00
	2	1	0.30
	1 + 0.6	2.5	0.69
	1 + 0.3 + 0.1	4	0.90
	1 + 0.2	6.3	1.10
	1	10	1.30
	0.6	25	1.69
	0.3	50	2.00
Photopic	1	10	1.30
	0.6	25	1.69
	0.3	50	2.00
	0.2	63	2.10
	0	100	2.30

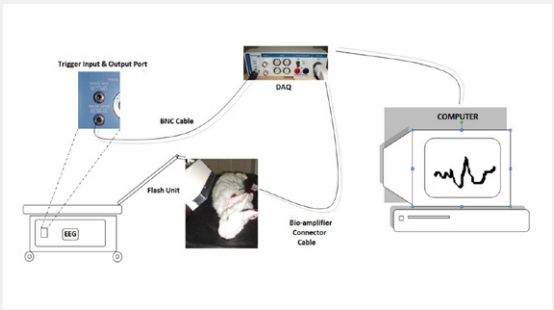

Fig. 1. Summary of the device set up in the experiment. All connections of the devices are shown in the figure.

Fig. 2. All frequencies can be manually adjusted and managed by the control button over the EEG device.

Interpretation of ERG

LabChart Reader software (LabChart Reader v8.0; ADInstruments Pty Ltd; New South Wales, Australia) was used for ERG analysis. Scotopic (dark-adapted) and photopic (light-adapted) amplitudes of the a-wave and b-wave were measured. A-wave amplitudes were measured from the preresponse baseline to the trough of the negative wave and reflect photoreceptor function (outer retina). B-wave amplitudes were measured from the trough of the a-wave to the peak of the b-wave and reflect Muller cell and bipolar cell function (inner retina). For oscillatory potentials of the 10- and 30-Hz flicker responses, the amplitude (OPs) was measured from the preresponse baseline to the peak. Implicit time for a- or b-wave was obtained by calculating the time between the stimulus and the top of the a- or b-peak. During analysis, we have used the average of the 10 ERG responses for every light stimulus with different strengths. Mean amplitudes of a- and b- waves were obtained by calculating the average of all a- and b-waves in all stimulus strengths.

Intravitreal saline injection

The needle was inserted infero-temporally through the conjunctiva into the pars plana 3–5 mm from the limbus. The globe was oriented so that the needle track was axial with no rotational movement. The needle was directed posteriorly towards the optic nerve to the central vitreous approximately 5 mm posterior to the apex of the posterior capsular pole. The needle was observed through the pupil, and care was taken not to nick the lens capsule or disrupt the vitreous. 0.05 ml isotonic saline were injected into the central of vitreus of the rabbits' right eyes after anesthesia. A cotton-tipped applicator was placed over the injection site for 30 s to minimize risk of reflux.

3. Results

We have obtained all components of an ERG measurement in this experimental set; such as, a- and b-waves, oscillatory potentials (OPs), photopic-negative response (PhNR),and i-wave (Fig. 3). ERG responses were obtained by short-duration light stimuli with different strengths in scotopic (-2.69; -1.69; 0.00; 0.30; 0.69; 0.90; 1.10; 1.30; 1.69; 2.00 log stimulus energy (log cd.s/m^2)) and in photopic conditions (1.3; 1.69; 2.0; 2.10; 2.30 log stimulus energy (log cd.s/m^2)). ERG traces in scotopic and photopic conditions, and flickers are shown in Fig. 4.

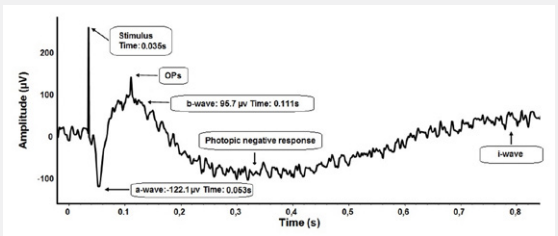

Fig. 3. The a- and b- waves, OPs, photopic-negative response (PhNR), and i-wave obtained in mesopic conditions with 0.90 log stimulus energy (log cd.s/m^2) are shown.

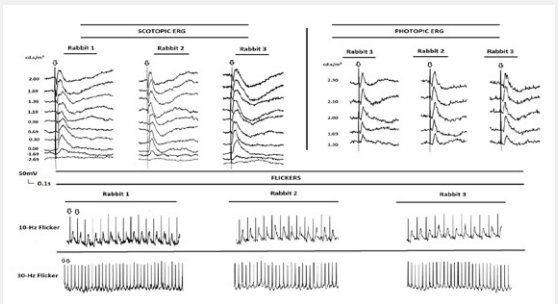

Fig. 4. All ERG traces in scotopic and photopic conditions and, flickers are shown. The alterations in the waves by the augmentation of the stimulus are seen. (Arrows show the stimuli).

Before saline injection, mean amplitude of a- and b- waves were -38.5 μv and 116.5 μv; respectively. Mean amplitude of a- and b- waves after saline injection were -35.3 μv and 104.4 μv, respectively. Implicit time of a- and b-waves before injection were

0.019 s and 0.045 s, and they were 0.015 s and 0.041 s after injection, respectively (Fig. 5). There was no statistically significant difference between before and after saline injection for these parameters (p>0.05).

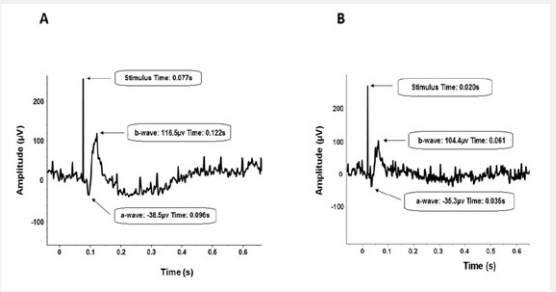

Fig. 5. Mean amplitudes of waves, the stimulus time and mean implicit time of waves are demonstrated in the ERG traces for baseline (A) and after saline injection (B).

4. Discussion

Experimental set of ERG may not be always available for all researchers. In our study, we defined a cost-effective and easily available technique to perform experimental ERG for the studies of retinal toxicity.

We have used an unemployed EEG device for photic stimulation. It can be easily synchronized with data acquisition device and we obtained precise measurements of implicit time in ERG traces by this synchronization. As a data acquisition device, we have used PowerLab 26T in our study. It has integrated data recording featuring a dual Bio Amp, an isolated stimulator and trigger input, and it includes Scope and LabChart software to quantify the ERG traces and analysis the data. This kind of devices are usually used in nearly all physiology laboratories for multiple purposes. By the control panel of EEG device (Fig. 2), it can be easy to change the frequency of the light stimulus. We have used 0.1Hz temporal frequency in photic stimulation for scotopic ERG and have used an average of 10-12 repeated flashes at 1Hz temporal frequency for photopic ERG to get maximum cone response. This represents the less variable intra-individual factor and thus enable comparison between the same animal from a session to another one (Rosolen et al., 2008; Perlman, 2009). So we have obtained similar results in ERG measurements before and after the saline injection for the amplitudes and implicit time of a- and b- waves. As a corneal electrode, we used ERG-jet equipped with a golden- metallic ring that does not generate artificial pupil and it is generally used for species with larger corneal diameter; such as human and rabbits. There is commercially available electrodes for an alternative electrodes to these expensive contact lens electrode, the fiber electrodes such as DTL are more popular (Dawson et al., 1979). DTL electrodes offer several advantages: painless even after several hours, no need for topical anesthesia and disposable. However, they must be used with great care and their positioning controlled as even minor changes in position could have a significant impact on the amplitude of the ERG parameters.

