

Patients' preference for administration of endocrine treatments by injection or tablets: results from a study of women with breast cancer

L. Fallowfield*, L. Atkins, S. Catt, A. Cox, C. Coxon, C. Langridge, R. Morris & M. Price

Sussex Psychosocial Oncology Group, Cancer Research UK, Brighton and Sussex Medical School, University of Sussex, Sussex, UK

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Background: Endocrine therapies for advanced breast cancer include tablets and intramuscular injections. When treatments have similar efficacy and tolerability profiles, addressing preferences about routes of administration is important.

Patients and methods: Two hundred and eight women >2 years post-breast cancer diagnosis were interviewed about their preferences for daily tablets or monthly intramuscular injections. Health-care professionals treating the women estimated patients' preferences.

Results: Sixty-three per cent of patients preferred tablets, 24.5% preferred the injection and 12.5% had no preference. The most cited reasons for tablet preference were convenience and dislike of needles; for injection preference, adherence and convenience. Variables associated with preferences were body mass index, educational level, attitudes towards injections and efficacy perceptions. Estimates about patients' preferences by health-care professionals varied widely. When asked to imagine scenarios where injections produced fewer hot flushes, or where two injections monthly improved efficacy, injection preference increased to 60.6% and 74.5%, respectively. Disturbingly, ~50% of patients admitted they sometimes forgot or chose not to take their current oral medication.

Conclusions: The majority of breast cancer patients preferred hormone therapy via daily tablets rather than monthly injections. Information about side-effects or improved efficacy altered these preferences. Adherence to treatment cannot be assumed; patients' preferences about drug administration may influence this.

Key words: breast cancer, fulvestrant injections, patient preferences, tablet adherence

introduction

Current and newly formulated endocrine therapies designed for patients with advanced breast cancer include tablets (e.g. tamoxifen, anastrozole, letrozole and exemestane) and intramuscular injections (e.g. fulvestrant) [1]. Where different treatments have broadly similar efficacy and tolerability profiles (e.g. tamoxifen and fulvestrant) [2], addressing patient preferences regarding the different routes of administration is important, especially as patients and health professionals may not share similar views about treatments [3, 4].

A better understanding of patients' preferences is fundamental to the shared model of medical decision-making, acknowledged as the preferred practice in determining treatment [5, 6]. Formulating plans that recognise patients' preferences enhances satisfaction and is associated with improved adherence [7]. Consideration must be given not only to concerns about the benefits and costs of different treatments, but also practical

implications [8]. Issues such as the ease of getting to a pharmacy, opening containers and remembering to take drugs all interfere with daily life, influencing how and when patients take their medication. Despite this, patients' understanding or concerns about treatment are rarely explored [7] and why patients choose particular treatments is poorly investigated [9].

Palliative oncology studies report that provided that efficacy is equivalent, most patients prefer oral treatment rather than insertion of central venous lines [4, 10, 11]. Factors influencing choice include convenience, problems with intravenous lines or needles, the environment in which the therapy is administered and concerns about side-effects [4, 10–12]. One of these studies employed a randomised crossover design and found different reasons for patients' preferences before and after they had experienced each treatment [11]. Initially, choices were dominated by toxicity fears, but after experiencing both oral and intravenous treatment, patients were more likely to indicate specific administration-related features.

Generally, health-care professionals consider that patients dislike injections, and consequently they are more likely to prescribe oral treatments, although true injection phobias, rather than dislike, only affect between 3% and 10% of the

*Correspondence to: Prof. L. Fallowfield, Sussex Psychosocial Oncology Group, Cancer Research UK, Brighton & Sussex Medical School, University of Sussex, Sussex BN1 9QG, UK. Tel: +44-1273-873015; Fax: +44-1273-873022; E-mail: L.J.Fallowfield@sussex.ac.uk

population [13, 14]. Injection site pain may be relevant in extremely thin patients, so body mass index (BMI) might be a further factor influencing preferences.

The potential for non-adherence is a major disadvantage of oral treatment. Patient adherence to oral anticancer medication is variable and difficult to predict [15, 16]. In one study of women prescribed adjuvant tamoxifen for breast cancer, nearly one-quarter risked inadequate clinical benefit due to poor adherence [16].

Women with breast cancer are often older, with comorbidities that necessitate the taking of many other drugs. One more tablet might not be viewed as a burden, but if tablet swallowing is difficult, a monthly injection might be seen as more desirable.

