



What occurs in the other 20% of cancer patients with chemotherapy-induced nausea and vomiting (CINV)? A single-institution qualitative study

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Abstract

Purpose Despite recent advances in prophylaxis and management, 20% of patients who receive moderately to severely emetogenic chemotherapy continue to experience nausea and vomiting. Relying on patients' own words, this study sought to capture and characterize the lived experience with chemotherapy-induced nausea and vomiting (CINV) for this important subgroup of patients.

Methods Solid tumor patients with a history of poorly controlled CINV provided informed consent and participated in a semi-structured interview, which was audio-recorded and transcribed. After data saturation, enrollment ceased, and inductive, qualitative analytic methods were employed.

Results The median age of the 20 enrolled patients was 56 years (range 27–83) with an equal gender split; half had gastrointestinal cancers. Two themes emerged. First, CINV is severe and multidimensional: “It’s like shredding your muscles... It’s doing it over and over again.” This symptom complex has psychosocial implications: “Isolation is a big thing.” Financial toxicity is also implicated: “I use [an antiemetic] when I feel like it is absolutely necessary because it is so expensive I cannot afford it anyway.” The second theme is underreporting of symptoms. Patients seemed to accept N/V as part of treatment and were therefore less forthcoming: “God, if you’re pumping poison in your system, you gotta expect some side effects.”

Conclusions These vivid data should motivate investigators to continue conducting clinical trials CINV and should remind healthcare providers about the importance of patient education on the availability of therapy for breakthrough symptomatology.

Keywords Nausea and vomiting · Antiemetics · Underreporting · Qualitative · Supportive care

Introduction

Described as a “quiet revolution,” palliative care has transformed cancer care in recent years, particularly with respect to chemotherapy-induced nausea and vomiting (CINV) [1]. The development of 5HT₃ receptor antagonists and NK₁

receptor antagonists, the success of combination drugs, such as NEPA, the availability of transdermal and oral dissolving formulations, and the repurposing of olanzapine have provided an armamentarium of antiemetics that have dramatically lessened the percentage of cancer patients who contend with chemotherapy-induced nausea and vomiting. Moreover, national and international organizations have developed clinical guidelines for the prevention and treatment of CINV; some of these organizations, such as the Oncology Nursing Society, have also provided important patient and healthcare provider resources to target CINV [2–5]. These guidelines match the emetogenic potential of each chemotherapy regimen to the most appropriate antiemetic regimen, thus enabling patients to receive the most effective prophylactic palliation up front and thus eliminating what had previously been a trial and error approach. Today, an estimated 80% of cancer patients who receive moderately to severely emetogenic chemotherapy

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have no nausea and vomiting or, at most, experience markedly attenuated symptoms [6].

But what occurs in the other 20% of cancer patients whose symptoms persist? Indeed, the published literature appears to focus on the successful management of CINV with an emphasis on the effective palliation of this symptom complex. Relatively little attention appears to be devoted to the subgroup of cancer patients who continue to be symptomatic. This qualitative study aimed to address this glaring void in the published literature. Relying on patients' own words, this study sought to characterize the experiences of this subgroup with the goal of identifying future areas of research and practice improvement.

Methods

Overview This study was conducted at the Mayo Clinic in Rochester, MN, where a guideline-based approach to CINV is integrated into the clinical practice [7]. The Mayo Clinic Institutional Review Board approved the current study (IRB#16-005748).

Patient eligibility and recruitment Patients were deemed eligible for this study if they had been diagnosed with a solid-organ malignancy and had experienced poorly controlled nausea and vomiting at any time point. Nurses in the outpatient chemotherapy unit identified patients who were receiving active cancer treatment and who otherwise met the above eligibility criteria. Patients provided written informed consent prior to study enrollment.

Interview process All interviews were conducted in the summer of 2016, and patients were interviewed only once. A single, trained, physician investigator (D.S.C.), who was not involved in the participants' clinical care, conducted a semi-structured interview with each patient in a private room in the chemotherapy unit. The interview guide, which appears in Table 1, was constructed based on the clinical experiences of the study team and a review of the published literature. The interviewer was allowed to rephrase the questions based in the needs of the patient or to ask follow-up questions as long as all such questions were in keeping with the primary goal of the study. Grounded theory was used in approaching and exploring this issue of refractory CINV. The interviewer explored responses or pertinent topics of interest as long as such questioning was in alignment with the original goals of the study which seeks to understand this symptom complex from the vantage point of patients.