Ganzfeld dome provides standardized media for homogenous light stimulus and it allows researcher to take ERG response from both eyes of the rabbit at the same time. Although we did not use any Ganzfeld dome in our study, we obtained similar results in ERG response before and after saline injection. Partial sphere with nearly 0.40 m diameter would be used for this purpose. Internal surface of it should be painted with a high reflectance, spectrally flat coating (for example: Avian D high reflectance coating, Avian Technologies, Wilmington, OH) (Harrison et al., 2005).

In the study, we have obtained all components of an ERG measurements such as, a- and b- waves, OPs, PhNR, and i-wave. The changes in these components by altering OPs the strength of light stimulus was clearly seen in Fig. 4. It is now accepted that in photopic conditions the leading edge of the a-wave (first 10 ms) reflects the photoreceptor response to bright light (Hood and Birch, 1996). It should be noted that there is no pure rod ERG a-wave as such because in scotopic condition, an a-wave is recordable only in response to flashes of light intensities, which are in the photopic range. These responses are usually referred to as mixed cone and rod ERG because both photoreceptors are claimed to contribute to their genesis (Rosolen et al., 2005). In the study, a-wave has appeared first at the level of 0.30 log stimulus energy (log cd.s/m^2) in scotopic ERG trace, and it was shown that a-wave has been augmented by the increase in stimulus strength for both scotopic and photopic conditions and has achieved the maximum at the level of 2.10 log stimulus energy (log cd.s/m^2) in our study. The b-wave, that was attributed to post-receptoral elements (ON-bipolar cells), has appeared first at the level of -1.69 log stimulus energy (log cd.s/m^2) in the study, and it was also correlated with the stimulus strength. We obtained decay in implicit time after saline injection. Even if there was a difference in implicit time (0.004 s) before and after saline injection, it should be noted that faster than normal responses are usually considered as a variation of normal (Rosolen et al., 2008).

The OPs of ERG, that are best visible with bright light stimulation, can be used to assess the functional integrity of the inner retina (Heynen et al., 1985; Wachtmeister, 1987). The PhNR is a negative-going wave that occurs following the b-wave and it was seen that PhNR have been more visible after the stimulus level of 0.30 log stimulus energy (log cd.s/m^2) in ERG trace. Since the origin remains undetermined, the PhNR is significantly reduced in human patients with primary open angle glaucoma (Viswanathan et al., 2001), anterior ischemic optic neuropathy (Rangaswamy et

al., 2004) and other optic nerve neuropathies (Gotoh et al., 2004), consistent with an origin in ganglion cells or their axons. The i-wave is a positive deflection that occurs approximately 20 ms after the b-wave which can easily be identified in a number of animal species (Rosolen et al., 2004). It is thought that i-wave might be attributed to the activation of the retinal ganglion cells and the optic nerve including the chiasm (Rousseau et al., 1996). The amplitudes of PhNR and i-wave were related with the strength of the light stimulus in our study.

We have obtained all components of an ERG measurement in our study, and we have used an unemployed EEG device for photic stimulation. It can be easily synchronized with data acquisition device and we obtained precise measurements of implicit time in ERG traces by this synchronization. According to our definition of the experimental set, researchers may easily perform experimental ERG, and precise and more accurate ERG measurements can be obtained for the studies of retinal toxicity.

Acknowledgements

This study was supported by Ondokuz Mayıs University. The authors have no proprietary or financial interest in the materials presented here. Involved in design and conduct of the study (V.Y,Y.S.); collection, management, analysis, and interpretation of the data (V.Y., O.S.); and preparation, review, or approval of the manuscript (V.Y.). The Ondokuz Mayıs University Animal Care and Use Committee, Samsun, Turkey, approved all aspects of this investigation, and the study adhered to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

REFERENCES

Dawson, W. W., Trick, G. L., Litzkow, C. A., 1979. Improved electrode for electroretinography. Invest. Ophthalmol. Vis. Sci. 18, 988-991.

Fylan, F., Edson, A. S., Harding, G. F., 1999. Clinical significance of EEG abnormalities during photic stimulation in patients with photosensitive epilepsy. Epilepsia. 40, 370-372.

Gotoh Y, Machida S, Tazawa Y., 2004. Selective loss of the photopic negative response in patients with optic nerve atrophy. Arch Ophthalmol. 122, 341-346.

Harrison, J. M., Glickman, R. D., Ballentine, C. S., Trigo, Y., Pena, M. A., Kurian, P., Najvar, L.K., Kumar, N., Patel, A. H., Sponsel, W. E., Graybill, J. R., Lloyd, W. C., Miller, M. M. Paris, G. Trujillo, F. Miller, A. Melendez, R., 2005. Retinal function assessed by ERG before and after induction of ocular aspergillosis and treatment by the anti-fungal, micafungin, in rabbits. Doc. Ophthalmol. 110, 37-55.

Heynen H., Wachtmeister L., van Norren D., 1985. Origin of the oscillatory potentials in the primate retina. Vision Res. 25, 1365-1373.

Hood D.C., Birch D.G., 1996. Assessing abnormal rod photoreceptor activity with the a-wave of the electroretinogram: Applications and methods. Doc. Ophthalmol. 92, 253-267.

Huang, W., Collette, W., Twamley, M., Aguirre, S. A., Sacaan, A., 2015. Application of electroretinography (ERG) in early drug development for assessing retinal toxicity in rats. Toxicol. Appl. Pharmacol. 289, 525-533.

Perlman, I., 2009. Testing retinal toxicity of drugs in animal models using electrophysiological and morphological techniques. Doc. Ophthalmol. 118, 3-28.

Rangaswamy, N.V., Frishman, L.J., Dorotheo, E.U., Schiffman, J.S., Bahrani, H.M., Tang, R.A., 2004. Photopic ERGs in patients with optic neuropathies: Comparison with primate ERGs after pharmacologic blockade of inner retina. Invest. Ophthalmol Vis. Sci. 45, 3827-3837.

Rosolen, S.G., Rigaudiere, F., Le Gargasson, J.F., Chalier, C., Rufiange, M., Racine, J., Joly, S., Lachapelle, P., 2004. Comparing the photopic ERG i-wave in different species. Vet. Ophthalmol. 7, 189-192.

Rosolen, S.G., Rigaudiere, F., Le Gargasson, J.F., Brigell, M.G., 2005. Recommendations for a toxicological screening ERG procedure in laboratory animals. Doc. Ophthalmol. 110, 57-66.

Rosolen, S. G., Kolomiets, B., Kolomiets, B., Varela, O., Picaud, S., 2008. Retinal electrophysiology for toxicology studies: Applications and limits of ERG in animals and ex vivo recordings. Exp. Toxicol. Pathol. 60, 17-32.

Rousseau, S., Mc Kerral, M., Lachapelle, P., 1996. The i-wave: Bridging flash and pattern electroretinography. Electroencephalogr Clin Neurophysiol. Suppl. 46, 165-171.

Viswanatha.n, S., Frishman, L.J., Robson, J.G., Walters, J.W., 2001. The photopic negative response of the flash electroretinogram in primary open angle glaucoma. Invest. Ophthalmol. Vis. Sci. 42, 514-522.

Wachtmeister, L., 1987. Basic research and clinical aspects of the oscillatory potentials of the electroretinogram. Doc. Ophthalmol. 66, 187-194.

Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Clinical Research

J. Exp. Clin. Med., 2018; 35(2): 41-44
doi: 10.5835/jecm.omu.35.02.003

Comparison of glue ablation and endovenous thermal ablation of small saphenous vein and early and midterm results

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ARTICLE INFO

Article History
Received 20 / 01 / 2019
Accepted 20 / 02 / 2019
Online Published Date 25 / 10 / 2019

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Keywords:
Glue ablation
Radio frequency
Small sapheneous vein
Thermal ablation
Treatment

ABSTRACT

The aim of our study was to evaluate and compare the early and midterm post-operative outcomes of glue ablation and endovenous thermal ablation of the small saphenous vein. From January 2015 to January 2017, 26 consecutive patients who had admitted to our clinic with symptomatic chronic venous insufficiency of small saphenous vein who underwent either glue ablation and endovenous thermal ablation were included in this retrospective study. A total of 26 patients (12 males, 14 females; mean age 39.69±9.88 years; range 27 to 62 years) with 30 legs who underwent either glue ablation and endovenous thermal ablation either tumescent or local anesthesia were included in this study. BMI was 25.6 ±2.3 (range, 18.8-32.7). 20 patients (76.9%) were CEAP 2 and 6 patients (23.1%) were in CEAP 3 classification. The mean size of the treated small saphenous vein was 4,7±1,6 mm (range, 2.5-6 mm). Simultaneous phlebectomy was performed to 28 limbs (93.3%) under local anesthesia. No technical failure and device-related complications were observed during procedure. The mean average follow-up was 14±2.6 months (range 12-18 months). In this study, we found that glue ablation with cyanoacrylate closure was found superior results in early term however; no difference was noted on the mid-term result. To sum up, both glue ablation with cyanoacrylate closure and endovenous thermal ablation with radio frequency under either local or tumescent anesthesia can be easy, safely and effectively performed with satisfactory results.

1. Introduction

Chronic venous insufficiency affects 21% of the population (40% of females and 17% of males, which reduces the life quality of people (Maurins et al, 2008). Small saphenous vein (SSV) constitutes 15% of chronic venous insufficiency (Almgren et al., 1990). Surgical high ligation, stripping, endovenous thermal ablation including laser and radiofrequency ablation, foam therapy, MOCA and glue ablation (cyanoacrylate closure) are the treatment modalities of small saphenous vein chronic venous insufficiency (Rutgers et al., 1994). Treatment of chronic venous insufficiency of the small saphenous vein is still a debate. Some authors reported high recurrence and complication rates (Winterborn et al., 2004). Sural nerve present close to the small saphenous vein which potentially constitutes injury during the intervention. The saphenopopliteal junction cannot be present in 22% of patients. The studies about the treatment of symptomatic chronic venous insufficiency of the small saphenous vein are lacking in contrast to great saphenous vein. Deep venous thrombosis (DVT), nerve injury pain, bruising, superficial phlebitis, hematoma, superficial infection, and skin irritation are the major complications of

treatment of chronic venous insufficiency of small saphenous vein (Park, 2017). Endovenous thermal ablation demonstrates faster recovery compared to surgery (Park, 2017). The need of tumescent anesthesia, which may lead to pain, hematoma, and ecchymosis, is the main advantage of endovenous thermal ablation, however, glue ablation (cyanoacrylate closure) can be successfully applied under local anesthesia (Park, 2017). The aim of our study was to evaluate and compare the early and midterm postoperative outcomes of glue ablation and endovenous thermal ablation of the small saphenous vein.

2. Materials and methods

Study population

From January 2015 to January 2017, 26 consecutive patients who had admitted to our clinic with symptomatic chronic venous insufficiency of small saphenous vein who underwent either glue ablation and endovenous thermal ablation were included in this retrospective study. Preoperative symptoms were considered as pain, aching, cramping, heaviness, edema, and restless leg syndrome. Physical examination and laboratory results, medical history, comorbidities and postoperative outcomes were analyzed. Treatment indications were considered as more than 2 seconds of reflux and more than 2.5 mm and less than 6 mm in diameter of small saphenous vein. All patients were divided into two groups with respect to the type surgery as group 1 glue ablation (cyanoacrylate closure) and group 2 endovenous thermal ablation with radio frequency. Table 1 summarizes the baseline characteristics. Anatomical success was considered as the primary outcomes confirmed by Doppler ultrasound. Major complications were considered as the secondary outcomes. Sural nerve injury leads to numbness and paresthesia. Doppler ultrasound was performed standing position to all patients before the intervention, which examines both superficial and deep venous system of the limbs. No exclusion criteria were considered. Patients were followed up on postoperative 2 weeks, first month, 6th month and annually and examined with Doppler ultrasound. The preoperative Clinical, Etiologic, Anatomic, Pathophysiologic (CEAP) classification was also applied to all patients.

Table 1. Prevalence of central obesity in different smoking strata divided by participant characteristics; Iran 2007.

Baseline Characteristics			
	n	**%**	**Mean±SD**
Age			39.69±9.88
Gender			
Male	12	46.1	
Surgical Side			
Right	15	57.6	
CEAP 2	20	76.9	
CEAP 3	6	23.1	
Current smoking	5	19.2	
Hypertension	3	11.5	
DM	2	7.6	
BMI			25.6 ±2.3

The clinical, demographic and laboratory features of patients.

Surgical technique

After introduced a 7F sheat with the guidance of Doppler ultrasound, the 5F catheter was introduced to the small saphenous vein during endovenous thermal ablation, which was positioned 5 cm distal to the saphenopopliteal junction. Compression was achieved via probe of ultrasound during thermal ablation. Tumescent anesthesia was applied to reduce the thermal injury of the procedure.

After introduced a 7F sheat with the guidance of Doppler ultrasound, the catheter was delivered to the 2 cm distal to the saphenopopliteal junction and 2 ml cyanoacrylate glue was administered during a glue ablation procedure and compression was achieved with ultrasound probe under local anesthesia. Occlusion was confirmed by Doppler ultrasound. Simultaneous miniphlebectomy were performed after the ablation was done. A compression bandage was applied to all patients after the procedure. Intravenous sedation was done in need of.

Statistical analysis

The Statistical Package for the Social Sciences Windows Version 21 (SPSS Inc, Chicago, IL, USA) was used to compare the data. The Kolmogorov-Smirnov test was used to analyze normally distributed continuous variables. Categorical variables were presented in percentages and frequencies. Continuous variables were presented in mean ± standard deviation (SD). The continuous variables were compared using the T-test and the Mann-Whitney U test. The categorical data were tested with the Chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

3. Results

Sample sizes and demographic features

A total of 26 patients (12 males, 14 females; mean age 39.69±9.88 years; range 27 to 62 years) with 30 legs who underwent either glue ablation and endovenous thermal ablation either tumescent or local anesthesia were included in this study. The clinical, demographic and laboratory features are shown in Table 1. Glue ablation with cyanoacrylate closure was applied to 19 limbs and thermal ablation with radio frequency was applied to 11 limbs. BMI was 25.6 ±2.3 (range, 18.8-32.7). 20 patients (76.9%) were CEAP 2 and 6 patients

(23.1%) were in CEAP 3 classification. The mean size of the treated small saphenous vein was 4.7±1.6 mm (range, 2.5-6 mm). Simultaneous phlebectomy was performed to 28 limbs (93.3%) under local anesthesia. No technical failure and device-related complications were observed during procedure. The mean average follow-up was 14±2.6 months (range 12-18 months). No deep vein thromboses were observed. No nerve injury was detected during follow up. All patients were followed up in our study. 2 patients underwent redo surgery due to continuous reflux. The early success rate of Glue ablation with cyanoacrylate closure and endovenous thermal ablation with radio frequency were 94.7% and 54.5%, respectively (p=0.015). Mid term success rate of Glue ablation with cyanoacrylate closure and endovenous thermal ablation with radio frequency were 84.2% and 54.5%, respectively (p=0.1).