Personality may also influence treatment choice and adherence, for example patients who have a sense of control over their treatment are more likely to choose oral therapy [4, 10, 11]. Anxiety is another factor that may potentially affect preferences. A putative benefit of monthly injections is more regular contact with a specialist nurse, which some patients, especially those with high anxiety, may value. Conversely, high anxiety might be associated with unwillingness to have extra contact with the clinic [17].

The objectives of the study reported here were: to elicit women's preferences for different routes of administration of hormone treatments for breast cancer, namely oral tablets or a monthly intramuscular injection, and to determine the factors associated with preferences. Additionally, the breast cancer clinicians and specialist nurses in participating centres were surveyed to elicit which of the treatments they thought their patients would prefer and reasons for their patients' choices.

materials and methods

participants and recruitment

Participants were a convenience sample of women with early or advanced breast cancer currently in remission or with stable disease. All were at least 2 years post-diagnosis and were currently receiving or had previous experience of at least one drug for breast cancer. The women were attending one of six outpatient clinics for routine follow-up. Clinics were chosen by the researchers in different parts of the UK to ensure a geographical spread of different socioeconomic groupings. Health-care professionals, usually the specialist nurse or treating clinician, identified potentially eligible patients fulfilling the broad criteria above, prior to their consultations. Consecutive, potentially eligible patients were then given written information by a researcher and invited to participate in the study. Those interested were telephoned and consenting patients were interviewed in their own homes by a trained researcher, using a semi-structured interview schedule. Written consent included permission for the interview to be audiotaped. The study had approval from multicentre and local research ethics committees.

interview content

Most interviews lasted under 1 hour, during which sociodemographic information was collected, together with details about current and previous breast cancer treatment and concurrent medication for comorbidities. Patients were asked about journey length to the clinic, ease and method of travelling, physical difficulties, convenience of attending clinics, and their relationship with clinic doctors and nurses. They were asked about their views on the efficacy of injections versus tablets and if any aspects of their current medication were difficult. Specific issues about oral medication were elicited including: whether or not they found swallowing tablets difficult,

if they ever forgot to take tablets, if they ever chose not to take tablets as prescribed and why, and if tablet taking interfered with their daily life. They were also asked about injections: previous experiences, anxiety and whether they had ever had a needle phobia.

Patients were then read a scenario: 'Imagine that you were going to be offered one of two new treatments that were designed to help prevent breast cancer from getting worse. Both these treatments would be equally effective and similar in terms of side-effects. One treatment would be a tablet taken by mouth once a day and you would continue to see your doctor for check-ups every 3–6 months. The other treatment would be an injection into the buttock, which is administered once monthly at your breast clinic by the nurse. You would continue to see your doctor every 3–6 months.'

Patients' preferences for tablets or injections were obtained immediately after hearing the scenario and then again after reflecting further on the benefits and disadvantages of both treatments. To ascertain the strength of preferences two final follow-up questions were posed. Patients were asked if preferences would remain the same if (i) the injection caused fewer hot flushes and (ii) an injection into both buttocks controlled the cancer better.

questionnaires

Participants completed two short standardised questionnaires, the State-Trait Anxiety Inventory (STAI) [18] and the Multidimensional Health Locus of Control Scale (MHLOC) [19]. The MHLOC assesses respondents' perceptions of control over their illness and the extent to which they feel powerful others and chance factors influence their general health.

health-care professionals' estimations of their patients' preferences

Twelve health-care professionals, comprising eight consultant oncologists and four specialist breast care nurses from the participating clinics, were sent questionnaires with the main patient scenario and follow-up variations (if injections caused fewer hot flushes or greater efficacy could be achieved with one injection in each buttock). They then estimated the proportion of patients who would opt for injections, tablets or have no preference, and reasons for these preferences.

statistical analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS). The *t*-test was used to examine differences between group means and the χ^2 -test to examine differences in proportions.

Audiotapes were checked by an independent researcher and inconsistencies resolved prior to analysis. Reasons for preferences were split into agreed thematic categories by a consensus group of three researchers.

results

Two hundred and seventy women expressed interest in the study of whom 208 (77%) were interviewed and completed questionnaires (35 refused when contacted and 27 were not contactable within the time-frame of the study). Patient characteristics are shown in Table 1. Most were married (62%) and educated up to secondary school level (53.9%). Mean STAI were slightly higher than the norms for women aged 50–69 years (31.79 and 32.20) [18], but similar to those for women with breast cancer [20]. MHLOC scores were similar to those seen in chronic patient populations and did not differ significantly between preference groups.

