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Influence of smoking, coffee and tea consumption on bladder pain syndrome in female twins

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Abstract

OBJECTIVES—To assess the influence of smoking, coffee and tea consumption on the risk for bladder pain syndrome (BPS) using the O'Leary Interstitial Cystitis Symptom Index (ICSI)

METHODS—In 2005, all twins born 1959–1985 in Sweden (n = 42 852) were invited to participate in a web-based survey to screen for complex diseases including BPS. Analyses were limited to female twins with information regarding bladder pain symptoms (n = 9 349). Women with an ICSI score of 6 or greater with required nocturia and bladder pain were defined as having BPS symptoms. Logistic regression was used to estimate odds ratios (ORs) with 95% confidence intervals (CIs). Environmental and genetic influences were assessed in co-twin control analysis

RESULTS—Tea consumption was associated with an increased risk for BPS (OR 1.26, 95% CI 1.02–1.55 for low tea consumption; OR 1.74, 95% CI 1.24–2.44 for high tea consumption). Coffee consumption was not a risk factor for BPS (OR 1.1, 95% CI 0.84–1.45). Former, and current smoking, were both associated with a higher risk of BPS (OR 1.5, 95% CI 1.18–1.89; and OR 1.49, 95% CI 1.16–1.92 respectively) but results from co-twin control analysis suggested that the association between smoking and BPS was confounded by familial factors.

CONCLUSIONS—Tea and smoking are environmental risk factors for BPS which are amenable to intervention. The effects of smoking on the risk for BPS may, however, be confounded by familial factors

Keywords

Bladder pain syndrome; Coffee; Smoking; Tea; Twins

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INTRODUCTION

Diagnosis of bladder pain syndrome (BPS) is based on the presence of chronic pelvic pain or discomfort related to the bladder and at least one other symptom such as urinary frequency.¹ Symptoms may wax and wane for years and are often severely debilitating. While risk factors for BPS are poorly understood, exacerbation of bladder pain is often reported after consuming particular foods or beverages such as coffee and tea.^{2–4} Also tobacco use, and in particular smoking, has been implicated as possible causative agents for BPS.^{5–8} However, current understanding on the importance of coffee, tea and smoking on the occurrence of BPS derive from studies with limited control for important confounders. Furthermore, it is uncertain to what extent these consumables influence the occurrence of BPS in the general population. Although widely agreed that symptoms are the same, the term BPS is preferred to that of interstitial cystitis (IC) in epidemiological studies in the absence of further diagnostic confirmation of BPS subtypes.⁹

A recent study has shown that BPS occurs more frequently in family members of patients affected by BPS,¹⁰ suggesting that familial factors such as genes and shared environmental factors may have play role in the etiology of the disease. For this reason it is important to evaluate if the studied associations are confounded by familial factors. This study aims to assess the influence of smoking, coffee and tea consumption on the risk for BPS and to evaluate if these associations are confounded by genetic and environmental factors in a cohort of young female twins.

METHODS

Study population

The Swedish Twin Registry contains data on nearly all twins born in Sweden since 1886. In 2005, all twins born 1959–1985 ($n = 42\,852$) were contacted with a letter inviting them to participate in a web-based survey to screen for common complex diseases and common exposures.¹¹ The present study was limited to female twins ($n = 9\,349$) participating in the survey.¹¹ Those not responding to the web questionnaire were offered to answer the survey through a computer-assisted telephone interview. After 2–5 months, 100 twins were contacted again to assess test-retest reliability. The kappa coefficients for agreement between the web questionnaire and telephone interviews ranged from good to excellent¹¹. This study was approved by the Regional Research Ethics Board at Karolinska Institutet and conforms to the STROBE guidelines for reporting observational studies (www.strobe-statement.org).

Measures

Presence of BPS was determined using the Interstitial Cystitis Symptom Index (ICSI) introduced by O’Leary.¹² The ICSI is characterized by asking how often one or several of four cardinal symptoms of BPS is experienced: urinary urgency; urinary frequency; nocturia; and bladder pain. Response alternatives using ordinal scales are provided to each question and a summary score can be calculated in a simple additive fashion, where a higher score indicates more distressful symptoms. The ICSI has shown a high sensitivity (89%) and specificity (97%) for interstitial cystitis.¹² Inclusion of a score of two or greater for nocturia and bladder pain as prerequisites for BPS diagnosis has been shown to further improve the specificity for the O’Leary index to identify individuals most likely to have BPS.¹³ In the present study we defined women with an overall ICSI score of 6 or greater and a score ≥ 2 for nocturia and bladder pain as affected by BPS.¹⁴