4. Discussion

In this study, we focused on the early and midterm results and comparison of Glue ablation with cyanoacrylate closure and endovenous thermal ablation with radio frequency. The main finding of this study was glue ablation with cyanoacrylate closure was found superior results in early term, however, no difference was noted on the mid-term results.

Allegra et al. (2007) reported a 132 patients study that the 5-year success rate of EVLA was in 70%. Of the 132 patients, the rate of paresthesia was 31% and the rate of DVT was 0.7%. Our results were superior that we did not observe any nerve injury or deep vein thrombosis. Allegra et al. (2007) noted that superiority was found between treatment modalities. The reported success rate of EVLA ranged 95%–100% with higher success rate compared to surgery (Allegra et al., 2007). Choosing the optimum treatment modality is scarce in the literature. Rashid et al. (2002) reported that the success rate of saphenopopliteal junction ligation was 59%. The rate of Paresthesia was 19.6% after surgery, 9.7% after RFA and 4.8% after EVLA (Allegra et al., 2007). The reported DVT rate ranged 0% to 1.2% after thermal ablation (van Eekeren et al., 2013). Glue ablation with cyanoacrylate closure reduces the rate of paresthesia; postoperative pain compared to endovenous thermal ablation and provides earlier return to work (van Eekeren et al., 2013, Morrison et al., 2015). Open surgery have reached a plateau however, newer techniques are developing (van Eekeren et al., 2013). Endovenous thermal ablation can be preferred to foam therapy. Surgery should be preferred in terms of failure. O'Hare et al. (2008) reported a 204 leg study that included 67 stripping of small saphenous varicose vein and found that the recurrence rate of reflux after stripping was 18% and 24% after saphenopopliteal junction ligation without any statistical significance. No difference was found in terms of paresthesia between stripping and ligation of saphenopopliteal junction (O'Hare et al., 2008). They concluded that the recurrence rate after stripping and ligation of saphenopopliteal junction were 13% and 32%, respectively ($P < 0.01$) (O'Hare et al., 2008). They thought that stripping reduced the recurrence of reflux (O'Hare et al., 2008). Our perioperative complication rates were found lower rather than the literature. In addition, stripping of the small saphenous vein is thought to be dangerous due to the potential injury of sural nerve during surgery (O'Hare et al., 2008). On contrast, no sural nerve injury was observed in our study. We found reasonable mid-term results in our study. Park (2017) reported that VenaSeal system was found to be safe and efficient for the treatment of reflux of small saphenous vein with 100% patient's satisfaction. The postoperative rate of phlebitis ranged was found 11.4% to 20% by Park (2017). In contrast to the previous study we did not observe any phlebitis. Phlebitis was thought to be due to foreign body or allergic reaction (Park, 2017). Park (2017) reported that no nerve injury was found after glue ablation so does we (Park, 2017).

This study has a number of limitations worth noting. First, we conducted a retrospective study. Second, the number of patients, which were included in our study, may seem relatively small compared to other studies. Third, it's a single-center design. Fourth, perforating veins were not assessed. Confirmation of our findings will require randomized controlled prospective studies.

Conclusion

In this study, we found that glue ablation with cyanoacrylate closure was found superior results in early term however; no difference was noted on the mid-term result. To sum up, both glue ablation with cyanoacrylate closure and endovenous thermal ablation with radio frequency under either local or tumescent anesthesia can be easy, safely and effectively performed with satisfactory results.

REFERENCES

Allegra, C., Antignani, P.L., Carlizza, A., 2007. Recurrent varicose veins following surgical treatment: Our experience with five years follow-up. Eur. J. Vasc. Endovasc. Surg. 33, 751–756.

Almgren, B., Eriksson, E., 1990. Valvular incompetence in superficial, deep and perforator veins of limbs with varicose veins. Acta. Chirurg. Scand. 156, 69–74.

Maurins, U., Hoffmann, B.H., Lösch, C., Jöckel, K.H., Rabe, E., Pannier, F., 2008. Distribution and prevalence of reflux in the superficial and deep venous system in the general population--results from the Bonn Vein Study, Germany. J. Vasc. Surg. 48, 680–687.

Morrison, N., Gibson, K., McEnroe, S., Goldman, M., King, T., Weiss, R., Cher, D., Jones, A., 2015. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). J. Vasc. Surg. 61, 985–994.

O'Hare, J.L., Vandenbroeck, C.P., Whitman, B., Campbell, B. Heather B.P, Earnshaw J.J., 2008. On behalf of the Joint Vascular Research Group. A prospective evaluation of the outcome after small saphenous varicose vein surgery with oneyear follow-up. J. Vasc. Surg. 48, 669-674.

Park I., 2017. Initial outcomes of cyanoacrylate closure, venaseal system, for the treatment of the ıncompetent great and small saphenous veins. Vasc. Endovascular Surg. 51, 545-549.

Rashid, H.I., Ajeel, A., Tyrrell, M.R., 2002. Persistent popliteal fossa reflux following saphenopopliteal disconnection. Br. J. Surg. 89,7 48–751.

Rutgers, P.H., Kitslaar, P.J., 1994. Randomized trial of stripping versus high ligation combined with sclerotherapy in the treatment of the incompetent greater saphenous vein. Am. J. Surg. 168, 311–315.

Winterborn, R.J., Campbell, W.B., Heather, B.P., Earnshaw, J.J., 2004. The management of short saphenous varicose veins: A survey of the members of the vascular surgical society of Great Britain and Ireland. Eur. J. Vasc. Endovasc. Surg. 28, 400–403.

Van Eekeren R. R. J. P., Boersma D, Konjin V, de Vries J.P.P.M, Rejinen M.M.J.P., 2013. Post-operative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. J. Vasc. Surg. 57, 445–450.

Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Case Report

J. Exp. Clin. Med., 2018; 35(2): 45-47
doi: 10.5835/jecm.omu.35.02.004

Hoigne's syndrome following the injection of repeating benzathine penicillin G: A case report

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ARTICLE INFO

Article History
Received 04 / 11 / 2015
Accepted 01 / 03 / 2016
Online Published Date 25 / 10 / 2019

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Keywords:
Benzathine penicillin
Emergency department
Hoigne's syndrome

ABSTRACT

Hoigne's syndrome is characterized by the development of acute neuropsychiatric symptoms which are mainly panic-like anxiety state and conversive neurosis. We here report a 60-year-old man with Hoigne's syndrome. Emergency physicians should always keep in mind Hoigne's syndrome.

1. Introduction

Hoigné described the first cases of pseudo-anaphylactic reactions induced by intramuscular administration of procaine penicillin G in 1959 (Hoıgne and Schoch 1959). Agitation, hallucinations and delirium are stated, to occured following the administration of intramuscular procaine penicilin. Hoigne's syndrome (HS) have been reported in the literature to our knowledge (Silber and D'Angelo, 1985; Schmied et al., 1990; Schreiber and Krieg, 2001).

Pathogenesis of HS is still unclear (Landais et al., 2014). In literature, it is stated that HS is caused by the administration of many different antibiotics such as ceftriaxone, cefoxcitin, clarithromycin, procaine penisiline, intralesional steroid and lidocaine (Rockney, 1987; Rallis et al., 2009; Baran, 2014; Landais et al., 2014; Thompson and Theobald, 2016). Allergic and non-allergic effects are occured following injections and infusions. Here we present a case of Hoigné's syndrome which was caused by intramuscular benzathine penicilin administration after obtaining patient consent.