Two members of the research team (D.S.C. and A.J.) met regularly to discuss interview data in a real-time manner. Patient recruitment was halted once it appeared that saturation, or the emergence of no new information, had occurred.

Table 1 Semi-structured interview guide

- (1) Can you start by telling me about your experience with chemotherapy-induced nausea and vomiting?
- (2) What were your expectations for nausea and vomiting prior to starting chemotherapy?
 - (a) How has the reality differed from your expectations?
- (3) How has nausea and vomiting affected your day-to-day life?
- (4) How have your symptoms affected relationships that are important to you?
- (5) Are there any other ways that nausea and vomiting has affected your quality of life?*
- (6) What made communication with your provider easy or difficult regarding the subject of nausea and vomiting?*
- (7) What, if any, were your hesitations about reporting the severity of your symptoms?*
- (8) Who did you look to for support in controlling your nausea and vomiting?*
- (9) What has been most helpful in coping with nausea and vomiting?
 - (a) What support do you still need?
- (10) How do you think your nausea and vomiting will be in the future?
- (11) How has nausea and vomiting impacted the decisions you make regarding your cancer?
 - (a) How has it impacted your motivation to continue treatment?

*Questions with yes/no answers or focused responses were further explored with follow-up questions at the discretion of the interviewer

Trained medical secretaries transcribed audio files; these transcripts were then reviewed for accuracy.

Data analysis Data were analyzed inductively using an approach that was based on the steps in thematic analysis described by Guest and Chapman [8, 9]. Two investigators (D.S.C. and A.J.) independently reviewed the transcripts multiple times to get a sense of the whole and independently developed codes (that is, short words or phrases that captured specific interview content) that were used to segment and organize the data. After discussion and comparison of these independently developed codes, the two investigators created a harmonized "codebook" for data analyses. They then independently reviewed and coded the entirety of the transcripts, meeting regularly to review coding decisions and to resolve coding differences. A third adjudicator was available, in the event coding differences were unable to be reconciled, but was never called upon. After merging all data elements that had the same coding, these two investigators met to identify associations or networks among the codes. Both the convergence and divergence of codes were explored and then reconciled in the process of developing themes. Themes were then checked against the raw data to ensure that the breadth of patients' experiences and messages were appropriately captured.

Results

Demographics All eligible patients who were approached for the study consented and enrolled, providing a total sample size

of 20 patients. Demographics are listed in Table 2. The most common category of malignancy was gastrointestinal cancer. The median interview duration was approximately 21 min with a range of 13 to 38 min.

Themes Two themes emerged from the data (Table 3): (1) the severe and multifaceted nature of this symptom complex and (2) patients' underreporting of nausea and vomiting. As relevant to this first theme, patients provided varied and visceral descriptions of their experience, many of which underscored extreme physical suffering: "It's just like shredding your muscles. It's contracting them so tight. It's doing it again and again, and you need to breath, but it won't let you." Another patient described, "Okay, if you stick your finger down your throat, that feeling you get just before everything comes up, that is the feeling I have . . . all the time." Others described the nausea and vomiting as "extreme torture" or "horribly painful." A patient who was on chemotherapy for testicular cancer used the term "yakapalooza," when describing the act of vomiting.

Of note, CINV was at times so severe and multifaceted that it sometimes seemed difficult for patients to characterize. In attempting to do so, some tied nausea and vomiting to the more familiar. For example, one patient explained it as "the sickening feeling like you've had the worst case of flu." A mother who was being treated for breast cancer described her nausea as "terrible morning sickness." By contrast, others thought of their symptoms as a unique experience, "It's kind of like there's a word in our language that's missing. Because nausea is 'I feel I'm going to be sick,' then there's *this* nausea. It seems there's a big blank space between. There's a missing word."