Daily coffee or tea consumption was reported by a total of 6 613 (70.8%) and 4 329 (46.4%) women respectively. For statistical purposes we categorized coffee and tea consumption in 3

groups: 0, 1–2, 3 or more cups daily. Smoking status was categorized as never, former and current use. Information on relevant covariates including age, number of childbirths, body mass index (BMI) and educational level was included in the survey. Age was categorized according to the quartile distribution in the cohort (19–26, 27–33, 34–40, and 41–47). BMI was arranged in four categories according to WHO guidelines¹⁵. Parity was defined as ever or never given birth. Educational level was divided into three categories depending on level of formal education (elementary, gymnasium and college/university degree).

Statistical Analysis

To evaluate the effect of smoking, coffee and tea consumption on BPS we used logistic regression models based on generalized estimating equations, which take into account the correlated (twin) structure of the data. Odds ratios (ORs) with 95% confidence intervals (CIs) were used as measures of associations. Using logistic regression we first provided crude estimates and subsequently adjusted for a number of covariates including age, BMI, parity, and educational level in multivariable models. In co-twin analysis we analyzed only women in pairs with information about zygosity and who were discordant for the outcome, i.e. one twin had BPS symptoms and the healthy co-twin was used as a matched control subject to the case.¹⁶ The matched nature of the co-twin control design minimizes confounding by factors shared within twin pairs such as intrauterine exposures, maternal factors, sharing 50% (dizygotic) or 100% (monozygotic) of their segregating genes, and childhood and adolescent environment. If familial factors confound the associations then within-pair associations are attenuated compared to the logistic regression estimates. If the attenuation is present for both mono- and dizygotic twins, then shared environmental factors contribute to the associations, while an attenuation of the estimates only among monozygotic twins speaks in favour of genetic confounding. ORs were estimated with 95% CIs and a p-value lower than 0.05 was considered significant in all analyses. All statistical analyses were performed using SAS software (version 9.2, SAS Institute, Cary, NC).

RESULTS

In Table 1, the distribution of lower urinary tract symptoms in relation to ICSI-scores are shown. Among women with ICSI ≥ 6 , 553/ 942 subjects (58.7%) had a bladder pain score of 2 or higher whereas 389/ 942 (41.3%) reported no or mild bladder pain. Moderate-severe symptoms of urinary urgency, frequency and nocturia were exceedingly more common in women with an ICSI score ≥ 6 . After adjustment for age, BMI, parity, educational level, smoking, and coffee and tea consumption, women with a co-twin affected by BPS-like symptoms had more than 4 times higher odds of BPS compared to women with an healthy cotwin (OR = 4.53, 95% CI 2.25–9.14).

Table 2 shows characteristics for women categorized as BPS and those not fulfilling the criteria for BPS. There was a significantly higher prevalence of current and former smokers, as well as, tea consumers among women with BPS symptoms compared to women without BPS. Coffee intake was similar in prevalence between those with and without BPS. No significant difference in age distribution was observed, but the prevalence of BMI > 30 was twice as high among those with BPS compared to those without. Women with BPS also had an overall lower educational level compared to women without BPS.

Crude and multivariable adjusted risk estimates for BPS are presented in Table 3. Women who consumed more than two cups of tea per day had a 74% greater odds of having BPS compared to non tea drinkers (95% CI 1.24–2.44) but also a low tea consumption was positively associated with BPS (OR 1.26, 95% CI 1.02–1.55). Current smokers had a 49% increased odds of BPS compared to non smokers (95% CI 1.16–1.92) and the risk remained practically the same among those who were former smokers (OR 1.50, 95% CI 1.18–1.89).

Coffee consumption was not associated with BPS symptoms in either the crude or adjusted analyses.

Table 4 shows the results from co-twin control analysis for tea consumption and smoking only since there was no significant association between coffee intake and BPS in logistic regression. When we looked at both mono- and dizygotic twins, smoking had no significant effect on BPS. However, a positive association (although not statistically significant) between smoking and BPS was observed among dizygotic twins (OR 1.73, 95% CI 0.36–8.22) suggesting that the association was confounded by genetic factors. When mono- and dizygotic twins were analyzed together, a significant positive association between tea consumption and BPS was observed (OR 2.24, 95% CI 1.08–4.67). When we looked separately at mono- and dizygotic twins, the significant association between tea consumption and BPS did not remain. However, the point estimates remained similar indicating a loss of statistical strength due to smaller sample sizes. These results indicate that the association between tea intake and BPS was not confounded by familial factors, such as genes or shared environment.