2. Case

A 50-year-old man was admitted to the emergency department (ED) in September 2014, complaining

of agitation and fear of death. He had an benzatine penicilin injection for treatment of an streptococcus infection. 2-3 min after injection, symptomps occured. Patient medical history was unremarkable except for routine monthly intramuscular benzathine penicillin injections. He didn't use any recreational drug, had no history of alcohol abuse. He was a nonsmoker. On admission to our ED, his blood pressure was 160/80 mmHg; his pulse was 90 beats/min; body temperature was 36º C. His general status was moderate, glasgow coma score was 13 (Eye: 4, motor: 5, verbal: 4). He was confused and in a panic-like anxiety state. Other his physical examination was normal and no focal neurological signs. On mental status examination, he was disoriented and uncooperative and conversive neurosis at the time. On cognitive testing he scored 18/30 on a screen of cognitive function (mini mental state examination) Laboratory tests were normal. He was started on intravenous diazepam infusion. After the initial stabilisation of the patient a CT-Scan, a MRI-Diffusion and a Cranial MRI were performed. None showed any abnormal findings. Over the next 1 day, his all symtoms resolved completely.

3. Discussion

We report a case afflicted by a reaction known as HS. Altough HS is reported in with the use of agents such as ceftriaxone, cefoxcitin, clarithromycin, HS usually occurs due to intramuscular procaine penisiline (Rockney, 1987; Landais et al., 2014; Sawa et al., 1977).

The pathophysiological mechanisms of which drugs may induce an acute neuropsychiatric episode, are not exactly known (Landais et al., 2014). However, pathogenesis of HS may be associated with an infectious disease and/or organic brain disease of other origin (Zdziarski, 2001). This case had no signs of infectious diseases or organic brain disease.

HS is characterized predominantly by different neurotic symptoms including severe psychomotor agitation with confusion, sensations of disintegration, depersonalization, and derealization, perceived changes of body shape, visual and auditory hallucinations, panic-like anxiety including fear of death as well as alterations of consciousness and seizures (Schreiber and Krieg, 2001). Our case had neuropsychiatric symptoms such as panic-like anxiety state and conversive neurosis. Although he had not all symptoms, he was diagnosed HS. Because there was not other diagnosis to explain the patient's condition

It is stated that HS may be manifested by repeating injections of procaine penicilin (Magiera et al., 1985; Araszkiewicz and Rybakowski, 1997;). Another clinical study, neuropsychiatric reactions were analysed during penicillin treatment and the most often symptoms were conversive neurosis, and subsequently the hypochondriac syndrome. In same study, HS had occurred after an average of sixth injections (Magiera et al., 1985). In 94% of the patients the neurotic symptoms manifested themselves within minutes after injections. A positive correlation between the age and intensity of the symptoms was found (Magiera et al., 1985). HS following the administration of intramuscular penicillin G procaine have been rare in the pediatric groups (Silber and D'Angelo, 1985). In our study, we report a geriatric patient who had a history of repeated benzathine penicillin injections and had severe neuropsychiatric symptoms.

As a result, emergency physicians should always keep in mind HS in patients with a history of penicilline use to properly manage disease and avoid unnecessary imaging. The dramatic and unexpected manifestation of this condition calls for an immediate diagnosis to decide the appropriate treatment.

REFERENCES

Araszkiewicz, A., Rybakowski, J. K., 1997. Hoigne's syndrome, kindling, and panic disorder. Depress. Anxiety. 4, 139-143.

Baran, R., 2014. Proximal nail fold intralesional steroid injection responsible for Hoigné syndrome. J. Eur. Acad. Dermatol. Venereol. 28, 1563-1565.

Hoıgne, R., Schoch, K., 1959. Anaphylactic shock and acute nonallergic reactions following procaine-penicillin. Schweiz. Med. Wochenschr. 89, 1350-1356.

Landais, A., Marty, N., Bessis, D., Pages, M., Blard, J.M., 2014. Hoigne syndrome following an intravenous injection of ceftriaxone: A case report. Rev. Med. Interne. 35, 199-201.

Magiera, P., Trojanowski, L., Leszczyński, L., 1994. Acute non-allergic reaction after administration of penicillin as a factor in the occurrence of neurotic symptoms. Psychiatr. Pol. 28, 677-685.

Rallis, E., Moussatou, V., Saltos, L., 2009. Clarithromycin-induced Hoigne syndrome in a patient treated for rosacea. J. Eur. Acad. Dermatol. Venereol. 23, 1093-1094.

Rockney, R.A., 1987. Variant of Hoigne's syndrome following intramuscular cefoxitin sodium? Am. J. Dis. Child. 141, 475-476.

Sawa, H., Balcar-Boroń, A., Kucharski, E., Olijewski, S., Slowik, J., 1977, Hoigńe syndrome: A non-allergic complication during penicillin administration. Pediatr. Pol. 52, 1285-1287.

Schmied, C., Schmied, E., Vogel, J., Saurat, J.H., 1990. Hoigné's syndrome or pseudo-anaphylactic reaction to procaine penicillin G: A still current classic. Schweiz. Med. Wochenschr. 120, 1045-1049.

Schreiber, W., Krieg, J.C., 2001. Hoigne syndrome. Case report and current literature review. Nervenarzt. 72, 546-548.
Silber, T.J., D'Angelo, L., 1985. Psychosis and seizures following the injection of penicillin G procaine. Hoigne's syndrome. Am. J. Dis. Child. 139, 335-337.
Thompson, T.M., Theobald, J.L., 2016. Hoigne syndrome: A little-known adverse effect of lidocaine. Am. J. Emerg. Med, 34, 679.
Zdziarski, P., 2001. Hoigne syndrome as an acute non-allergic reaction to different drugs: Case reports. Pol. Merkur. Lekarski. 10, 453-455.

Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Case Report

J. Exp. Clin. Med., 2018; 35(2): 49-52
doi: 10.5835/jecm.omu.35.02.005

A composite tumor in the adrenal gland: Pheochromocytoma and ganglioneuroma

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ARTICLE INFO

Article History
Received 13 / 12 / 2015
Accepted 05 / 03 / 2016
Online Published Date 25 / 10 / 2019

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Keywords:
Adrenal medulla
Composite tumor
Ganglioneuroma
Pheochromocytoma

ABSTRACT

Composite tumor in the adrenal medulla is a rare tumor containing endocrine and neural components. Pheochromocytoma together with ganglioneuroma combination is the most common compound tumor in the adrenal medulla. Pheochromocytoma originates from the chromaffin cells in adrenal medulla and the ganglioneuroma originates from autonomic ganglion cells. A 49-years-old male patient refers to hospital with the complaint of abdominal pain which had started 1month ago. A mass was detected in his right adrenal gland, and he underwent right adrenalectomy. Macroscopic study of the adrenalectomy material section revealed a 7 x 5 x 4.5 cm dark brown-yellow mass. Histopathological studies revealed that the tumor was consisted of two components 1) areas compatible with pheochromocytoma characterized by islands of polygonal cells with eosinophilic cytoplasm, round-oval nucleus and a prominent nucleolus, and forming small nodules with well-defined margins in a fibrovascular stroma and 2) mature ganglion cells scattered in a stroma with Schwann-like cells. In immunohistochemical study, pheochromocytoma foci were stained positive for chromogranin, synaptophysin and tyrosine hydroxylase. Schwann and ganglion cells were stained positive with S100. On the basis of histomorphological and immunohistochemical findings, the patient diagnosed with compound tumor of pheochromocytoma and ganglioneuroma. Although ganglioneuroma is encountered as a rare tumor, it should be kept in mind in the differential diagnosis of the adrenal masses.

