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Cimetidine in the management of colorectal cancer: A survey of the knowledge and opinions of pharmacy students

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Abstract

This survey was conducted at Howard University (HU) College of Pharmacy as part of a Drug Information course, in which First-Year Pharmacy students learn how to perform literature search on a pharmacy topic and run a survey. A total of 42 student respondents participated in the survey. Nearly 64% (*n*=27) wrongly thought that cimetidine reduces the risk of colon cancer, while 57.1% (*n*=24) gave a wrong response that, even though cimetidine is FDA-approved for other indications, it can be taken for the prevention of colorectal cancer. Twenty-seven (64.3%) correctly believed that cimetidine is used for other health problems than colorectal cancer. The majority gave the correct response (*n*=25; 59.5%) that prescription medications are more useful than dietary supplements for the prevention of colorectal cancer. The highest number of correct responses (*n*=28; 66.7%) was obtained for the question of cimetidine passing through breast milk. The opinions of survey respondents were evenly divided in recommending cimetidine for the prevention of colorectal cancer (50%, *n*=21), and knowing someone or oneself taken for other than colorectal cancer (50%, *n*=21). Opinions varied unevenly for the other three opinion-based questions.

Keywords: Cimetidine; Histamine-2 Blocker; Colorectal Cancer; Knowledge; Opinion; Likert's score

1. Introduction

Cimetidine is a histamine-2 (H2) blocker that inhibits basal gastric acid secretion that is stimulated by food, histamine, pentagastrin, caffeine, and insulin. Its indications include gastric ulcers, erosive esophagitis, systematic mast cell disease, Zollinger- Ellison syndrome, and ulcers of the duodenum. Side effects of cimetidine typically are not severe. Common reactions include headache, diarrhea, dizziness, drowsiness, and breast enlargement. Very uncommon but severe adverse effects include depression, hallucinations, and mood related changes [1]. It is an FDA-approved drug for gastroesophageal reflux disease (GERD), hypersecretory conditions such as Zollinger-Ellison syndrome, and ulcers of the duodenum and stomach. Cimetidine is available both as a prescription and non-prescription over-the-counter product.

A few studies have been published on the potential benefits of cimetidine in colorectal cancer patients. Colorectal cancer, which is commonly known as colon cancer for short, is a cancer that occurs in the colon or rectum. The colon is the large intestine, and the rectum is the passageway that connects it to the anal opening. They are both a part of the digestive tract where the colon aids in the absorption of water and salt from food, and the rectum has the function of storing the remaining water from the colon until it is excreted during bowel movement [2].

Colorectal cancers form from a polyp that grows on the inner wall of the colon or rectum. The polyps are then removed and examined to determine if they are cancerous or not. Some signs that the polyp may be cancerous are if they are

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larger than 1 cm or if many polyps are found in an area. Current approaches for managing colorectal cancers include local treatments directed at the tumor without affecting the rest of the body. Performed in the early stage of the disease, these procedures include polypectomy and colectomy. Systematic treatments include drugs that target cancer cells throughout the body. During chemotherapy, immunotherapy, and targeted therapy treatments, the side effects typically include nausea, diarrhea, fatigue, loss of appetite, and low white blood cell counts [3].

Besides its approved uses, cimetidine has several non-FDA indications. One of these uses is in the treatment of acute intermittent porphyria (AIP). In a case report, the use of cimetidine was described in a 40-year-old man who presented with signs and symptoms consistent with AIP. The patient was treated with oral cimetidine at 800 mg/day and had as a result a complete clinical resolution after 12 days of treatment [4]. Similar benefits have been shown in other case studies. [5]. Preliminary evidence suggests that cimetidine may be a useful adjunct in treating acute intermittent porphyria; however, further clinical studies are required to fully evaluate the efficacy of cimetidine in treating this disease state.

In allergic rhinitis, 72% of the 40 patients with perennial allergic rhinitis who received cimetidine at 3 mg/kg/day once daily dose for 18 days showed clinical improvement versus placebo [6]. Moreover, several clinical reports and clinical studies indicate that intravenous cimetidine may have a role in the therapy of acute allergic reactions. Additionally, cimetidine has been used in combination with an H-1 blocker for the prevention of allergic reactions [7,8].

