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- Analysis of 1429 tonsillectomy cases on single surgeon experience
- Radiologically isolated syndrome (RIS) to definite multiple sclerosis

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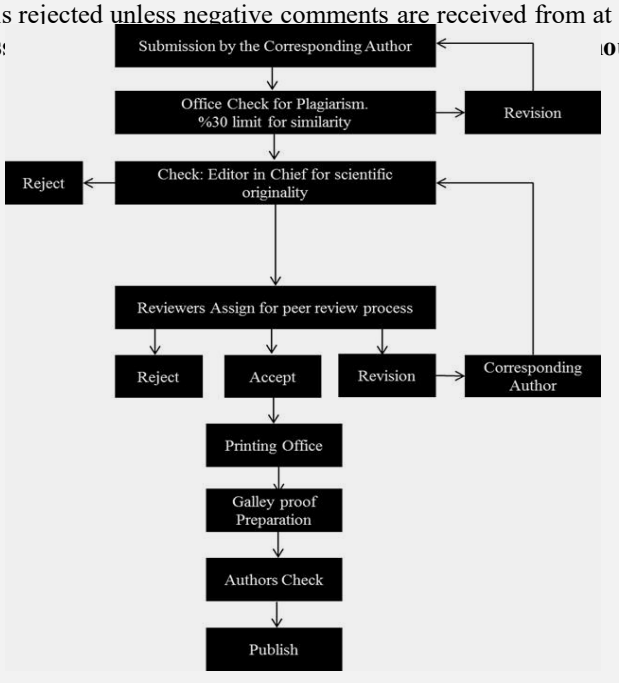

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Evoked potentials and other guiding factors of conversion from radiologically isolated syndrome to definite multiple sclerosis

Serkan Demir[1*], Eyup Duzgun[2], Cahit Kafadar[1], Rifat Erdem Togrol[1], Mehmet Guney Senol[1], Akin Cakir[3]

Abstract

Objective: Radiologically Isolated Syndrome (RIS) has become a popular subject recently with quite a number of follow-up and other clinical studies being done. A consensus on the approach to the patient with RIS is being tried to be established. The aim of our study was to assess the role of visual evoked potential (VEP) and somatosensory evoked potential (SEP) as a guiding factor for the conversion from Radiologically Isolated Syndrome (RIS) to definite Multiple Sclerosis (MS).

Material and methods: 49 RIS patients who were referred to GATA Haydarpasa Training Hospital Neurology Department between 2011-2015. All of the patients fullfillied the 2009 Okuda criteria for RIS and other differential diagnosis were excluded accordingly. VEP and SEP examinations made during the pre-MS RIS period were scanned retrospectively. For the VEP examination, the P100 latency and amplitudes, for the SEP examination, the P40 latency and amplitude was analysed.

Results: 49 patients were included in this study, the mean time of follow-up was 21,8 months. 63% of patients were female, while 37% were male. The mean age was 31,2 years. Among the four patients with abnormal SEPs, MS developed in three of them (75%) over time. This is statistically significant ($p = 0.011$). VEP and/or SEP was abnormal in 8 patients and MS developed in 4 (50%) of those ($p=0.017$). The following factors have a positive statistically significant correlation with conversion to MS: Presence of active plaques ($r=0.461$, $p<0.001$), presence of more than 9 plaques ($r=0.287$, $p=0.046$), VEP and/or SEP pathologies ($r=0.402$, $p=0.004$) and number of plaques ($r=0.309$, $p=0.031$). The most important factor for the transformation is the presence of active plaque which increases the risk 8.1-fold. The second important factor seems to be the presence of VEP and/or SEP abnormality, but this factor does not reach statistical significance.

Conclusion: In the conversion to MS risk from RIS, VEP- SEP examinations are important and should take its place in the follow-up of these patients.

Key words: Multiple syclorosis, Evoked potential, Radiological isolated syndrome

Introduction

As the imaging methods have become prevalent, more and more cases are being encountered with no specific complaints, symptoms or neurological examination findings but with lesions of their white matter in their magnetic resonance imagings (MRIs) that have been performed for various neurological complaints not implying multiple sclerosis (MS). This is usually called “asymptomatic MS” or nowadays more commonly, "Radiologically Isolated Syndrome (RIS)"(1,2). It is known that some of these patients are known to turn into definite MS over the years. While RIS may lead to definite MS, the observed asymptomatic MRI lesions are lack of the pathological confirmation.

Evoked potential investigations (EPs) are used to evaluate a physiological system in real time. Physiological system here refers to sensorial afferent pathway functions (i.e visual, touching and hearing). Usually both latency and amplitude of the potential are evaluated and compared to normal values in these. The study to evaluate the visual pathways with the help of giving stimulations to one eye in the form of flash or changing checkerboard pattern is called "Visual Evoked Potential (VEP)”. Sensory information is evaluated on the physiological level is evaluated by the "Somatosensory Evoked Potentials (SEP)". VEP and SEP show the real-time status of the visual and somatosensory afferent pathways function.

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Although it has been removed from the revised McDonald criteria in 2010, VEP and SEP are still known to occupy a very important place in the diagnosis and follow-up of patients.

In this study, VEP and SEP examinations of patients were scanned before the "pre-MS" RIS period retrospectively, reviewed for any abnormality at this stage, and tried to determine whether there is a guiding factor for the transformation or not.