COMMENT

In this nationwide population of young female Swedish twins we identified a positive association between tea consumption, as well as, previous and current smoking with BPS. However, in the subsequent co-twin control analysis we found that the positive association between smoking and BPS was confounded by genetic factors, while the association between tea intake and BPS was not confounded by familial factors.

Previous studies have shown that caffeinated beverages may exacerbate symptoms of BPS.^{3,4} Shorter et al.⁴ reported that both coffee and tea consumption aggravated bladder pain in patients meeting the National Institute for Diabetes and Digestive and Kidney Diseases diagnosis criteria for IC. In our study, tea was positively associated with BPS symptoms, whereas coffee was not. Since the amount of caffeine in tea is approximately one-third of that in coffee,¹⁷ our results suggest that tea may contain components other than caffeine that may be involved in the pathways leading to BPS. Furthermore, when only discordant twin pairs were analyzed, our results suggest that the association between tea and BPS symptoms is not attributed to familial confounding factors such as shared drinking habits or micturition patterns within the family. The lack of an association between a high coffee consumption and BPS symptoms could be explained by the lack of a true direct effect but we recognise that it could also be attributed to patients with BPS having been advised to decrease their coffee consumption or done so by their own initiative.

Metabolites from cigarette smoking have been identified as a bladder carcinogen and irritant, yet results concerning the association between cigarette smoking and BPS are divergent.^{5–8} An association may be explained by an altered permeability of the bladder urothelium in patients with BPS, allowing penetration of allergens, chemicals, drugs, or toxins such as those from tobacco into the bladder wall.¹⁸ In the present study we found that both current and former smoking was associated with BPS but the lack of association with BPS among monozygotic twins favours the hypothesis of genetic confounding underlying the positive relation.

Even if it was not originally intended for epidemiological surveying purposes, the ICSI has been established as a useful instrument for population based screening of BPS.⁶ However, use of the O'Leary questionnaire can be associated with serious misclassification, which is exemplified in the present study by the fact that more than 40% of women with an overall score of 6 or greater did not report significant bladder pain and were actually more likely to be afflicted by overactive bladder (i.e. urgency, frequency and nocturia without bladder

pain) rather than BPS despite a high ICSI score. Thus, results from studies using the O'Leary index where bladder pain is not singled out as a requirement for classification of BPS should be treated with caution. Although it is widely accepted that symptoms of BPS and of the classic IC are interchangeable we have not been able to ascertain cases of Hunner type IC in the absence of diagnostic confirmation by cystoscopy and histological findings. Because BPS is a heterogeneous diagnostic term which may include several conditions associated with bladder pain such as endometriosis of the bladder and chronic bacterial cystitis, it is plausible that a minority of cases with BPS in our study would be attributed to classic IC.

Strengths of our study include the large scale collection of population-based data, a well characterized cohort of women, the ability to adjust for several important confounders, and the twin study design which allows the distinction between genetic and environmental influences on the studied associations. Furthermore, our results are unbiased by volunteer-based ascertainment of cases with BPS. An important limitation of our study lies within its cross-sectional nature: since disease and exposure are measured at the same time we cannot conclude whether the exposure preceded or resulted from the disease. In addition to individuals' smoking habits, the type and amount of coffee and tea consumption may vary over time causing exposure misclassification. Lack of control for such trends should, however, be of limited importance on a population-based level since during the last ten years the coffee consumption per capita in Sweden did not change notably.¹⁹ Moreover the misclassification of smoking status, due to the fact that women with BPS may have decided to quit smoking to ameliorate their symptoms, biases the estimates towards the null. Thus, the positive association between smoking and BPS observed in our study is probably an underestimation of the real association which presumably is greater.

CONCLUSION

In conclusion, this population based study among female twins suggests that tea and smoking are positively associated with BPS, but also that the association with smoking is likely to be confounded by genetic factors, while the association with tea intake is not confounded by familial factors.

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Table 1

Prevalence of lower urinary tract symptoms in relation to ICSI-score.