In aspiration pneumonitis, cimetidine has consistently been found to raise the pH above 2.5 minimizing the risk of developing pneumonitis. Cimetidine 300 mg orally, administered 2 to 2.5 hours prior to anesthesia induction, significantly increased gastric pH and reduced residual volume compared to placebo. In Barrett esophagus, gastric epithelial cells are replaced by esophageal squamous epithelium secondary to damage from gastroesophageal reflux. Two studies have reported that cimetidine at a dose of 1 to 1.6 g orally daily was effective in treatment of Barrett esophagus [9,10].

Hyperparathyroidism is also found to be responsive to cimetidine therapy, but only if it is due to adenomatous disease. Cimetidine's effect is believed to be due to its ability to decrease plasma parathyroid hormone and calcitonin levels [11]. Cimetidine has been used in the measurement of renal clearance. It is known that creatinine clearance (CrCl) overestimates GFR in the presence of renal insufficiency. Cimetidine improves the precision and accuracy of CrCl as an estimate of GFR, apparently by inhibiting the tubular secretion of creatinine [12]. The beneficial effects of cimetidine in the management of pancreatitis and steatorrhea were found either ineffective or inconclusive. [13,14].

In colorectal cancer patients, Matsumoto and co-workers demonstrated the beneficial effects of cimetidine. The study enrolled 64 patients, and co-administration of cimetidine with 5-fluorouracil increased the survival rate of colorectal patients significantly when compared to patients who received only 5-fluorourcacil [15]. Between 1996 and 2006, the use of cimetidine was investigated in patients with stage III colorectal cancer. Tumor recurrence was evaluated in the days between tumor resection and colorectal cancer recurrence. Thirty-eight patients met the inclusion criteria of the American Joint on Cancer Committee (AJCC) stage III colorectal cancer patients by having undergone surgical resection of the tumor and receiving chemotherapy [16]. Ten of the 38 patients received cimetidine at a median daily dose of 750 mg for 369 days with chemotherapy. The use of cimetidine showed a positive effect in prolonging recurrence of colorectal cancer.

A detailed review article examined the role of histamine and histaminergic receptors in colorectal cancer pathogenesis and the benefits of HR2 receptor antagonists (HR2A), including cimetidine. According to the review, HR2A's can be beneficial in colorectal cancer patients, because they promote lymphocyte growth which in turn helps with improved immune response to the tumor, suppression of the adhesion of molecules that favor metastasis, and increasing production of some cytokines that may counteract tumor growth [17].

In a previous publication, we reported the results of a survey on the knowledge and opinions of pharmacy students regarding the use of metformin in colorectal cancer [18]. In the current paper, from the same previous pool of respondents, we wish to report on their knowledge and opinions regarding the use of cimetidine in the same disease state.

2. Methods

The survey enrolled 45 incoming first professional year pharmacy students at Howard University College of Pharmacy. Of these, 42 students completed the survey, with a-93% response rate. The optional questionnaire was distributed to students during a drug information course. All questions, demographic data, and responses were analyzed using

Qualtrics. The survey consisted of 8 demographic inquiries, 5 knowledge-based and 5-opinion-based questions. A 4-point Likert scale (1=strongly agree; 2=agree; 3 = disagree; 4=strongly disagree) was used to score responses. The responses were then aggregated as 'agree" and "disagree," respectively. A mean Likert score was computed for each set of data on knowledge-based and opinion-based questions by dividing the respective scores by the total number of respondents (*n*=42). Demographic data, including age, gender, state of residence, work experience, annual income, and education were collected through the survey. Results were analyzed using IBM SPSS, and statistical analysis was completed by using a crosstab.

3. Results and discussion

Most of the survey participants (*n*=31; 73.8%) were in the age range 21 to 26 years (Table 1). There were more female respondents (n=27; 64.3%) than males (*n*=15; 35.7%). Thirty-four (81%) had a bachelor's degree prior to entering the pharmacy program. About 57% (*n*=24) reported as living in the Maryland/Virginia/Washington, D.C. area. Other demographic data are also summarized (Table 1).