Material and Methods

The 49 patients who were hospitalized to GATA Haydarpasa Training Hospital Neurology Department between 2011-2015 whom, neurological symptoms not typical for MS, and with no neurological examination findings for MS, while having demyelinating lesions in their cranial MRI were included in the study. All of the patients fullfillied the 2009 Okuda criteria for RIS and differential diagnosis were excluded accordingly. None of the evaluated patients had any other medical condition that could create an abnormality in the electrophysiological studies.

VEP test protocol

The VEP were performed by using a MEDELEC TM Multimedia EMG/EP Synergy Monitoring System (London, United Kingdom) in abidance of the current guideline for pattern VEP of the International Societyfor Clinical Electrophysiology of Vision (3). Complete ocular examinations of anterior and posterior segments were done by the two ophthalmologists, and then patients went to VEP test.

VEP measurements were obtained with the patient wearing a visual aid, if needed and each eye tested separately. A steel needle recording electrode was placed at Oz' (2 cm above the inion) and the reference electrode at Fz. Stimulation was performed according to standard protocols by checkerboard pattern reversal by using a computer screen at a distance of 1 m with a check size of 60 minutes of arc.

VEP test results assessed by two ophthalmologists and one neurologist. The mean P100 VEP latencies of the right and the left eyes of each patient were measured. According to laboratory normal values, the upper latency limit for the P100 latency was 120 ms. P100 latency was considered abnormal if there is not any wave, latency longer than 120 ms in each of eyes or a difference equal or more than 6 ms between two eyes.

SEP test protocol

For SEP recordings, subjects lay on a couch in a warm and semidarkened room. All SEP examinations were made using MEDELEC TM Multimedia EMG/EP Synergy Monitoring System (London, United Kingdom). SEPs were elicited by electrically stimulating the posterior tibial nerves by superficial electrodes at the ankle on medial malleolus. The ground electrode was placed 10 cm distal to the active electode. Square wave stimuli of 0.2 ms duration were delivered via a bipolar surface stimulator with a frequency of 3/sec. The stimulus intensity was adjusted to be slightly above the motor threshold, which in most cases was also twice the threshold for radiating paresthesia towards the toes.

The cortical potentials were recorded with electrodes placed on the head of the subject. One recording electrode (impedance below 5 kQ) was placed at the Cz' while another was placed at the Fpz (according the 10–20 system) as the reference electrode. The analysis time was 120 ms, including also 10 ms of preanalysis. The amplifier bandpass was 100–2000 Hz. Two averages of 500 trials each were obtained for each condition and printed out by the computer on a printer. It is well known that movement attenuates the early cortical SEPs, thus patients were asked to stay still during the procedure. For tibial SEP, latency and amplitude of the positive peak around 38-40 ms after the stimulating pulse (p40) was evaluated.

Tibial nerve SEPs were evaluated using established standards of our laboratory by two neurologist. (4). The criterion of a pathologic event in the SEP was defined as an increase of latency or a reduction of amplitude. Changes in SEP were considered pathological only if they were repeatable and sustained across at least two consecutive testings.

Statistical analyses

Statistical analyses were performed using SPSS software version 15. The univariate analyses to identify variables associated with MS occurence during follow up, was investigated using Fisher's exact test, and chi square tests, where appropriate. Since the data were non-normally distributed and ordinals, the correlation coefficients and their significance were calculated using the Spearman test. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into the logistic regression analysis to determine the independent predictors of MS occurance. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. A 5% type-I error level was used to infer statistical significance.

Results

The 49 patients were included in this study which was designed as a retrospective cohort study. The mean time of follow-up was 21.8 months. 63% of patients were female, while 37% were male. The mean age was 31.2 years. Most frequent age range was 26-35 which is 39% of all the patients. The following factors have a positive statistically significant correlation with conversion to MS: Presence of active plaques ($r = 0.461$, $p < 0.001$), presence of more than 9 plaques ($r = 0.287$, $p = 0.046$), VEP and/or SEP pathologies ($r = 0.402$, $p = 0.004$).

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The most common complaints at the time of referral was headache (55%). 77% of the patients had more than two plaques. More than 9 plaques were detected in 21 cases (% 42.8). 7 cases (14.2%) had abnormal VEP results while 4 cases (8,1%) had abnormal SEP results. Among all the patients, 21 of the cases (42.8%) developed MS over time. Demographic and clinical data of the patients are summarized in Table 1.