Sixty-one respondents were taking four or more tablets a day for any illness or condition and 28 were not on any medication. Almost two-thirds (131 of 208; 63%) were currently receiving medication for their breast cancer (Table 2), the majority taking

Table 1. Patient characteristics

Characteristic	All patients (<i>n</i> = 208)	Injection preference (<i>n</i> = 51)	Tablet preference (<i>n</i> = 131)	No preference (<i>n</i> = 26)
Mean age, years [SD (range)]	59.72 [11.51 (32–88)]	58.27 [12.35 (34–81)]	59.02 [11.21 (32–88)]	66.08 [9.43 (51–86)]
Mean BMI, kg/m ² [SD (range)]	26.43 [5.04 (17–42)]	28.57 [5.88 (20–42)]	25.69 [4.63 (17–42)]	25.95 [4.17 (19–34)]
Education [<i>n</i> (%)]				
Secondary	111 (53.9)	35 (70.0)	60 (46.1)	16 (61.6)
Further	41 (19.9)	6 (12.0)	30 (23.1)	5 (19.2)
Higher	54 (26.2)	9 (18.0)	40 (30.8)	5 (19.2)
Partnership status [<i>n</i> (%)]				
Single	24 (11.6)	6 (11.8)	14 (10.7)	4 (15.4)
Married	129 (62.0)	31 (60.8)	86 (65.6)	12 (46.2)
Living with partner	5 (2.4)	2 (3.9)	3 (2.3)	0 (0)
Separated/divorced	24 (11.5)	6 (11.7)	13 (9.9)	5 (19.2)
Widowed	26 (12.5)	6 (11.8)	15 (11.5)	5 (19.2)
Trait mean anxiety [SD (range)]	37.82 [10.50 (20–72)]	39.49 [10.33 (23–63)]	37.72 [10.58 (20–72)]	35.13 [10.24 (22–59)]
State mean anxiety [SD (range)]	38.45 [9.94 (20–72)]	39.85 [8.91 (24–59)]	38.56 [10.09 (20–72)]	35.08 [10.66 (21–57)]
Multidimensional health locus of control				
Internal mean [SD (range)]	23.73 [5.14 (11–34)]	23.66 [5.07 (11–32)]	23.70 [5.38 (11–34)]	24.00 [4.08 (14–31)]
Chance mean [SD (range)]	18.26 [5.28 (8–34)]	18.81 [5.21 (9–28)]	17.95 [5.26 (10–34)]	18.83 [5.64 (8–30)]
Powerful others mean [SD (range)]	19.06 [6.21 (6–36)]	20.00 [5.06 (10–30)]	18.33 [6.27 (6–36)]	21.08 [7.42 (7–36)]

SD, standard deviation; BMI, body mass index.

either tamoxifen (34.6%) or anastrozole (17.3%). Five patients were receiving injections (excluding intravenous infusions) and four patients were receiving chemotherapy.

The majority had no physical disabilities affecting their ability to get around (195 of 208; 93.8%) and most (191 of 207; 92.3%) found attendance at clinics easy and convenient, even though 111 of 207 (53.6%) said the journey took more than 30 min. Most reported good relationships with their doctors (203 of 207; 98.1%) and nurses (193 of 198; 97.5%).

When asked if they thought that tablets or injections were more effective in general, 92 of 200 (46%) respondents said they did not know and 55 of 200 (27.5%) thought that both methods were equally effective; 44 of 200 (22%) considered injections to be more effective and nine of 200 (4.5%) felt that better efficacy was likely from tablets.

Most patients had no problems swallowing tablets (184 of 208; 88.5%) and said that tablet taking did not interfere with everyday life (183 of 194; 94.3%). However, approximately half said that they sometimes forgot (94 of 193; 48.7%) or deliberately omitted (25 of 191; 13.1%) taking their tablets at times. Approximately one-third (78 of 208; 37.5%) said they were generally anxious about having injections; 36 of 208 (17.3%) said that feelings of anxiety or dislike of needles might cause them to avoid injections if possible. However, true needle phobia, rather than anxiety or dislike, was reported by 28 of 208 (13.5%) of patients at some time.

Immediately after hearing the scenario, most patients (131 of 208; 63%) preferred daily tablets to the monthly injection, almost one-quarter (51 of 208; 24.5%) preferred injections and 26 of 208 (12.5%) had no preference.

Patients gave 256 reasons for their initial preferences, which were grouped into 12 thematic categories (Table 3).

