Association between irritable bowel syndrome and cardiac rhythm abnormalities: a case control study

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الخلاصة:

العلاقة بين متلازمة القولون العصبي(متلازمة تهيج الامعاء) واضطراب ايقاع القلب : دراسة الحالات المقترنة بحالات ضابطة

د سعد عبد فرحان البدري كلية الطب جامعة واسط

مقدمة :العلاقة بين متلازمة القولون العصبي (متلازمة تهيج الامعاء) واضطراب ايقاع القلب كانِت موضوع جدل للدراسات والابحاث في هذا المجال فبعض الدراسات اثبتت واخرى نفت وجود هذة العلاقة وقد اجري هذا البحث لدراسة هذة العلاقة واضافة بحث لهذا الموضوع

شملت الدراسة عينة من خمسون مريضا تم تشخيصهم في مستشفى الكرامة التعليمي كمصابين بمتلازمة القولون العصبي (متلازمة تهيج الامعاء) وخمسون متطوعا سليما كحالة ضابطة و اجري للمجموعتين فحص مراقبة تخطيط القلب لمدة 24 ساعة بجهاز هولتر

اتضح من خلال الدراسة وجود علاقة مهمة احصائيا بين متلازمة القولون العصبي(متلازمة تهيج الامعاء) والضربات البطينية المبكرة حيث سجلت هذة الضربات عند 60 % من المرضى وعند 32% من المجموعة الضابطة (الاصحاء)ولم يسجل فرق مهم احصائيا بين المجموعتين بالنسبة لباقي اضطرابات نسق القلب

الاستنتاج:وجود علاقة بين متلازمة تهيج الامعاء واضطرابات ايقاع القلب وتبرز الحاجة الى دراسات اخرى مكملة لدراسة العلاقة واسبابها.

Abstract

The issue of association between IBS and cardiac rhythm abnormalities has been raised in few published literature; however there is substantial amount of controversy in such a way that some authors deny this association while others support this association when one take into consideration particular symptoms and signs like severity of pain, pattern of sleep and associated anxiety and depression. The current study involved 50 patients diagnosed with irritable bowel syndrome and 50 apparently healthy control subjects and both groups was subjected to about 24 hour holter monitoring. The results showed significantly higher rate of cardiac premature ventricular complexes in patients with irritable bowel syndrome than that in control group 60% versus 32% ($P<0.05$)with no significant association with other rhythm abnormalities.

Conclusion: Irritable bowel syndrome is significantly associated with premature ventricular complexes and further studies are needed to clarify exact pathophysiology.

Key words: Irritable bowel syndrome; cardiac rhythm abnormalities

Introduction

Irritable bowel syndrome (IBS) is defined as a functional abnormality typified by episodic abdominal discomfort or pain that is accompanied by changes in stool frequency or form and being well after passing motion [(1)].Irritable bowel syndrome (IBS) is the most common gastrointestinal condition diagnosed in clinical practice and the most common cause for consultations to gastroenterology clinics with over all prevalence estimated to range from 10% up to 25% in various regions [(2)(3)]There is no specific diagnostic clinical or laboratory test for IBS as well as no definite structural abnormality that can be used clinically to confirm the diagnosis(3). Over the last decades , many clinical criteria have been developed based on symptoms to diagnose IBS.Rome III criteria is the most commonly used for establishing the diagnosis of IBS which include the following: abdominal pain or discomfort that affect the patient at least three days a month over the last three months accompanied by ≥2 of the following (improvement with passing motion; change in stool frequency and change in stool form at onset of diagnosis) in the absence of organic cause. [(4)].

The pathophysiology of this disease is still unclear; however, there are a lot of proposed mechanisms that include: altered intestinal motility, impaired autonomic regulation and increased visceral sensitivity as well as alteration in intestinal flora and minor mucosal inflammation[(5) (6) (7) (8)(9)(10)].It had been well documented that the symptoms of IBS extend beyond the gastrointestinal tract[(11)]but few literature studied the link to cardiac rhythm abnormalities [(12)]and few studies investigate the association between abnormalities in heart rate variability and IBS (13). It is well documented that the use of heart rate variability will help in assessing autonomic functions [(14)]. Abnormality in heart rate variability is associated with poor outcome in patients with myocardial infarction and can predict ischemic heart disease in patients with diabetes mellitus [(15, 16)]. Debate about association between IBS and autonomic nervous system dysfunction is well known in published literatures; however there is substantial amount of controversy in such a way that some authors deny this association [(17-18)] while others support this association when one take into consideration particular symptoms and signs like severity of pain, pattern of sleep and associated anxiety and depression [(19-20)]. It should be pointed out that great amount of association between autonomic dysfunction and risk of atherosclerosis [(21)]. From another point of view, a common inherited pathology for both cardiac arrhythmia and IBS might explain the co-existence of these abnormalities in same patients simultaneously. Patients with Sodium Voltage-Gated Channel Alpha Subunit 5 (SCN5A) mutations have been described to suffer irritable bowel syndrome (IBS). In one of the studies, 2% of patients with IBS exhibited SCN5A mutations, and in one case, administration ofmexiletine caused restitution of normal bowel habits, so it may be suggested that channelopathies are involved in the pathogenesis of IBS somehow [(22-23)].Few literatures studied the link between cardiac rhythm abnormalities and irritable bowel syndrome although they may share some pathophysiological bases