Table 1: Patient charecteristics

Patient	Gender	Age	Symptoms	Number of Plaques	Gd (+) plaque	Spinal plaque	VEP P100 latance	SEP P40 latance	OKB
1	F	18	Syncope	2	-	-	N	N	X
2*	F	28	Epilepsy	5	-	-	N	N	Neg
3	F	38	Backache	>9	1	1	N	N	Pos
4	F	29	Peripheral Facial Palsy	2	1	-	N	N	X
5	M	22	Headache	>9	-	-	N	N	Neg
6	F	42	Headache	3	-	-	N	N	X
7	F	34	Headache	3	-	-	N	N	X
8	M	24	Headache	2	-	-	N	N	Neg
9	F	36	Vertigo	>9	1	1	N	N	Pos
10	M	30	Headache	>9	-	-	N	N	X
11	M	36	Headache	>9			N	N	X
12	F	35	Vertigo	>9	-	-	N	N	X
13	F	28	Headache	>9	-	-	R>	N	Neg
14*	F	48	Vertigo	>9	2	1	N	R>L	Pos
15	F	45	Headache	>9	-	-	N	N	X
16	F	38	Vertigo	4	-	-	N	N	X
17	F	25	Headache	6	-	-	N	N	Pos
18	F	30	Headache	>9	-	-	N	N	X
19	F	27	Headache	2	-	-	N	N	X
20*	F	35	Vertigo	4	1	-	L>	N	Pos
21	F	27	Epilepsy	6	-	-	N	N	X
22*	M	27	Headache	>9	2	-	N	N	Pos
23*	F	32	Head Travma	>9	5	-	R>	L>	X
24	F	37	Headache	>9	-	-	N	N	Neg
25	F	18	Headache	7	-	-	N	N	X
26	M	21	Tremor	2	-	-	N	N	X
27	F	33	Headache	2	-	-	N	N	X
28	M	41	Headache	2	-	-	N	N	Neg
29*	F	23	Headache	>9	2	2	R/L>	R/L>	Pos
30	M	21	Headache	5	1	-	N	N	Neg
31*	F	20	Vertigo	2	-	-	N	N	X
32	M	21	Head Trauma	6	-	-	N	N	X
33	F	32	Headache	>9	-	-	N	N	X
34*	M	26	Vertigo	>9	-	1	N	N	Pos
35	F	36	Vertigo, Cramps	2	-	-	N	N	X
36	M	24	Headache	2	-		N	N	X
37	M	22	Epilepsy	>9	-	-	R/L>	R/L>	Pos
38	M	21	Headache	3	-	-	N	N	X
39	F	49	Headache	5	-	-	N	N	X
40	F	30	Headache	2	-	-	N	N	X
41	M	22	Headache	5	-	-	N	N	X
42	F	42	Headache	>9	-	-	N	N	Neg
43	M	26	Headache	>9	-	-	R/L>	N	X
44	F	47	Headache	5	-	-	N	N	X
45*	M	44	Peripheral Vertigo	>9	-	-	N	N	Pos
46	F	55	Peripheral Vertigo	>9	-	-	N	N	X
47	M	21	Peripheral Vertigo	5	-	-	L>	N	X
48	F	35	Peripheral Vertigo	5	1	-	N	N	X
49	M	31	Uveitis	4	-	-	N	N	Pos

* the patients that converted to MS,
N: normal, R: right, L: left , X : patients with no CSF studies

Table 2: Conversion rates of risc factors to MS

Risc factors	Did not develop MS	Developed MS	Total	p value*
Number of patients with VEP abnormality, n (%)	4(57%)	3(42.8%)	7(14.2%)	0.075
Number of patients with SEP abnormality, n (%)	1 (25%)	3 (75%)	4(8.1)	0.011
Number of patients with VEP and/or SEP abnormality, n (%)	4(50%)	4(50%)	8(16.3%)	0.017
Active plaque	5(50%)	5(50%)	10(20.4%)	0.005
Patients with >9 plaques	15(71%)	6(28.5%)	21 (42.8%)	0.060

*Fisher exact test.

Table 3: Spearman correlation analysis of the MS, active plaque, plaque number, >9 plaque number and age.

		Presence of Active plaque	>9 plaque	VEP and/or SEP negative	Plaque number	Age
MS existence	r	0.461	0.287	0.402	0.309	0.084
	p value	<0.001	0.046	0.004	0.031	0.566

Table 4: Multiple logistic binary regression analysis.

Risk factors	RR*	%95 Confidence interval (CI)	p value
Presence of active plaques	8,103	(1.232-53.285)	0.029
Abnormal VEP or SEPs	4,511	(0.562-36.244)	0.156
More than 9 plaques	3,262	(0.428-24.839)	0.254
Age	1,015	(0.904-1.141)	0.797

*RR: estimated relative risk shown by odds ratio and 95 % confidence intervals.

Among the four patients with abnormal SEP, MS developed in three of them (75%) over time. This is statistically significant (p = 0.011). VEP and/or SEP was abnormal in 8 patients and MS developed in 4 (50%) of those (p = 0.017). Of the 10 patients with an active plaque, 5 of them (50%) developed MS (p = 0.005).

Of the 7 patients with only an abnornal VEP response, conversion to MS was observed in only 3 (42.9%) (p = 0.075). MS developed in 6 out of 21 patients (28.6%) with more than 9 plaques (p = 0.060). Univariate analysis findings are summarized in the Table 2.

The following factors have a positive statistically significant correlation with conversion to MS: Presence of active plaques (r = 0.461, p <0.001), presence of more than 9 plaques (r = 0.287, p = 0.046), VEP and/or SEP pathologies (r = 0.402, p = 0.004) and number of plaques (r = 0.309, p = 0.031). These all have a statistically significant positive low-to-moderate correlation. No significant statistical relationship between age and conversion to MS was found. (r = 0.084, p = 0.566) (Table 3).

When the relationship between the presence of abnormality in VEP and/or SEP and the number of plaques, and the presence of more than 9 plaques is evaluated, a positive low-to-moderate statistically significant correlation is calculated (r = 0.309, p = 0.031; r = 0.287, p = 0.046; respectively) . There is a mild positive statistically significant correlation between SEP deterioration and spinal plaques (r = 0.392, p = 0.005).

In order to to calculate how effective these risk factors are in the transformation to MS, we have created a logistic regression model and we have seen that the most important factor for the transformation is the presence of active plaque. (Table 4) The presence of active plaque increases the risk 8.1-fold. The second important factor seems to be the presence of VEP and/or SEP abnormality, but this factor does not reach statistical significance. Similarly, the presence of 9 or more plaques does not reach statistical significance.

In the power analysis using G power 3.1.9.2 belonging to this multiple binary logistic regression analysis, the power was found to be 0.934.