Table 1 Demographic characteristics of respondents

Characteristics	Respondents (n, %)	95% CI (% range)[1]
Age (years)		
21-23	14 (33.3)	19.1-47.6
24-26	17 (40.5)	25.6-55.3
27-29	5 (11.9)	2.1-21.7
>29	6 (14.3)	3.7-24.9
Gender		
Male	15 (35.7)	21.2-50.2
Female	27 (64.3)	49.8-78.8
Education		
Some college	1 (2.4)	0.0-7.0
Associate Degree	1 (2.4)	0.0-7.0
BA/BSc	34 (81)	69.1-92.8
MSc	4 (9.5)	2.7-22.6
PhD/Professional	2 (4.8)	0.0-11.2
Residence		
Washington, D.C. Maryland	4 (9.5) 13 (31)	0.7-18.4 16.9-44.9
Virginia	7 (16.7)	5.4-27.9
Other States	18 (42.9)	27.9-57.2
Working now		
Yes	9 (21.4)	9.0-33.8
No	33 (78.6)	66.2-90.9
Work experience		
Never worked	2 (4.8)	0.0-11.2
Short-term	3 (7.1)	0.0-14.9
Part-time	16 (38.1)	23.4-52.8
Full-time	21 (50)	34.9-65.1

Type of job		
Pharmacy related	16 (38.1)	23.4-52.8
Other healthcare	12 (28.6)	14.9-42.2
Non-health related	13 (31)	16.9-44.9
Not applicable	1 (2.4)	0.0-7.0
Annual income		
< USD 10,000	13 (31)	16.9-44.9
10,001-20,000	7 (16.7)	5.4-27.9
20,001-30,000	6 (14.3)	3.7-24.9
30,001-40,000	5 (11.9)	2.1-21.7
>40,000	11 (26.2)	12-9-39.5
Years worked		
None	1 (2.4)	0.0-7.0
1-2	19 (45.2)	30.2-60.3
3-4	11 (26.2)	12.9-39.5
>4	11 (26.2)	12.9-39.6

[1]CI = Confidence Interval; normal approximations of binomial exact values.

Table 2 Responses to knowledge-related survey questionnaire statements

	Survey Statement*	**Response [*n*, (%)]**						**LK (m ±SD)**
		Correct Responses		**Incorrect Responses**		**T. Responses**	**T. Responses**	
		S. Agree	**Agree**	**Disagree**	**S. Disagree**	**Correct**	**Incorrect**	
1.	Cimetidine reduces the risk of colorectal cancer	4 (9.5)	11 (26.3)	18 (42.9)	9 (21.4)	15 (35.7)	27 (64.3)	2.24±0.91
2.	Cimetidine passes through breast milk in breast feeding mothers	8 (19.1)	20 (47.6)	10 (23.8)	4 (9.5)	28 (66.7)	14 (33.3)	2.24±0.88
3.	I believe cimetidine can be used for health issues other than colorectal cancer	7 (16,7)	20 (47.6)	9 (21.4)	6 (14.3)	27 (64.3)	15 (35.7)	2.33±0.93
4.	Prescription medications are more useful for prevention of colorectal cancer than dietary supplements	6 (14.3)	19 (45.2)	12 (28.6)	5 (11.9)	25 (59.5)	17 (40.5)	2.38±0.88
5.	Cimetidine is approved by FDA, and I am comfortable taking it if it helps prevent colorectal cancer	5 (11.9)	13 (30.9)	19 (45.2)	5 (11.9)	18 (42.8)	24 (57.1)	2.43±0.86

Abbreviations: S Agree =strongly agree; S. Disagree=strongly disagree.; T. Agree=total agree; T. Disagree =total disagree; LK=; Likert score; m ± SD=mean ± standard deviation.; *Correct number of total answers: 15 for question 1; 28 for 2; 27 for 3, 17 for 4 & 18 for 5.