Another aspect of this multifaceted symptom complex was psychosocial. One patient described social isolation when

trying to relate to others, "Because they had never gone through it before, they don't understand. They understand what it is like to be sick with the flu or something like that but to feel sick every day and not be able to eat or have dinner with my family, they did not understand what that feeling was like." Refractory symptoms left many patients feeling as if they were a burden to their families and caregivers, "I kind of feel like sometimes I'm being a burden, but everybody puts up with me."

Yet, another aspect of this multifaceted symptom complex centered on financial toxicity as relevant to antiemetics. One patient explained, "I use [the antiemetics] when I feel like it is absolutely necessary because it is so expensive I cannot afford it anyway."

The second theme is the underreporting of symptoms to healthcare providers. One reason for underreporting was because patients did not want to be perceived as complaining, "I've just been born and raised as the kind that you don't complain, so I guess people tell me that I have to start telling them. I think it's just my nature that I don't complain." A second reason was that patients did not want to bother their healthcare providers "I don't want to bother anybody. They have lives and stuff. It's like I know if it's 2 o'clock in the morning, I'm not going to call [my healthcare provider] and let her know I'm throwing up and it's really bad." A third reason centered on worries that chemotherapy would be stopped; one patient described how complaining would "[give] them [their healthcare providers] more reason to say 'no' to more treatment." Along the same line, many patients were willing to tolerate the CINV to gain benefit, noting "If I want to live, I have to do it. It's kind of like putting a gun to your head." Finally, CINV was occasionally accepted as part of cancer treatment, "I just put up with it. You're getting chemo. God, if you're pumping poison in your system, you gotta expect some side effects," and "to us, it just seemed like, this is just part of the treatment. It's going to happen."

Of note, underreporting also pertained to adverse events from antiemetics. One patient described, "The two drugs that I take cause constipation, and then you gotta fight that, and it isn't an enjoyable regimen of anti-nausea things to take because there are side effects from that, too." This same patient went on to explain, "Then, I was worried about constipation, and I'd stop taking them too soon, but I should've maybe taken them a few more days."

Discussion

To our knowledge, this is the first study in the era of highly effective antiemetic therapy to use qualitative methods to capture and characterize patients' lived experience with CINV. Perhaps the most important message in this report is that, despite recent therapeutic breakthroughs, CINV remains a

Table 2 Patient demographics

Median age at interview in years (range)	55.5 (27, 83)
Median duration of interview in minutes (range)	20.7 (12.6, 37.7)
Sex	
Female	10 (50)
Male	10 (50)
Cancer type	
Gastrointestinal	10 (50)
Breast	4 (20)
Gynecologic	3 (15)
Lung	2 (10)
Testicular	1 (5)