Discussion

Patients with MRI investigations made for any reason that is compatible with MS incidentally, while having no clinical data or medical clinical examination findings are termed or identified as RIS (1,2 5,6). At this stage, there is no consensus on this clinical entity and no suggested treatment today (5,7,8,9). None of the patients admitted in the RIS phase, which is included in our study were receiving a conventional MS treatment. Most common complaint among the RIS patients was identified to be headache in various studies as found in this study (1,5,10).

RIS is a popular topic of recent times. 2009 Okuda criteria are used in the diagnosis of RIS. There have been a number of studies on this subject and some clinical follow-up work is being done. It is intended to achieve a consensus on the approach to these patients.

It is usually stated that while RIS may usually lead to definite MS, the observed asymptomatic MRI lesions most often than not lack pathological confirmation. Pathologically confirmed inflammatory demyelinating disease compatible with MS have been reported in a limited number of patients where the pathology of RIS has been described as "indistinguishable from classic MS pathology" (11). Of course, not all RIS patients develop clinically definite MS.

Findings consistent with RIS were observed in 23 out of 2783 psychiatric patients in a study made in 1996 (12). Studies have been published in which demyelinating lesions were reported in less than 0.5% of the radiological scans of asymptomatic patients without any complaints (13-15). RIS is seen more frequently in people with family members with MS than those without (16). Data of the twin studies also support this statement. It seems that genetic predisposition is a risk factor.

Neurological symptoms develop during follow-up in proportion of patients at different ratios in various studies. Approximately in two-thirds of the patients develop radiographic progression within the first 5 years. When the number of lesions in the MRI is high (> 9), gadolinium (Gd) enhancement of the asymptomatic lesions is present and in particular if cervical cord lesions are seen, clinical conversion rate is higher (2,5,6,7,17,18,19). In our study, 8 of 49 patients had subsequent neurological episodes during the follow-up period, and thus began to be followed by a diagnosis of Clinically Isolated Syndrome (CIS) - MS accordingly. 6 of these 8 patients had more than 9 plaques at the beginning and 5 had Gd-enhancing active plaques at the time of RIS diagnosis. All the patients are still being followed up and the subsequent revisions of this text in the following years, the diagnosis of the patients that are still being followed up with RIS diagnosis and Gd-enhancing lesions arouses interest. Thus whether or not a treatment is feasible for RIS patients that are highly probable to turn into definite MS over the years is still debatable (7,9).

MS is perhaps the most common area of use in the practice of neurology the EPs are used today. They are especially utilized in patients when MS is considered, where the sign and symptoms are not adequate or definite, while the electrophysiological conduction defects due to the subclinical lesions in the background are shown (20-22). Although they are not required in the 2010 revised McDonald criteria, they are still frequently used in the follow-up of patients.

VEP is extremely sensitive in showing lesions in the anterior visual pathways. While it gives objective information on acute optic neuritis, it also gives an idea by providing data on the chronic period. Therefore, one can conclude that VEP examination is more sensitive and less expensive compared to MRI for showing optic nerve lesions, and a normal VEP examination can more or less virtually rule out the possibility of an optic nerve and/or chiasm lesion in a patient (22-24). The superiority of VEP examination to other methods for showing early demyelination of the optic nerve and follow-up, including OCT and retinal nerve fiber examinations have been are reported in some studies (24).

SEP are obtained from appropriate regions by stimulating a sensory nerve anywhere in the body, after giving mechanical, electrical or magnetic stimuli. Unlike EEG, they are not affected by general anesthesia or sedatives (25). Most frequently central responses obtained after mixed nerve stimulation (median and/or posterior tibial nerve) are evaluated. Pathological processes in the central nervous system that cause SEP abnormalities are most frequently in the spinal cord. The main purpose of this investigation in demyelinating diseases is to show "silent" lesions. Lesions that belong to a specific region of the nervous system with no evidence in clinical examination or history can be detected with SEP. In demonstrating a "silent" lesion, SEP is almost as sensitive as VEP (20,26). The main pathology in MS is demyelination and axonal degeneration. Accordingly, slowing of the transmission in nerve fibers occurs, this transmission becomes dispersed or is completely blocked. This functional disorder is reflected in the EPs. The median and ulnar SEP studies are rarely abnormal in MS patients, while the studies made by the stimulation of lower extremity have pathological or abnormal results more often. This situation is explained by the longer way in the spinal cord the somatosensory pathways go from the lower extremities and are therefore more likely to come across an area of demyelination (27). Sometimes even in patients with the definite diagnosis of MS, EPs are known to be used to "confirm the diagnosis", in reality to show the lesions with no radiographic or clinical findings. On the other hand, EPs may be used serially to follow-up patients. This is applicable for both SEP and for VEP. Tsao et al. have used SEP in their study for monitoring neuromyelitis

optica prognosis and have reported it to be beneficial (28).

There are very few studies that have examined the relationship of EPs with RIS. In a study that have compared CIS and RIS patients who have been examined with oligoclonal bands, antinuclear antibodies and VEP has shown that VEP pathology is still an important parameter to show demyelination episode. RIS patients have been determined to have a lower percentage of OCB positivity and VEP abnormality compared to CIS patients, which implies that every RIS patient will not eventually become a CIS, or eventually MS patient (24).