1. Introduction

Composite tumor is a rare tumor which occurs most frequently in the adrenal medulla and is consisted of endocrine and neural components (Rai et al., 2012). The dominant component in this tumor is pheochromocytoma, and the second component is ganglioneuroma in 60-80% of the cases. Rare secondary components are the ganglioneuroblastoma and the neuroblastoma and more rarely the malignant peripheral nerve sheath tumor (Comstock et al., 2009; Menon et al., 2011; Gorgel et al., 2014). Little is known about its biological potential and molecular genetic profile (Comstock et al., 2009). Since these tumors are rarely seen, we would like to present our case of composite tumor of pheochromocytoma-ganglioneuroma together with the data in the literature.

2. Case

The patient was a 49-years-old male. He referred to our hospital with the complaint of abdominal pain which had started 1 month ago. A mass was detected in the right adrenal gland of the patient who had a hypertension history, and he underwent right adrenalectomy.

The macroscopic study of the 10 x7x4.5 cm adrenalectomy material section revealed a 7 x 5 x 4.5 cm tumor. Tumor's margins were well-defined, and it

was covered with a dark brown-yellow fibrous capsule. In histopathological examination, tumor was observed with relatively well-defined margins that had normal adrenal gland tissue around itself. Tumor was also included foci of necrosis and hemorrhage. There were 2 main components in the tumor. Areas compatible with pheochromocytoma were characterized by islands of polygonal cells with eosinophilic cytoplasm, round-oval nucleus and a prominent nucleolus, and forming small nodules with well-defined margins in a fibrovascular stroma (Figs. 1, 2). Second component was consisted of mature ganglion cells scattered in a stroma with Schwann-like cells (Fig. 3). Neuroblastoma-like immature small cell components were not observed. Mitosis was rare in both components. There were large areas of necrosis in the tumor, but no lymphovascular invasion was seen. The tumor showed limited extensions into the neighboring fat tissue.

In the immunohistochemical study, pheochromocytoma foci showed positive staining with chromogranin (monoclonal antibodies, SP12, 1:200, Thermo Scientific, Fremont, USA), synaptophysin (monoclonal antibodies, Clone EP158, 1:200, BioSB, Santa Barbara, USA) and tyrosine hydroxylase (Clone 1B5, 1:40, Novocastra, USA) (Fig. 4). Sustentacular cells showed positive stainingwith S100, and Ki-67 index was lower than 1% (polyclonal Antibodies, Genemed, San Francisco, USA). Typical zellballen islets were observed with the help of silver (Fig. 5). As for ganglioneuroma component, it showed focal positive staining with chromogranin, positive with synaptophysin and tyrosine hydroxylase and diffuse-strongly positive for s100 (Fig. 6). Ki-67 index was lower than 1%. On the basis of the histomorphological and immunohistochemical findings, the patient was diagnosed with compound tumor of pheochromocytoma-ganglioneuroma.

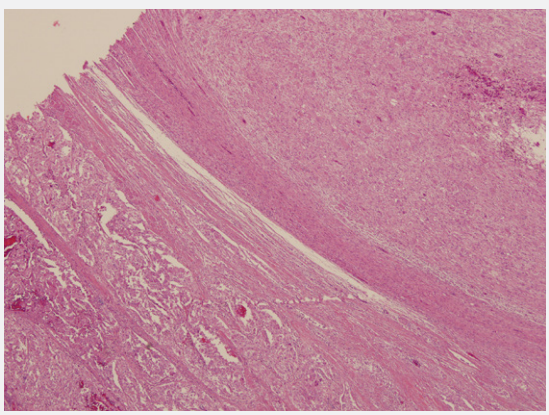

Fig. 1. Two distinct component of tumour (HE X 40).

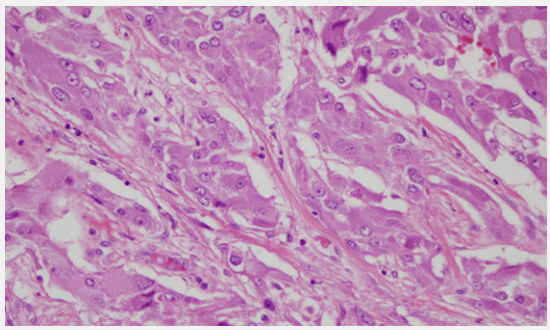

Fig. 2. Pheochromocytoma component (HE X400).

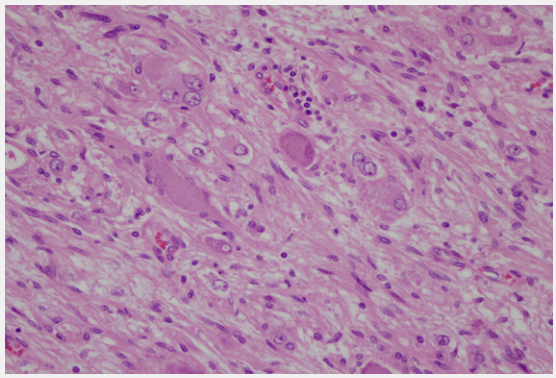

Fig. 3. Ganglioneuroma component (HE X 400).

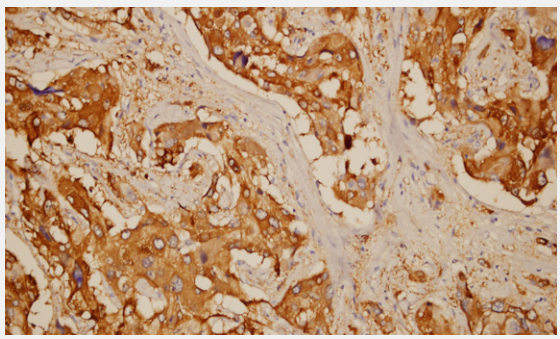

Fig. 4. The chromaffin cells were strongly positive of Tyrosine Hydroxylase (DAB X 200).

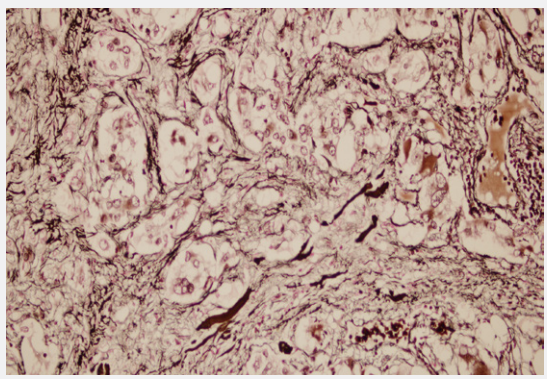

Fig. 5. Zellballen islets (Silver X 200).

Fig. 6. Ganglioneuroma component showed diffuse-strongly positive for S100 (DAB X 400).

3. Discussion

Composite tumors of the adrenal medulla are rare tumors, and they account for less than 3% of the sympatho adrenergic pheochromocytomas (Choi et al., 2006; Rao et al., 2014). While pheochromocytoma originates from adrenal medulla chromaffin cells, ganglioneuroma develops from autonomic ganglion cells. Embryologically, chromaffin and ganglion cells arise from neural crest cells and from the migration into somatic field. Compound tumor can occur due to faulty migration into the somatic area or due to disrupted development of neural crest cells (Choi et al., 2006; Rao et al., 2014). Both components of the compound tumor can cause hormonal hypersecretion, and symptoms related to hypersecretion can occur. Clinically headache, tachycardia, excessive sweating can be observed in 50% of the patients with active pheochromocytoma. A continuous or paroxysmal hypertension is the basic symptom of pheochromocytoma (Choi et al., 2006; Rai et al., 2012; Rao et al., 2014). Moore et al. reported hypertension only in 4 patients out of 13 patients with composite tumor (Choi et al., 2006). Our patient also had a hypertension history. Aqueous diarrhea due to increased vasoactive intestinal peptide (VIP) has been reported in some patients. Both components of the composite tumor can secrete VIP (Mahajan et al., 2010; Hu et al., 2013).