Data in parentheses are percentages unless otherwise noted

Table 3 Themes, subthemes, and representative quotes from patients

Themes	Subtheme	Representative quotes from the interviews (patient identifier in parentheses)
Theme 1: Severe and multifaceted nature of CINV symptom complex	Varied and visceral descriptions of CINV	<p>“It’s just like shredding your muscles. It’s contracting them so tight. It’s doing it again and again, and you need to breath, but it won’t let you.” (1)</p> <p>“Okay, if you stick your finger down your throat, that feeling you get just before everything comes up, that is the feeling I have . . . all the time.” (18)</p> <p>“[It feels] like a bubble of air or something, and it pushes. I feel like something going to come out, and it’s not coming out.” (8)</p> <p>“The muscle starts to tighten up and then there’s a release and then the tightening again and then the cramping. Then you just know that, at some point, it’s going to start to move up to your stomach and those muscles; I can feel those muscles moving. . . moving. I can feel them contracting. And then there’s that release of. . . I have got to relieve this—whatever it is that’s contracting my stomach. And that’s when I get into the vomiting or the dry heave. That’s the nausea; it’s the muscle contracting movement.” (7)</p> <p>“This nausea is a constant churning of my intestines.” (7)</p> <p>“Um, it’s a different feeling; it’s hard to describe. Um, I can look at food and smell food, but it’s like my body just shuts down and does not want any food in it.” (15)</p> <p>“How do I feel? I get a tightness on my diaphragm area. It’s just a strange thing, and I’ll know I better get to the sink or get that bucket.” (4)</p> <p>“It’s [like] tightness on my diaphragm. I wouldn’t say heartburn because I didn’t have the chest pain.” (3)</p> <p>“I knew I’d be throwing up a bit. I knew I’d probably hack once or twice a day, but I didn’t realize it’d be every five minutes or every time I put something in my mouth.” (1)</p> <p>“When I first started taking this stuff I could eat and everything was fine and all of a sudden, yakapalooza.” (1)</p> <p>“All I can say is it sucks, it sucks, it sucks. I wish it would go away. It’s horrible.” (1)</p> <p>“I have something that I think is nausea that just doesn’t seem to go away. It is minimized, but it is just always there. Lying down doesn’t seem to change the nausea part, it just follows you to bed.” (20)</p> <p>“Well, I just never imagined that I could look at some of my favorite foods and just almost throw up. I just never imagined that; that would be inconceivable.” (20)</p> <p>“Even bringing a pill to my mouth would make me vomit. The smell of food would make me vomit. I constantly was nauseous. I am constantly nauseous.” (2)</p>
	Ability versus inability to tie CINV to something familiar	<p>“[It’s like] <i>terrible</i> morning sickness.” (15)</p> <p>“Oh, just the sickening feeling like you had the worst case of flu.” (17)</p> <p>“[It’s like] gas, but there’s not a lot of gas that comes with this either.” (7)</p> <p>“I don’t know that I can describe it any other way.” (6)</p> <p>“It’s a different kind of nausea. It’s not anything like you would expect it to be.” (3)</p> <p>“It’s kind of like there’s a word in our language that’s missing. Because nausea is ‘I feel I’m going to be sick,’ then there’s THIS nausea. It seems there’s a big blank space between. There’s a missing word.” (7)</p>
	Psychosocial impact	<p>“I kind of feel like sometimes I’m being a burden, but everybody puts up with me.” (18)</p> <p>“Because they had never gone through it before, they don’t understand. They understand what it is like to be sick with the flu or something like that but to feel sick every day and not be able to eat or have dinner with my family, they did not understand what that feeling was like.” (19)</p> <p>“Well, it seemed like everybody in the family would just leave me alone because they knew I was sick, so they would not sit with me. They kinda go off in a different room because they did not want to bother me and the lights were usually down. So, I could not socialize with them. That was hard, little depressing because they did not like seeing me going through what I was going through at the time.” (19)</p> <p>“Isolation is a big thing.” (2)</p> <p>“So, I try to keep a smile on my face and try to keep the nausea within the confines of my own personal space and not let people see it in public or my family members.” (2)</p> <p>“I have teenagers at home that their mom’s in the hospital and they don’t want to come see me sick, and I don’t want to be sick around them.” (2)</p> <p>“I don’t leave the house anymore. I want to stay close to my own toilet.” (2)</p> <p>“I’m sick I can’t go with him places. It affects a lot.” (3)</p> <p>“They’ll say, ‘do you want to go out to lunch?’ And I’ll say, ‘No, I’m probably going to get sick that day or queasy and I don’t want to get in a car.’ So yeah, it hasn’t really affected any relationships.” (4)</p> <p>“I’m really sick of being sick. And I’m really tired of this whole thing. And you start to get, I don’t know, upset, but it’s just a stressor that I’m feeling sick all the time, and I can’t contribute, or I can’t go places.” (5)</p>

Table 3 (continued)