The small number of patients and the lack of the number of RIS patients who eventually turned to CIS or MS are the weak points of that study. In another study in which 70 patients were followed-up prospectively, abnormal VEP, younger age, and Gd enhancement on follow-up MRI were more frequent in clinically definite MS than in MS determined by MRI (29). In a review of American Academy of Neurology, it is reported, based on various publications, that those with a probable MS and abnormal VEP investigations have 2.5-9 times more probability to develop clinically deifinite MS compared to those with normal VEP studies. Likewise, in the same review it can be seen that some studies have reported 2.4-3.9 times more likelihood to develop clinically definite MS in those with SEP abnormalities; but several other studies have not replicated this finding (30).

Our opinion is that all patients with RIS should be evaluated with EPs. Because, RIS patients with an abnormal VEP or SEP abnormality have a higher risk of having an attack and developing CIS/MS according to the results of this study. The presence of active plaque has been found to be most important factor for convertion to MS. The second important parameter is abnormal VEP/SEP. This is even more valuable and significant than the number of plaques.

On the other hand, these patients should also be serially followed-up with EPs. This is true for both SEP and VEP. EPs can reveal lesions simulating that can not be detected with MRI (25). If an abnormal response from a patient that is not having an attack due to a silent lesion is obtained, this abnormality is expected to continue. Similarly, if an abnormal response due to a silent lesion from an asymptomatic patient with only radiological findings (RIS) is obtained, this abnormality is expected to continue. This rules out the technical problems and mistakes. Additionally, serial follow-up is helpful in monitoring the development of disease, determining prognosis and demonstrating new areas that are being affecting during the progression of the disease, i.e. new lesions.

There are some limitations of our work. Follow-up time is less than 2 years and our study is retrospective. We didn't use median SEP study on our patients.

Conclusion

Finally, we believe that all patients with RIS should be evaluated with EPs and followed-up serially with them. In order to understand the exact place of EPs in the follow-up of RIS, greater series with longer period of follow-up is needed.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: SD: Examination of patients, collecting of data, writing of manuscript, Revision of Article, **ED, CK, RET, MGS, AC:** Examination of Patients, Collecting of Data

Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

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Secondary tonsillar hemorrhage requiring surgical intervention: Analysis of 1429 tonsillectomy cases on single surgeon experience

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Abstract

Objective: Determination of risk factors affecting secondary tonsillar hemorrhage of the requiring surgical intervention.

Material and methods: The 1429 tonsillectomy cases were performed with three different dissection techniques (dissection and snare, bipolar and monopolar dissection) by a single surgeon were examined retrospectively. Age, sex, surgical knowledge, indications and postoperative tonsillar hemorrhage day of the patients were recorded. Patients who were operated on for hemorrhage were evaluated statistically in terms of technique used, age, sex and indications.

Results: A total of 25 cases of a secondary hemorrhage cases requiring surgical intervention were detected. The relationship between age and bleeding was statistically significant (p=0.003). Hemorrhage frequency requiring surgical intervention was significantly higher in patients with recurrent tonsillitis than in patients with tonsillar hypertrophy (p = 0.001). 19 of the 25 patients who were operated on for hemorrhage were in the group of tonsillectomy patients due to recurrent tonsillitis. There was no meaningful relationship in terms of sex. The hemorrhage rate in the dissection and snare technique was 1.74% (12 patients), the hemorrhage rate in bipolar dissection was 2.78% (9 patients), and the monopolar dissection- hemorrhage rate was 0.96% (4 patients). There was no statistically significant difference between the results (p = 0.170). It was determined that the hemorrhage required surgery at most was between 6th and 10th days.

Conclusion: While there was no significant relationship between the incidence of secondary tonsillar hemorrhage requiring surgery and gender and dissection techniques, it has been observed that the risk was increased in patients operated due to recurrent tonsillitis and older age group.

Key words: Tonsillectomy, Hemorrhage, Risk factors

Introduction

Tonsillectomy is one of the oldest and most commonly applied otolaryngologic procedures (1). A post-tonsillectomy hemorrhage rate, which is one of the complications of this procedure, varies from 2.1% to 12% when all age groups are taken into consideration (2-4). In general, the rate of second surgical procedure due to tonsillar hemorrhage is between 1.2% and 6% (3,4). Post-tonsillectomy hemorrhages are classified as primary (within 24 h postoperatively) and secondary (after 24 h postoperatively) (5). It is known that primary hemorrhage depends on inadequate bleeding control during surgery. Secondary hemorrhage occurs due to the decrease of the crusts in the tonsillar fossa (6).

Currently described tonsillectomy techniques are cold dissection, bipolar and monopolar dissection, bipolar scissor dissection, laser, cryosurgery, ultrasonic excision, microdebrider, coblation, thermal welding and plasma knife methods (7,8). These methods have been developed to achieve less intraoperative hemorrhage, less surgical time, and less postoperative pain (8).

Previously reported risk factors in tonsillar hemorrhage include age, gender, indications, surgical techniques and instruments used, and the surgeon's experience (9-14). Electro-surgery in some publications has been described as a risk factor for postoperative hemorrhage or secondary tonsillar hemorrhage (15-17). In addition, a significant association between primary tonsillar haemorrhages that occur in the first 4 hours postoperatively, and cold dissection has been reported (18). Cold technical tonsillectomy has more hemorrhage intraoperatively; however, postoperative pain is less than electrosurgical methods (6).

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This study was designed to determine the risk factors affecting the secondary tonsil hemorrhage requiring surgical intervention through the experience of a single surgeon.