	ICSI score < 6 n= 8407	ICSI score ≥6 n= 942
Urgency		
0 = not at all	7991 (95.0)	696 (73.9)
1 = less than 1 time in five	411 (4.9)	241 (25.6)
2 = less than half the time	4 (0.05)	4 (0.4)
3 = about half the time	1 (0.01)	0
4 = more than half the time	0	1 (0.1)
Frequency		
0 = never	4816 (57.3)	16 (1.7)
1 = rarely	1909 (22.7)	44 (4.7)
2 = sometimes	1379 (16.4)	350 (37.1)
3 = often	269 (3.2)	372 (39.5)
4 = always	34 (0.4)	160 (17.0)
Nocturia		
0 = none	3349 (39.8)	7 (0.7)
1 = once	3513 (41.8)	78 (8.3)
2 = two times	1231 (14.6)	247 (26.2)
3 = Three times	277 (3.3)	268 (28.4)
4 = Four times	29 (0.3)	187 (19.8)
5 = Five or more times	8 (0.1)	155 (16.4)
Bladder pain score		
<2	7538 (89.7)	389 (41.3)
≥2	869 (10.3)	553 (58.7)

Figures are number of subjects (%).

ICSI denotes Interstitial Cystitis Symptom Index.

Table 2

Characteristics of the female twin population and of women with BPS symptoms in relation to potentially associated factors

	Women without BPS [†] n= 8866	Women with BPS [†] n= 470	P-value [*]
Age			
19–26	2158 (24.3)	111 (23.6)	0.82
27–33	2188 (24.7)	118 (25.1)	
34–40	2439 (27.5)	123 (26.2)	
41–47	2081 (23.5)	118 (25.1)	
Smoking			
No	5272 (59.5)	227 (48.3)	< 0.001
Former	1808 (20.4)	120 (25.5)	
Current	1736 (19.6)	122 (26.0)	
Missing	50 (0.6)	1 (0.2)	
Coffee/day			
0	2562 (28.9)	129 (27.4)	0.31
1–2	2731 (30.8)	136 (28.9)	
3+	3541 (39.9)	205 (43.6)	
Missing	32 (0.4)	-	
Tea/day			
0	4742 (53.5)	232 (49.3)	0.01
1–2	3416 (38.5)	186 (39.6)	
3+	675 (7.6)	52 (11.1)	
Missing	33 (0.4)	-	
BMI			
<18.5	328 (3.7)	27 (5.7)	< 0.001
18.5–24.9	6526 (73.6)	287 (61.1)	
25–29.9	1400 (15.8)	96 (20.4)	
≥30	438 (4.9)	51 (10.9)	
Missing	174 (2.0)	9 (1.9)	
Parity			
No	3873 (43.7)	191 (40.6)	0.17
Yes	4955 (55.9)	279 (59.4)	
Missing	38 (0.4)	-	
Education			
Low	370 (4.2)	36 (7.7)	< 0.001
Medium	4241 (47.8)	251 (53.4)	
High	4216 (47.6)	182 (38.7)	
Missing	39 (0.4)	1 (0.2)	

[†] BPS criteria defined as an overall ICSI score ≥6, a score ≥2 for bladder pain and nocturia.

Figures are number of women (%).

*
Chi-square test

Table 3

Risk for BPS symptoms in relation to smoking, coffee, and tea consumption among female twins born 1959–1985.

	Crude OR (95% CI)	Adjusted [†] OR (95% CI)
BPS		
N	9 304	9 089
Cups of coffee/day		
0	1.0	1.0
1–2	0.99 (0.77–1.27)	1.04 (0.80–1.35)
3+	1.15 (0.91–1.44)	1.1 (0.84–1.45)
Cups of tea/day		
0	1.0	1.0
1–2	1.13 (0.93–1.37)	1.26 (1.02–1.55)
3+	1.56 (1.14–2.13)	1.74 (1.24–2.44)
Smoking		
Never	1.0	1.0
Former	1.55 (1.23–1.94)	1.50 (1.18–1.89)
Current	1.62 (1.29–2.03)	1.49 (1.16–1.92)

[†] Adjusted for age, parity, BMI, and educational level.

Table 4

Co-twin control analyses for smoking and tea consumption in female twins discordant for BPS.

	Adjusted [†] OR (95% CI)		
	All	MZ	DZ
BPS			
N*	234	132	102
Cups of tea/day			
No tea drinkers	1.0	1.0	1.0
Tea drinkers	2.24 (1.08–4.67)	2.16 (0.74–6.3)	3.06 (0.96–9.7)
Smoking			
Never	1.0	1.0	1.0
Ever	1.18 (0.55–2.53)	0.93 (0.34–2.58)	1.73 (0.36–8.22)

[†] Adjusted for parity, BMI, coffee consumption and educational level.

MZ denotes monozygotic twins, DZ dizygotic twins.

* N denotes number of single twins subjects