Themes	Subtheme	Representative quotes from the interviews (patient identifier in parentheses)
Theme 2: Underreporting to healthcare providers	Financial toxicity	“It’s just a stressor that I’m feeling sick all the time, and I can’t contribute, or I can’t go places or whatever.” (5)
		“The nausea makes me feel... tied down, not able to...it didn’t make me feel independent.” (7)
		“I don’t have control of it. Today, I relinquished myself to mentally giving up to it, so I am willing to grab one of those cups, and have no embarrassment, dry heaving right out in public.” (7)
		“Social activities, I tend to not want to participate because I don’t feel good. And then I always feel like I’m there, but I feel like crap so it’s not like I’m really participating.” (5)
		“I’m not young and strong, I’m sick all the time.” (7)
		“Um, for me...um, it’s frustrating because I can’t control it. It...you can’t. There’s just nothing you can do. Even the anti-nausea medication, you know, I mean, I take it with great hopes that this is gonna work <i>really</i> good this time or the more I get into me, the <i>better</i> I’m gonna feel tomorrow! And it’s not the truth. Psychologically, it’s just another nuisance I have to deal with.” (15)
		“It affects me quite a bit. Like I’ve said before, I don’t know that I would do chemo again.” (3)
		“I thought well, if I am going to be sick like this I cannot do it.” (19)
		“I can’t do this every month. This is taking a big toll on me. Then, it starts working on my mental.” (15)
		“You’ve gotta have kids or a pet. So kids are a good thing ‘cause they don’t care if you’re nauseous. They’ve still gotta get places. I mean, they care, but they still have to be places. They have to be fed. They have to...they just keep going forward. That’s good ‘cause it gets ya outta the house or get you moving or whatever, so you don’t just sit there and you’re not miserable.” (16)
		“I mean, it’s fine just sitting here, getting fluids put in my arms, the chemo, the people, the ins and outs, the constant visits, the lack of energy. That’s all fine. It’s just that one, that one variable that kills it for me, is the throwing up. I can’t go through that.” (1)
		“I use [the antiemetics] when I feel like it is absolutely necessary because it is so expensive I cannot afford it anyway.” (18)
		“I asked was there an Emend that I could take on day 3, 4, 5 at home without having to come in, but evidently it’s a very expensive pill and MOST insurance companies don’t approve it.” (4)
		“So then they started giving me Emend along with my chemotherapy. And that was amazing and just like someone flipped a switch and I was not sick anymore.” (19)
Underreporting of CINV	“It [reporting CINV] would have given them more reason to say ‘no,’ you know.” (9)	
	“To us, it just seemed like ‘Okay, this [CINV] is just part of the treatment.’ It’s going to happen.” (11)	
	“I just thought it was one of the things that was going to happen, you know.” (13)	
	“I just put up with it. You’re getting chemo. God, if you’re pumping poison in your system, you gotta expect some side effects.” (17)	
	“I have never even asked if there was anything else. I assume that that is the normal.” (13)	
	“You get super forgetful during chemo, and you forget what you’re supposed to feel like and you put up with a lot. It becomes a part of your day.” (16)	
	“It [CINV] becomes your constant companion, and you just, it’s just the way it is.” (16)	
	“I don’t know. I don’t want to bother anybody. They have lives and stuff. It’s like I know if it’s 2 o’clock in the morning, I’m not going to call [my provider] and let her know I’m throwing up and it’s really bad.” (1)	
	“I don’t want to end up in here. I’ve just been born and raised as the kind that you don’t complain, so I guess people tell me that I have to start telling them. I think it’s just my nature that I don’t complain, so I don’t usually unless it’s bad.” (2)	
	“I’m an old German so I just tough it out. It’s like, ‘you’ll feel better in a couple days, just tough it out.’” (5)	
	“Sometimes I didn’t report it because I felt like it’ll pass, [and] I’ll get through it.” (4)	
	“I think it’s a human nature, for me, it’s my nature. They already know. There’s not much more they can do for me. I’m already in it. I’m already in it, so I’ll tough it out. All of those natural tendencies kick in, which then prevents me from picking up the phone and going ‘okay, this is what’s happening.’” (7)	
	“I didn’t really communicate because I expected that I could be nauseous. I wasn’t throwing up anything unusual, so no, I didn’t have to communicate with them.” (4)	
	“I felt I had enough of the medications—they’d been giving me so many of it that surely all of those medications have to be doing something for me somewhere.” (7)	

Table 3 (continued)