Material and Methods

The 1429 tonsillectomy operation performed by a single surgeon between 2010-2017 was included in the study. Patients who underwent only tonsillectomy and also adenoidectomy were included in the study. Tonsillectomies performed as part of the uvulopalatopharyngoplasty, tonsillectomies with malignancies suspected patients, tonsillectomies performed with nasal operations, and those with insufficient knowledge of the records were excluded from the study. The medical records were examined retrospectively in the electronic records. Age, sex, and indications were noted on the day of the patients who underwent hemorrhage control under general anaesthesia because of the most objective hemorrhage from patient data.

Indications for tonsillectomy disease were determined due to recurrent tonsillitis (⩾7 over one year, ⩾5 over two years, ⩾3 over three years) and/or tonsil hypertrophy resulting in snoring or drowsiness in sleep. Informed consent form was obtained from each patient or parent. All tonsillectomies were performed under general anaesthesia. Patients were discharged after approximately 6-8 hours of follow-up on the operation day. The patient was given a brochure containing the patient's tonsil diet and the surgeon's phone number without exception to call in case of hemorrhage. Each patient was prescribed 2nd generation cephalosporin and metamizole as a pain reliever. In case of allergy, macrolide group antibiotic and ibuprofen as an alternative for metamizole were prescribed. Additional diclofenac in intramuscular form was recommended for adult patients.

The surgeon used the dissection and snare technique in tonsillectomy performed between 2010 and 2013. After this date, the surgeon started using dissection with bipolar cautery. After using this technique till 2015, the surgeon was used dissection with monopolar cautery and still uses this technique.

A mucosa incision was performed in the anterior, superior and posterior tonsillitis in a dissection and snare technique using a tonsil knife. The upper pole of the tonsil was held with an Allis forceps and the extracapsular plan was inserted with the help of scissors and elevator to provide a dissection. Inferior pole was excised with the help of snare. It was waited for 7 minutes by performing tamp.

Subsequent bleeds were stopped by cauterizing with bipolar cautery. Bonding and suturing were rarely used in hemorrhage from large diameter vessels. Extracapsular dissection was performed only in bipolar dissection using Allis forceps and bipolar cautery.

The monopolar dissection was performed in the same manner using Allis forceps and monopolar cautery alone. Bipolar dissection and monopolar dissection and hemorrhage control were performed in 20-watt power mode electrocautery.

Statistical analyses

SPSS 22.0 (IBM Corporation, Armonk, New York, United States) program was used to analyse the variables. The normal distribution of the data was evaluated by the Shapiro-Wilk test and variance homogeneity of the date was assessed by the Levene test. Independent-Samples T test along with Bootstrap results was used when comparing two independent groups according to quantitative data. Pearson Chi-Square and Fisher Exact tests were used to compare categorical variables. Exact results were tested with the Monte Carlo Simulation technique. Quantitative variables and categorical variables were shown as mean ± SD (standard deviation) and as n (%), respectively, in Tables. Variables were examined at 95% confidence level and $p < 0.05$ was accepted as significant.

Results

Due to the analysis of demographic data of patients, there was no statistically significant difference in terms of age, sex, and indications between the patient groups in which three different dissection techniques were applied. The distribution of the patients and the demographic data are shown in Table 1.

There was no statistically significant relationship between hemorrhage and sex ($p = 0.316$). When the association between hemorrhage and age was examined, there was a statistically significant relationship between age and hemorrhage risk ($p = 0.003$). While the general average of the patient population was 7.57, the mean ages of the patients, who were operated on for hemorrhage, was 14.32. The hemorrhage was found to be statistically significantly higher in patients operated for recurrent tonsillitis ($p = 0.001$). In total, 19 of 25 patients who were operated on due to hemorrhage were patients who underwent tonsillectomy because of recurrent tonsillitis.

When the dissection methods used were compared with each other, the highest hemorrhage rate in percentage was bipolar dissection with 2.78%. This rate was 1.75% in the dissection and snare method and 0.96% in the monopolar dissection. There was no statistically difference between these three methods ($p = 0.170$).

When the day of the hemorrhage was observed, the secondary hemorrhage was seen between the 4th and 13th day. Most of the haemorrhages were between the 6th and 10th days. It was seen that 19 out of 25 bleedings were on within these day (Figure 2).