Aim of the study :to investigate the association between irritable bowel syndrome and cardiac rhythm abnormalities in young patients.

Patients and methods

This case control study included 50 patients with established diagnosis of irritable bowel syndrome (IBS)based on Rome III criteria and 50 healthy age and sex matched volunteers. It was carried out in Al-Karama teaching hospital in Kut city/ Wasit province / Iraq from June 2015 through May 2016.All the patients and control subjects wereassessed clinically by comprehensive and detailed history and physical examination and investigated with complete blood count and ESR, blood sugar , thyroid function test and 12 leads ECG with transthoracic echocardiography and thyroid function test .Exclusion criteria include history of ischemic and valvular heart disease , cardiomyopathy , thyroid disease , hypertension , acute illness ,patients on treatment for IBS known to cause arrhythmias like tricyclic antidepressants and history of symptomatic cardiac arrhythmia .All patients and control subjects were assessed for cardiac rhythm using 24 hour Shiller MT 2000 holter ECG systemwith the following data obtained :age and sex ,total time of recording, maximum heart rate , minimum heart rate , average heart rate ,premature ventricular complexes and if present in bigemeny , trigeminy or couplets and premature atrial complexes , supraventricular and ventricular tachycardia .

Data were analyzed using Statistical Package for Social Science (SPSS version 22). categorial variables were expressed as number and percentage , where as numerical variables were expressed as mean , median standard deviation and interquartile range (IQR). Chi-Square test was used to study the association between two categorialvariables , risk was estimated using Odds ratio and 95 % confidence interval .

Whitney U test was used to study difference in median ,Spearmancorrelation was used to study the correlation between numeric and ordinal variables .

The level of significance was considered at P value of ≤ 0.05

Results

The present study included 50 patients with irritable bowel syndrome IBS with a mean age of 25.76 ±7.24 years and an age range of 16-39 years. According to sex there were 34 male patients (68%) and 16 female patients (32%). ECG monitoring was performed for durations ranging from 18 to 24 hours with a mean of 21.87 ±2.04 hours. The duration of disease ranged from 1 to 7 years and averaged 3.44 ±1.05 years. Their mean body mass index (BMI) was 26.56 ±3.44 kg/m^2 and ranged from 19.96 to 32.11 kg/m^2. Also the study included 50 age and sex matched control group. Patients characteristics and that of the healthy control group are shown in table 1.

Types of cardiac premature complexes are shown in table 2. Premature ventricular complexes were seen in 30 patients (60%) and in 16 (32%) of the healthy control subjects; the difference was highly significant (P=0.005). Couplet were observed in 2 patients (4%) and 2 (4%) control subjects, Triplet in 6 patients (12%), Bigeminy in 10 patients (20%) and Trigeminy in 6 patients (12%), while premature atrial complexes (PAC) were encountered in 8 patients (16%) and 12 (24%) control subjects with no statistical significance (P=0.317). Table 3 showed mean number of premature complexes per patient.

There was no significant impact of any of the following variables: gender, age, minimal hear rate, average heart rate, duration of the disease and

body mass index on occurrence of PVC (P>0.05), table 5; however, there was significant positive correlation between maximum heart rate and rate of PVC (r = 0.166, P=0.028), table 4.

Table 1: Characteristic of the study sample

Characteristic	IBS (n = 50) Median (IQR)	Control (n = 50) Median (IQR)	P*
Age median (IQR) years	25.00 (10.00)	28.00 (10.00)	0.051*
Gender (Male : Female)	30/20	34/16	0.405†
Duration median (IQR) hr	22.00 (4.00)	22.33 (2.61)	0.104*
Mini.HR median (IQR) beat /min	44.00 (11.25)	45.00 (8.50)	0.287*
Maxi.HR median (IQR) beat /min	136.00 (27.25)	127.00 (21.00)	0.061*
Average HR median (IQR)	73.00 (14.25)	75.00 (14.50)	0.508*

IQR: interquratile range; n: Number of cases; min.: minimal; max.: maximum; hr: hour; * Mann Whitney U test; †: Chi-Square test.