About 64% (*n*=27) replied that cimetidine reduces the risk of colon cancer, while 57.1% (*n*=24) gave a response that cimetidine is an FDA-approved drug, and that it can be taken for the prevention of colorectal cancer. Both answers were wrong. On the other hand, 27 (64.3%) correctly believed that cimetidine is used for other health problems than colorectal cancer. The majority gave the correct response (*n*=25; 59.5%) when asked if prescription medications are more useful than dietary supplements for the prevention of colorectal cancer. The highest number of correct answers (*n*=28; 66.7%) was gleaned in response to the question that cimetidine passes through breast milk (Table 2). The

opinions of survey respondents were evenly divided on recommending cimetidine for the prevention of colorectal cancer (*n*=21, 50%), or knowing someone or oneself has taken it for other than colorectal cancer (*n*=21, 50%) (Table 3). There is a disconnect between the knowledge of the respondents favoring the use cimetidine for colorectal cancer (57.1%) and yet holding the correct opinion that it not advisable to use it for colorectal cancer (61.9%), or serious illnesses such as colon cancer should not be treated with dietary supplements or over the counter medications such as cimetidine (66.7%) (Table 3).

Table 3 Responses to opinion-related survey questionnaire statements

Survey Statement	Response [*n*, (%)]						LK (m ±SD)
	S. Agree	Agree	Disagree	S. Disagree	T. Agree	T. Disagree	
I may consider cimetidine as a recommendation to my patients for prevention of colorectal cancer	5 (11.9)	16 (38.1)	14(33.3)	7 (16.7)	21(50.0)	21 (50.0)	2.55±0.92
I know someone who has taken cimetidine, or I have taken it myself outside of colorectal cancer	4(9.5)	17 (40.5)	9(21.4)	12 (28.6)	21(50.0)	21 (50.0)	2.69±1.00
I believe other dietary supplements are as equally effective as cimetidine in preventing or treating colorectal cancer	8(19.0)	17 (40.5)	11(26.2)	6 (14.3)	25(59.5)	17 (40.5)	2.36±0.96
I do not believe in taking cimetidine or advising patients to take medications such as cimetidine that are not fully approved for illnesses including colorectal cancer	12 (28.5)	14 (33.3)	12(28.5)	4 (9.5)	26(61.9)	16 (38.1)	2.19±0.97
Serious illnesses such as colorectal cancer should be treated with dietary supplements or with OTC medications such as cimetidine	11(26.2)	17 (40.5)	8(19.0)	6 (14.3)	28 (66.7)	14 (33.3)	2.21±1.00

Abbreviations: S. Agree=strongly agree; S. Disagree=strongly disagree; T. Agree =total agree; T. Disagree =total disagree; LK= Likert score; m ± SD=mean ± standard deviation

4. Conclusion

A survey of 42 first year pharmacy students at HU revealed the majority had fairly good level of knowledge about two of the five knowledge-based questionnaire items; twenty-seven (64.3%) correctly believed that cimetidine is used for other health problems than colorectal cancer, and 25 (59.5%) thought prescription medications are more useful than dietary supplements for the prevention of colorectal cancer. However, 27 (64%) wrongly thought that cimetidine reduces the risk of colon cancer, and 24 (57.1%) believed, even though cimetidine is FDA-approved for other indications, it can be taken for the prevention of colorectal cancer. The majority gave a correct response (*n*=25; 59.5%) that prescription medications are more useful than dietary supplements for the prevention of colorectal cancer. The highest number of correct responses (*n*=28; 66.7%) was obtained for the question of cimetidine passing through breast milk. The respondents were evenly divided in their opinions on recommending cimetidine for the prevention of colorectal cancer (50%, *n*=21), and knowing someone or oneself taken for other than colorectal cancer (50%, *n*=21). Opinions varied unevenly for the other three opinion-based questions.

Limitations

The limitation of this study is the small sample size, with only 42 participants in the survey. For this reason, the findings cannot be extrapolated to future incoming pharmacy students at HU, or first-year pharmacy students in other institutions.

Compliance with ethical standards

Acknowledgments

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Approval

The survey was approved by Howard University IRB as part of a Drug Information course given by one of us (BH).

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

This survey was conducted as part of HU College of Pharmacy drug information course offered by one of us (BH); therefore, it didn't require informed consent of survey participants.

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