Themes	Subtheme	Representative quotes from the interviews (patient identifier in parentheses)
		<p>“You think what you’re prescribed at the onset is what you have to do the entire way and to know that there are options available and they can adjust to what works for you—that would be easy to overlook if you didn’t have a vocal person.” (16)</p> <p>“At the beginning, it would be nice if they would have a list of available things that have helped control those [symptoms] before so that if one thing wasn’t working, you know, we could have tried another one sooner.” (4)</p> <p>“When I feel nauseated, I usually don’t want to talk. I mean, it makes me feel worse when I talk, so I don’t feel like a phone call would be something I wanted to do.” (10)</p> <p>“Now that I’ve sorted out in the hospital, and I have the palliative care people and the surgical people in the units and the oncology people. It’s sometimes more difficult [to know with whom to report]. . . If I’m smart, I talk to the nurses.” (9)</p>
	Underreporting of antiemetic side effects	<p>“The two drugs that I take cause constipation, and then you gotta fight that, and it isn’t an enjoyable regimen of anti-nausea things to take because there are side effects from that, too.” (5)</p> <p>“Then, I was worried about constipation, and I’d stop taking them too soon, but I should’ve maybe taken them a few more days.” (5)</p> <p>“I was pretty tired too from the Compazine, I think. Was that the one?” (11)</p> <p>“[The antiemetics] made me sleepy.” (11)</p> <p>“Honestly. How many medications am I taking now? Oh my goodness gracious. I think I’m taking five or six nausea medications right now. Are they interacting with each other? Am I taking them in the right order? I don’t think there’s anything they can do. I really don’t.” (7)</p> <p>“He can’t keep down the nausea meds. Then, you gotta go to suppositories. Well, if you’re using suppositories, you ain’t going nowhere.” (7)</p>

major problem for a sizable subgroup of cancer patients. This poorly controlled symptom complex is not only physically uncomfortable but has far-reaching psychological implications, such as isolation, guilt, and helplessness. In view of the high cost of antiemetics, our data also highlight that financial toxicity can be considered another important aspect of this symptom complex. Patients may struggle to justify the cost of additional expensive medications for the purpose of managing the side effects of treatments like chemotherapy and radiation that are, themselves, expensive. Thus, within the context of the important palliative breakthroughs described earlier, the current study provides a vivid reminder that a subgroup of cancer patients continues to suffer from CINV with notable downstream effects. In essence, the current study should serve as a motivating force to continue to find interventions to help control this symptom complex.

Underreporting of nausea and vomiting was another important theme. Some patients reported feeling they should accept this symptom complex as part of treatment (“poison”); others expressed a perceived threat that treatment would be stopped. Regardless of the underlying reason for staying silent, patients who do not report their experiences with nausea and vomiting fail to receive further breakthrough medication for palliation. Hence, an important lesson emerges from this study: patients should be encouraged to be forthcoming about their own experiences with nausea and vomiting without fear of negative consequences (e.g., stopping treatment). Additionally, patients should be informed that, although prophylactic approaches are highly successful, healthcare providers are also able to provide therapy for breakthrough symptoms. This reassurance is

important because Passik and colleagues have shown that patients’ fears regarding chemotherapy evolve during the course of treatment and respond to the provision of adequate management [10]. In conjunction with antiemetic drug therapy, patient education might serve an important role in mitigating symptoms.

Furthermore, at least three aspects of the current study require additional comment. First, this study was conducted within a quaternary cancer center. As a result, the experience of CINV, as captured here, might not be representative of what occurs in a more community-based oncology practice or in an otherwise dissimilar practice setting. It might be that patients within a quaternary medical center have more advanced cancer and therefore greater symptomatology. In concert with this same point, our patient population included a notably high percentage of patients with gastrointestinal malignancies. It is unclear whether this high percentage reflects a heavy predisposition of symptomatology within this group of patients, a high incidence of these cancer types in the population at large, institutional expertise in managing patients with these cancer types, or all the above. Nonetheless, this high percentage should be noted. Second, as a result of purposive sampling, we interviewed patients with more severe symptoms. Although this approach enriched our ability to understand this symptom complex, one should keep in mind that the majority of patients who receive cancer therapy truly do acquire good control of chemotherapy-induced nausea and vomiting. Third, future research on this topic might want to more fully query patients on what has helped the most when they have had to contend with CINV. In the future, it might be important to ask

patients specifically about complementary and integrative therapies and about the availability (or lack thereof) of external resources to help allay the high costs of antiemetics.

In summary, despite advances in palliative care, a subgroup of patients continues to experience a multifaceted symptom complex that stems from CINV—sometimes with severe and far-reaching consequences. Better antiemetic therapy coupled with better patient education continues to be necessary to help palliate this symptom complex in the 20% of patients who remain symptomatic.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Control of the data The authors have full control of all primary data and agree to allow the journal to review it if requested.

Ethical statement The Mayo Clinic Institutional Review Board approved this work.

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