The patients reported in the literature are usually over 30 years old, most of them are in the fifth decade. Similar to the patients in the literature, our patient was 49 years old. Tumor is equal in males and females. Significant numbers of the patients are sporadic. But it can rarely be comorbid with the syndromes of hereditary pheochromocytoma/paraganglioma outside the adrenal gland, syndromes of familial tumor such as neurofibromatosis type 1 (NF), multiple endocrine tumor (MEN) syndromes or adrenocortical tumors (Lam and Lo 1999; Gücin et al., 2003; Comstock et al., 2009; Hu et al., 2013; Shida et al., 2013). In our patient, MEN, NF or adrenocortical tumor were not observed.

The differential diagnosis includes adrenocortical adenoma or hyperplasia and other adrenal tumors such as of adrenocortical carcinoma and pheochromocytoma. Pathological study is essential in determining the components of compound tumor. Microscopic study should be performed carefully in large areas. In a study including 46 patients, compound tumor with ganglioneuromatous component was detected in 4 patients. The cases displayed heterogeneous radiological, macroscopic and microscopic features (Menon et al., 2011). Compound tumors in the bladder, retroperitoneum and caudaequina have also been reported (Hu et al., 2013). It is difficult to estimate the biological behavior of the compound tumor. Prognosis of these tumors varies. Metastatic lesions of compound tumor almost always develop from the neural component. Accordingly, in microscopic evaluation, immature neuroblastic component should be studied carefully for the metastatic potential. Autopsies revealed liver metastasis only in one of the patients with pheochromocytoma ganglioneuroma (Comstock et al., 2009; Rao et al., 2014). In one study, N-myc amplification was studied both in the compound tumor and pheochromocytoma. It was found out that neuroblastic elements in the compound tumor had low mitotic- karyorrhectic index and positive histological features, but no N-myc amplification was detected. These results indicate that neuroblastic elements have no prognostic importance in composite tumors (Comstock et al., 2009; Rao et al., 2014). In our study, neuroblastoma-like immature small cell components were not observed. The main treatment of compound tumor is surgical resection. Clinical follow-up is recommended for the malignancy potential (Hu et al., 2013).

In conclusion, composite tumor of pheochromocytoma-ganglioneuroma is a rare tumor. Components of tumors can be identified in the adrenal tumor resection specimens with careful macroscopic, microscopic and immunohistochemical study. Metastasis is rare. It is mostly observed together with ganglioneuroblastoma, so microscopic examination should be performed carefully in large areas. Neuroblastoma-like foci elimination is important for the recurrence and follow-up of metastasis.

REFERENCES

Choi, E.K., Kim, W.H., Park, K.Y., 2006. A case of a composite adrenal medullary tumor of pheochromocytoma and ganglioneuroma masquerading as acute pancreatitis. Korean J Intern Med 2, 141-145.

Comstock, J.M., Willmore-Payne, C., Holden, J.A., Coffin, C.M., 2009. Composite pheochromycitoma. A clinicopathologic and molecular comparison with ordinary pheochromocytoma and neuroblastoma. Am. J Clin. Pathol. 132, 69-73.

Gorgel, A., Çetinkaya, D.D., Salgur, F., Demirpence, M., Yılmaz H., Karaman, E.H., Tutuncuoglu, P., Oruk, G., Bahceci, M., Sari, A.A., Altinboga, A.A. and Paker, İ., 2014. Coexistence of gastrointestinal stromal tumors (GISTs) and pheochromocytoma in three cases of neurofibromatosis type 1 (NF1) with a review of the. Intern. Med. 53, 1783-1789.

Gücin, Z., Geçer, M.O., Aksoy, B., 2003. Nörofibromatozis eşliğinde non-sporadik adrenal kompozit feokromositom. Feokromositom-ganglionörom birlikteliği. Olgu sunumu. Turk Patoloji Derg. 19: 42-44.

Hu, J., Wu, J., Cai, L., Jiang, L., Lang, Z. et al., 2013. Retroperitoneal composite pheochromocytoma- ganglioneuroma: A case report and review of literature. Diagn. Pathol. 8, 63.

Lam, K.Y., Lo, C.Y., 1999. Composite Pheochromocytoma-Ganglioneuroma of the Adrenal Gland: An Uncommon Entity with Distinctive Clinicopathologic Features. Endocr. Pathol. 10, 343-352.

Mahajan, H., Lee, D., Sharma, R., Chin, P. et al., 2010. Composite phaeocromcytoma-ganglioneuroma, an uncommon entity: Report of two cases. Pathology. 3, 295-297.

Menon, S., Manajan, P., Desai, S.B., 2011. Composite adrenal medullary tumor: A rare cause of hypertension in a young male. Urol. Ann. 3, 36-38.

Rai, R., Gajanthody, S., Jayaram, J., Chauhry, R.K., 2012. Composite pheochromycitoma. South Asian J. Cancer. 1, 98-99.

Rao, R.N., Singla, N., Yadav, K., 2013. Composite pheochromycitoma-ganglioneuroma of the adrenal gland: A case report with immunohistochemical study. Urol. Ann. 5, 115–118.

Shida, T., Igawa, T., Abe, K., Hakariya, T., Takehara, K., Onita, T. and Sak, H., 2015. Composite pheochromocytoma of the adrenal gland: A case series. BMC Res. Notes. 8, 257.

Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Case Report

J. Exp. Clin. Med., 2018; 35(2): 53-55
doi: 10.5835/jecm.omu.35.02.006

Twin pregnancy in a woman with hypogonadotropic hypogonadism and uterus didelphys: A case report and literature review

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ARTICLE INFO

Article History
Received 26 / 04 / 2016
Accepted 20 / 06 / 2016
Online Published Date 25 / 10 / 2019

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Keywords:
Cesarean
Hypogonadotropic hypogonadism
Infertility
Uterus didelphys

ABSTRACT

Hypogonadotropic hypogonadism is a rarely seen medical condition arising from absence or decrease of hypothalamic pituitary function. Hormone plasma concentrations are either can not be determined or are at very low rates. Uterus didelphys is a congenital uterine about medial fusion defects of mullerian ducts. A 22-year-old female patient applied to our clinic due to premier infertility. The diagnosis of uterus didelphys was confirmed as a result of hysterosalpingography. Recombinant FSH was started on ovulation induction. In the transvaginal ultrasonography performed 3 weeks later, 2 gestational sacs and fetal heartbeats in both cavities were observed. After cesarean operation, strassmann procedure was performed and both cavities were combined in the same session.

1. Introduction

Hypogonadotropic hypogonadism is a rarely seen medical condition arising from absence or decrease of hypothalamic pituitary function. In hypogonadotropic hypogonadism, follicle stimulating hormone (FSH) and luteinizing hormone (LH) plasma concentrations are either can not be determined or are determined at very low rates (Awwad et al, 2013).