Table 2: Comparison of arrhythmia type between IBS and control groups

Arrhythmia	IBS	Control	P	Odds ratio	95% CI
PVC	30 (60)	16 (32)	0.005	3.188	1.403 -7.241
Couplet	2 (4)	2 (4)	1.000	---	---
Triplet	6 (12)	0 (0)	0.027	---	---
Bigeminy	10 (20)	0 (0)	0.001	---	---
Trigeminy	6 (12)	0 (0)	0.027	---	---
PAC	8 (16)	12 (24)	0.317	---	---

Table 3: Cardiac arrhythmia type and frequency in patients with IBS

Type	Number of patients (%)	Mean number per positive cases/hr	Range /hr
PVC	30 (60%)	2544.6/24 hr	1-33129/hr
Couplet	2 (4%)	5/24 hr	Single patient
Triplet	6 (12%)	1/24 hr	1-1/24 hr
Bigeminy	10 (20%)	185.8/ 24hr	1-1836 /24hr
Trigeminy	6 (12%)	168.7 /24 hr	11-420 /24 hr
PAC	8 (16%)	267.38 /24hr	2.5-934 /24 hr

Table 4: Factors predicting PVC

Characteristic	Positive PVC (n = 30)	Negative PVC (n = 10)	P
Gender (M/F)	22/12	8/8	0.322 *
Age (mean ±SD) years	26.47 ±7.95	24.70 ±6.27	0.656 †
Mini.HR (mean ±SD) Beat/min.	45.47 ±7.28	41.90 ±7.28	0.173 †
Maxi.HR (mean ±SD) Beat/min.	128.67 ±20.51	143.10 ±18.36	0.076 †
Average HR (mean ±SD) Beat/min.	77.20 ±26.94	77.80 ±10.00	0.085 †
Duration of IBS (mean ±SD) years	3.67 ±1.35	3.10 ±1.73	0.254 †
BMI (mean ±SD) kg/m^2	26.33 ±3.52	26.90 ±3.46	0.542 †
Type of IBS (P, D, C)	(12, 1, 2)	(5, 3, 2)	0.172**

*Corrected Chi-Square test; † Man Whitney U test; **Spearman correlation

Table 5: Correlation between rate of PVC and independent variables

Variables	r	P
Age	-0.035	0.308
Sex	0.427	0.951
Minimal HR	-0.140	0.271
Maximum HR	0.166	0.028*
Average HR	0.948	0.654
Duration of IBS	0.269	0.820
BMI	-0.149	0.689
IBS type	-0.084	0.766

HR: heart rate; *Significant correlation at <0.05.

Discussion

The present study demonstrated significant association between the occurrence of premature ventricular complexes and IBS.Most of studies in this field concentrate on heart rate variability as an indicator of autonomic nervous system dysfunction in patients with IBS and despite using Holter monitoring for data collection and analysis , parameters other than heart rate variability were not investigated in these studies and data regarding this subject is lacking[12][13][14][15].

Premature ventricular contractions were seen in about 40–75% of apparently healthy adults screened by 24–48 hour (Holter) ECG monitoring[24]. According to the result of the present study, there should be an explanation for the susceptibility of patients with IBS for development of ventricular premature complexes. After thorough search in the published literature it was found that the pathophysiologic explanation resides in one of two major hypotheses. Some literature prefer autonomic dysfunction as a proposed mechanism for the occurrence of cardiac rhythm abnormalities in patients with IBS [12][17][19][25]whereas others suggest the presence of genetic predisposition of a common pathology like sodium channel abnormality that can explain both IBS and cardiac rhythm disturbances in same patients [22] [23].

It is preferred to link the pathophysiology to autonomic dysfunction rather than to genetic mutation as there is lack of significant number of patients with IBS and mutation at the same time. Maximum heart rate was a good predictor for occurrence of PVC in the present study and can be used to monitor and predict such cardiac abnormal rhythm in patients with IBS. Nevertheless, a more detailed study with lager sample and more variables to be included in order to exactly estimates the prevalence of cardiac rhythms abnormalities especially PVC in patients with IBS and understand the pathophysiologic role of IBS in correlation to cardiac rhythm disorders and the possible use of ambulatory Holter monitoring in the diagnosis and guiding management of both conditions.

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