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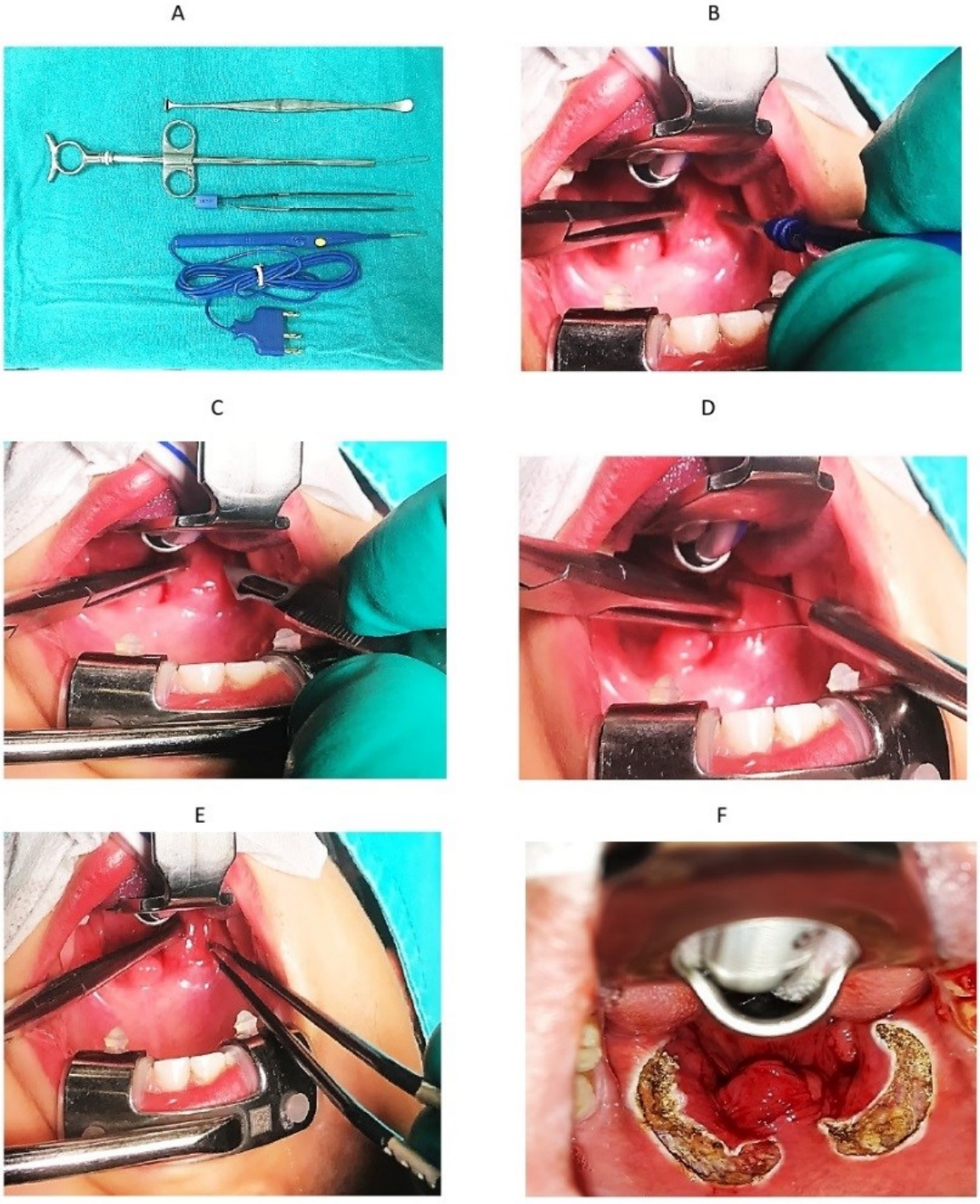


Figure 1: Intraoperative appearance of dissection methods. A: instruments of dissection, B: Monopolar dissection technique, C, D: dissection and snare technique, E: Bipolar dissection, F: Appearance of tonsil bed after haemostasis

Table 1: Demographic characteristics of patients

	Dissection and snare	Bipolar dissection	Monopolar dissection	Total	P value
	(n=689)	(n=324)	(n=416)	(N=1429)	
	n(%)	n(%)	n(%)	N(%)	
Gender					
Female	378(54,86)	174(53,70)	227(54,57)	779(54,51)	0,943
Male	311(45,14)	150(46,30)	189(45,43)	650(45,49)	
Indications					
Recurrent tonsillitis	265(38,46)	116(35,80)	162(38,94)	543(38)	0,756
Tonsil hypertrophy	366(53,12)	181(55,86)	226(54,33)	773(54,09)	
Both	58(8,42)	27(8,33)	28(6,73)	113(7,91)	
Hemorrhage					
Occurred	677(98,26)	315(97,22)	412(99,04)	1.404(98,25)	0,170
Not occur	12(1,74)	9(2,78)	4(0,96)	25(1,75)	

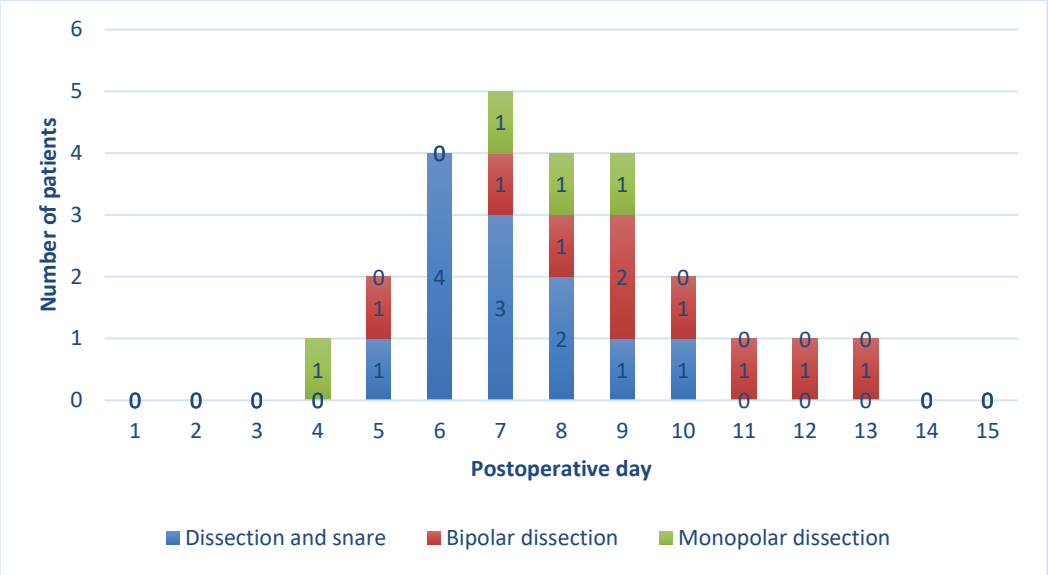
Pearson Chi-Square Test(Monte Carlo)