Table 2. Summary of current medication for breast cancer

	Drug	<i>n</i> ^a (% total sample)
Endocrine, antibody or bisphosphonate therapy	Tamoxifen	72 (34.6)
	Anastrozole	36 (17.3)
	Exemestane	9 (4.3)
	Letrozole	6 (2.9)
	Zoledronic acid	4 (1.9)
	Goserelin	3 (1.4)
	Megestrol	3 (1.4)
	Trastuzumab	2 (1.0)
	Fulvestrant	1 (0.5)
	Leuprorelin	1 (0.5)
Chemotherapy	Capecitabine	1 (0.5)
	Paclitaxel	1 (0.5)
	Vinorelbine	1 (0.5)
	Not named	1 (0.5)

^aEight patients were taking two drugs and one patient was taking three drugs.

Convenience was the most common reason for choosing tablets, followed by a dislike of needles. A few patients commented that they would rather have an injection if it could be given at home or by their general practitioner rather than at the cancer clinic. Convenience was also the most common reason cited for preferring injections, followed by the desire to ensure adherence.

An exploratory analysis was performed to determine which factors affected preferences. Patients who expressed an initial preference for injections or tablets (*n* = 182) were compared. Patients educated up to secondary school level were twice as likely to choose injections (35 of 95; 36.8%) as those educated beyond this level (15 of 85; 17.6%) ($\chi^2 = 8.24$; *P* = 0.004).

Table 3. Reasons for initial preferences

Categories	Injection (<i>n</i> = 51) [<i>n</i> (% ^a)]	Tablet (<i>n</i> = 131) [<i>n</i> (% ^a)]	No preference (<i>n</i> = 26) [<i>n</i> (96%)]	Total (<i>n</i> = 208) [<i>n</i> (% ^a)]
Convenience	24 (47.1)	92 (70.2)	2 (7.7)	118 (56.7)
Clinical contact	3 (5.9)	0 (0)	0 (0)	3 (1.4)
Control	1 (2.0)	10 (7.6)	0 (0)	11 (5.3)
Adherence	22 (43.1)	1 (0.8)	1 (3.8)	24 (11.5)
Side-effects	2 (3.9)	3 (2.3)	1 (3.8)	6 (2.9)
Pain	0 (0)	10 (7.6)	0 (0)	10 (4.8)
Efficacy	5 (9.8)	6 (4.6)	1 (3.8)	12 (5.8)
No preference	0 (0)	1 (0.8)	13 (50.0)	14 (6.7)
Psychological	7 (13.7)	13 (9.9)	0 (0)	20 (9.6)
Swallowing/tablet taking	4 (7.8)	9 (6.9)	0 (0)	13 (6.3)
Needle dislike	0 (0)	23 (17.6)	0 (0)	23 (11.1)
Financial	0 (0)	2 (1.5)	0 (0)	2 (1.0)

^aPercentage of respondents who gave multiple reasons for their preference.

Patients who preferred injections had a higher mean BMI than those preferring tablets (28.57 versus 25.69; $t = 3.14$; $P = 0.002$). Neither age, partnership status, anxiety nor any dimensions of health locus of control were significantly associated with preferences.

Negative feelings about injections led to self-reported needle avoidance in 30 of 131 (22.9%) of the patients who chose the tablet option compared with five of 51 (9.8%) of those who preferred injections ($\chi^2 = 4.05$; $P = 0.044$). Preferences were not significantly associated with any other aspects of current treatment including convenience and relationship with health-care professionals or general views about medication.

Despite the scenario describing treatments as 'equally effective', 56 of 182 (30.8%) thought one treatment was better than the other. Patients who preferred injections were more likely to feel one treatment was better than the other compared with patients who preferred tablets (22 of 51, 43.1% versus 34 of 131, 26%; $\chi^2 = 6.51$; $P = 0.039$). Of the 56 patients who thought one method was better than the other, 21 of 22 (95.4%) of those who preferred injections thought injections were better and 20 of 34 (58.8%) of those who preferred tablets thought tablets were better.

After weighing up the pros and cons of the different options, respondents reconsidered their preferences. This made very little difference: 134 of 208 (64.4%) preferred the daily tablet, 55 of 208 (26.5%) preferred the injection and 19 of 208 (9.1%) had no preference. However, varying the side-effects or efficacy of treatment options altered preferences. When patients were asked to choose again given hypothetical information that injections resulted in fewer hot flushes, the proportion choosing tablets decreased to 57 of 208 (27.4%), the proportion opting for injections increased to 126 of 208 (60.6%) and 25 of 208 (12%) remained undecided. When patients were asked to choose between a daily tablet and two monthly injections (one in each buttock) that would better control the cancer, 155 of 208 (74.5%) chose injections, 40 of 208 (19.2%) tablets and 13 of 208 (6.3%) gave no preference.