Uterus didelphys is a congenitaluterine abnormality caused by medial fusion defects of mullerian ducts. Women with abnormality of uterus didelphys need infertility treatment more frequently than those with other uterine abnormalities. Moreover, multiple pregnancy is a rarely seen condition in the women with uterus didelphys (Bhattacharya and Mistri, 2010). We presented twin pregnancy in a woman with uterus didelphys and hypogonadotropic hypogonadism after ovulation induction with gonadotropin. On the 3rd

day of menstruation, 75 IU/day recombinant FSH was started on ovulation induction. The diagnosis of uterus didelphys was confirmed as a result of hysterosalpingography and radiopaque material was present in both bilateral fallopian tubes. On the 3rd day of menstruation, 75 IU/day recombinant FSH was started on ovulation induction. The diagnosis of uterus didelphys was confirmed as a result of hysterosalpingography and radiopaque material was present in both bilateral fallopian tubes. On the 3rd day of menstruation, 75 IU/day recombinant FSH was started on ovulation induction.

2. Case

A 22-year-old female patient applied to our clinicdue to premier infertility. The patient had been married for 3 years and had never received infertility treatment. Spontaneous menstruation was not realizing in her anamnesis and she was taking combined oral contraceptive for menstruation.

In her gynecological examination, longitudinal vaginal septum and two cervical dilations were observed. The laboratory findings of the patient (FSH: 0.1 mıu/ml, LH: 0.1 mıu/ml, estradiol; E2:3 pg/ml) were compatible with hypogonadotropic hypogonadism.The diagnosis of uterus didelphys was confirmed as a result of hysterosalpingography and radiopaque material was present in both bilateral fallopian tubes. On the 3rd day of menstruation, 75 IU/day recombinant FSH was started on ovulation induction. The dose was increased as 150 IU on the 7th day of the cycle. Due to the observation of 2 dominant follicles withapproximately 18-mm length in the transvaginal ultrasonography made on the 14th day of the cycle, and the determination of E2 value as 650 pg/ml, recombinant human chorionic gonadotropin (hCG) was administered subcutaneously. 36 hours later, intrauterine insemination was performed. In the transvaginal ultrasonography performed 3 weeks later, 2 gestational sacs and fetal heartbeats in both cavities were observed. Her pregnancy follow-ups were normal.Antenatal screening tests were not performed. The patient was admitted in our hospital with regular and painful uterine contradictions in the 34th gestational week. In her vaginal examination, 3-cm cervical dilation and effacement of 60 % were observed. In the 34th week, elective cesarean operation was performed through bilateral sub-segment transverse incision. Strassmann procedure was performed and both cavities were combined in the same session (Fig. 1). Weights of the first and the second infants were relatively 1900 and 2000g. Apgar scores were 7/8. The infants did not need neonatal intensive care. No preoperative complication developed. Postoperative period was normal. She and her infants were discharged on the 6th postoperative day without any complication.

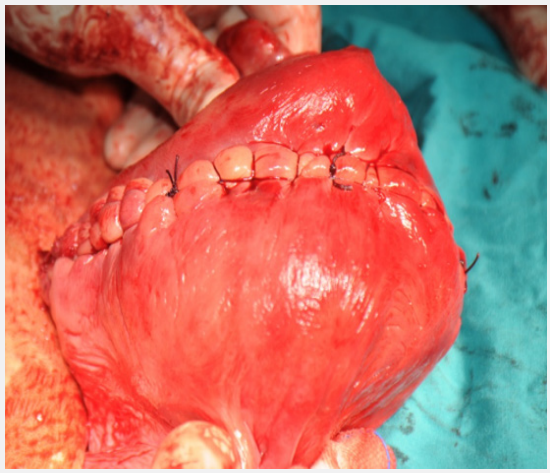

Fig. 1. Strassmann metroplasty.

3. Discussion

It is quite hard to determine the incidence of mullerian abnormalities in general population. The most common ones are uterus didelphys, bicornuate uterus, and unicomate uterus (Meiling et al., 2011). Most of these congenital abnormalities are defined as a potential cause of fetal malpresentation, preterm labor, recurrent pregnancy wastage, and infertility (Chan et al., 2011). In our case,the labor was preterm but malpresentation did not occur. Reproductive performance of uterus didelphys is rather low (Raga et al., 1997). Most authorshad different thoughts on the obstetric results of uterus didelphys. According to some authors,women with uterus didelphys need infertility treatment more frequently than those with other uterine abnormalities (Zhang et al., 2010). The infertility in women with hypogonadotropic hypogonadism is associated with inadequate secretion of hypothalamic gonadotropin releasing hormone (GNRH).

This situation causes decreasing of plasma levels of FSH and LH. These hormones should be relapsed. Ovulation induction is required for successful pregnancy (Hsing-Tse et al., 2012). Gonadotropin treatment can be used as an alternative to pulsatile GNRH or menopausal gonadotropins to ensure pregnancy in infertile patients with hypogonadotropic hypogonadism. We used purified FSH as gonadotropin and achieved a successful pregnancy. The patients with mullerian abnormality who conceived by using human menopausal gonadotropin –human chorionic gonadotropin are reported in the literature (Tanaka et al., 1998). In the literature 88% of the women with mullerian abnormality are stated to have pregnancies resulting in live birth after strassmann operation. Pregnancy periods of these were normal, ended within the term and they had cesarean sections. The rate of taking live infant to home is reported to be 100% (Lolis

et al., 2005). We performed strassmann metroplasty operation in order to prevent possible recurrent pregnancy wastage and preterm labor in case of future pregnancies of the patient. Successful pregnancies can be achieved by using ovulation induction agents in theuterus didelphys patients with hypogonadotropic hypogonadism. Strassmann metroplasty can be performed in order to prevent preterm recurrent pregnancy wastage and malpresentation.

REFERENCES

Awwad, J.T., Farra, C., Mitri, F., Abdallah M.A., Jaoudeh, M.A., Ghazeeri, G. 2013. Split daily recombinant human LH dose in hypogonadotrophic hypogonadism: A nonrandomized controlled pilot study. Reprod. Biomed. 26, 88-92.

Bhattacharya, S., Mistri, P.K., 2010. Twin pregnancy in a woman with uterus didelphys. Online J Health Allied Scs. 9(4): 24.

Chan Y.Y., Jayaprakasan, K., Tan, A., Thornton, J.G., Coomarasamy, A., Raine-Fenning, N.J., 2011. Reproductive outcomes in women with congenital uterine anomalies: A systematic review. Ultrasound Obstet. Gynecol. 38, 371–382.

Hsing-Tse, Y., Chyi-Long, L., Hong-Yuan, H., Yung-Kuei, S., 2012. Successful pregnancy in a woman with kallmann's syndrome using human menopausal gonadotropin followed by low-dose human chorionic gonadotropin in the mid-to-late follicular phase. Taiwanese J. Obstet. Gyn. 2, 300-302.

Lolis D.E., Pashopoulos, M., Makrydimas, G., Zikopoulos, K., Sotiriadis, A., Paraskevaidis, E., 2005. Reproductive outcome after strassman metroplasty in women with a bicornuate uterus. J. Reprod. Med. 50, 297-301.

Meiling, H., Anthony, O., George, A., 2011. Congenital uterine anomalies and a diverse pregnancy outcomes. Am. J. Obstet. Gynecol. 205, 558.

Raga, F., Bauset, C., Remohi, J., Fernando, Bonilla-Musoles., Carlos, Simon., Antonio, Pellicer., 1997. Reproductive impact of congenital mullerian anomalies. Hum. Reprod. 122277-2281.

Tanaka, T,. Fujimoto, S., Matsuzaki, N., Sakuragi, N., Ichinoe, K., 1988. Twin gestation induced with hMG-hCG in a patient witha bicornuate uterus: Report of a successful delivery. Int. J. Fertil. 33, 33-35.

Zhang, Y., Zhao, Y., Qiao, J., 2010. Obstetric outcome of women with uterine anomalies in china. Chinese Med. J. 123, 418-422.

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e-ISSN 1309-5129