Table 2: Clinical–demographic characteristics of patients presenting with secondary hemorrhage requiring surgical intervention

	No bleeding (n=1404)	Bleeding (n=25)	Total (N=1429)	P Value
	Mean±SD	Mean±SD	Mean±SD	
Age	7,45 ± 5,33	14,32 ± 6,77	7,57 ± 5,43	**0,003**
	n(%)	n(%)	n(%)	
Gender				
Female	768(54,70)	11(44)	779(54,51)	0,316
Male	636(45,30)	14(56)	650(45,49)	
Indications				
Recurrent tonsillitis	524(37,32)	19(76)	543(38)	**0,001**
Tonsil hypertrophy	767(54,63)	6(24)	773(54,09)	
Both	113(8,05)	0(0)	113(7,91)	

Independent T Test(Bootstrap) - Pearson Chi-Square Test (Exact) - Fisher Exact Test(Monte Carlo) - SS.:Standart deviation

Fig. 2. Periods of hemorrhage



Discussion

Electrocautery dissection is preferred because it causes less intraoperative hemorrhage and shortens the operation time. However, studies in which hot instrumentation increases postoperative bleeding are included in the literature (15-17). The records of primary and non-surgical hemorrhage were not evaluated because they were inadequate in our data, but the hemorrhage rates required for surgical intervention were similar to the rates of hemorrhage for cold dissection in the literature. When evaluating the results of these three different tonsillectomy techniques using hot instrumentation, it cannot be said that the hot instrumentation has increased the hemorrhage rate. In all patients included in the study, the rate of second surgery for secondary hemorrhage was 1.7%, which was consistent with rates of 1.2% and 6% in the literature (3,4). When we compared the dissection and snare method with bipolar dissection, although the percentage of second hemorrhage required in the bipolar dissection is not statistically significant, it can be explained by the more intensive use of the hot instrument in bipolar technique. In fact, it is stated in the literature that the use of hot instrumentation increases the hemorrhage and the use of bipolar technique to only control hemorrhage has moderate risk (17,19). On the other hand, secondary hemorrhage requiring a second surgery has a decline in percentage in monopolar dissection. Although the results show that monopolar cortical dissection has the best rate in terms of secondary hemorrhage requiring surgery, the data on which technique is better seems inadequate in the literature (20). Furthermore, there was no statistically significant difference in terms of the rate of secondary hemorrhage requiring surgery among the three techniques used. The choice of instrumentation is determined by the surgeon and the facilities owned. On the other hand, it is argued that every surgeon must learn and apply cold dissection before learning other methods (21).

Some publications have found hemorrhage rates associated with age (9,12,17,22,23), but others have not established such a relationship (24,25). There is a publication in the literature, which indicates that the age of the seconder hemorrhage under 6 years of age is less than all other age groups and hemorrhage rates in adults and adolescents are 5 times higher (26). Tomkinson and colleagues reported a 3-fold increase in the proportion of severe hemorrhage in patients over 12 years of age in 17,480 tonsillectomy cases (12). In this retrospective study, there were no patients under 6 years of age in the patients who were operated for secondary hemorrhage and the patients were predominantly 12 year old and older. When the patient ages are considered, the results showed that the risk of hemorrhage is significantly higher at 12 years of age and over.

The current literature suggests that post-tonsillectomy hemorrhage risk in patients who have been selected for recurrent and chronic tonsillitis is higher than that for patients with tonsil hypertrophy (27). The data in this study also supports this statement.

Male gender is regarded as a risk factor for bleeding after tonsillectomy by various authors (9,12,17,22). However, there was no significant relationship between gender and hemorrhage risk in this study.

Seconder tonsil haemorrhages tend to occur in the first week after surgery (5,28) and rarely require surgery after the first 10 days (29,30). When the patient data in the study were examined, it was observed that the hemorrhage occurred mainly between postoperative 6th and 10th days and there was no hemorrhage requiring surgery after the 13th day of surgery. The most common hemorrhage was on the 7th day.

This retrospectively designed study does not provide information on primary and non-surgical haemorrhages. Another weakness of the study is the use of hot instrumentation in hemorrhage control in all three methods. On the other hand, it was observed in this study that the method of dissection did not significantly change the hemorrhage rates.

In summary, if the factors related to the surgeon affecting bleeding rate are taking into consideration (11,12,31), in this article which compares three different dissection methods based on single surgeon experience, while it was shown that age, recurrent tonsillitis and used instrumentation affect secondary bleeding rates, it has been observed that in monopolar cautery dissection the percentage required for surgery is reduced in the number of hemorrhage compared to dissection and snare technique and bipolar dissection. However, the differences are not statistically significant.

This study allowed us to evaluate the effect of different surgical techniques on the frequency of secondary hemorrhage regardless of surgeon experience. In addition, it provided the opportunity to evaluate the risk factors mentioned in the literature in a wide range series of tonsillectomy performed by a single surgeon.

Conclusion

Bleeding from time to time as a post-tonsillectomy complication can be life threatening. It can be very annoying for the surgeon when the family and the patient are in serious anxiety. In this study, which was based on single surgeon experience, an increase was determined in patients operated due to recurrent tonsillitis and in the frequency of secondary tonsil hemorrhage requiring surgical intervention in older age groups. On the other hand, it was observed that gender and methods used in dissection did not affect the hemorrhage risk.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: SMC, EU, ID: Collecting of patients data, Patient examination and operation, writing and revision of article, HC: Statistical analysis of findings.

Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

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