Health-care professionals assumed tablets would be more popular than injections, but gave a wide range of estimates concerning the proportion of patients who would opt for tablets

(41–100%), injections (0–50%) or have no preference (0–20%). Estimates concerning patient preferences also varied when the side-effects and efficacy of treatments in the scenarios were changed. Estimates of the proportion of their patients with a needle phobia ranged between 0% and 60%. Most assumed that those who chose injections would do so to facilitate adherence and those patients who chose tablets would do so for reasons of convenience.

discussion

This study, examining patients' preferences for different routes of treatment administration, showed the majority (63%) preferred daily tablets rather than monthly injections. Nevertheless, a sizeable minority (24.5%) would prefer an intramuscular route of administration. These findings are similar to a recently reported telephone survey of 260 women with metastatic breast cancer conducted in the USA [21].

Analysis of reasons for choice revealed convenience to be an important issue whatever preference patients had. Some patients commented that they would prefer injections if these could be administered by a district nurse or primary care physician rather than at the hospital clinic. Although a minority of those who opted for tablets cited a general dislike of needles as a reason for their choice, only 17.3% of all respondents said that their concerns about injections would mean they avoided having one. Some patients commented that their negative feelings towards injections were more related to their experiences with the side-effects of previous intravenous chemotherapy than anything else.

Patients, even those with life-threatening disease, often fail to take their tablets as prescribed; disturbingly, almost half the patients currently on oral medication reported forgetting to take their tablets from time to time and 13.1% deliberately chose not to take them. Indeed one of the primary reasons given by 43.1% of the patients who preferred injections was that this method would ensure that they received their treatment. It is worth considering whether or not the figure for non-adherence might in fact be an underestimate. During a face-to-face interview patients might have had difficulty revealing that they choose not to take their medication, whereas admitting that they forgot is

more acceptable. From a behavioural point of view, maintenance of long-term endocrine therapy poses several interesting issues; if women remain asymptomatic of breast cancer or recurrence then they may not see the value of taking pills regularly. If the medication also produces iatrogenic harm or unpleasant side-effects, which are relieved by stopping the pills, then a reinforcing pattern of non-adherence is set up. These issues merit more attention given the huge amount of resources spent on treatment.

Factors significantly associated with preference were BMI, educational group, avoidance of injections and perceptions about the efficacy of different routes of administration. The association of higher BMI with injection preference is logical, as thinner patients might well find intramuscular injections more uncomfortable. Why those with lower educational attainment were twice as likely as those educated to higher levels to choose injections is not entirely clear. The finding concerning 'perceived' efficacy is perhaps surprising as the scenario informed patients that both treatments were equally effective. Of the 56 patients who thought one treatment was more efficacious than the other, almost all (95.4%) of those preferring injections thought injections were better, but unexpectedly only 58.8% of those preferring tablets thought that tablets were better. This suggests that beliefs concerning the efficacy of treatments may have been more of an influence on preference for those choosing injections. Interestingly, efficacy features such as 'I thought it was a stronger medicine' ranked very low overall compared with other reasons for post-treatment preferences in a crossover study that asked patients to compare palliative treatments for advanced colorectal cancer [11].

The methodology and specific wording used in studies may affect treatment preferences [11]. This study asked about preferences regarding hypothetical treatment choices, but preferences and reasons for them might be different if patients had actually experienced both methods of treatment [11]. The majority of women were on oral medication and only five patients were currently receiving injections (excluding intravenous infusions) for breast cancer treatment. Prospective studies are needed to examine whether preferences are related to actual treatment and whether preferences change over time [3].

Other factors expected to be associated with preference including: relationship with nurses and doctors at the clinic, ease of attending clinics, needle phobia, difficulties swallowing tablets, and psychological factors such as health locus of control and anxiety, demonstrated no significant association.

Although convenience was an important reason for treatment preference, nearly all the respondents in this study found their own breast clinics very convenient and very few reported problems regarding their current treatment. Similarly, most said their relationships with professionals were very good. The high level of satisfaction with health services might explain why no associations were found with preferences.

There was little change in preferences when patients reconsidered their choices after reviewing the advantages and disadvantages of each treatment option, but varying the description of side-effects and efficacy of treatments in the scenario produced interesting shifts.

Previous research regarding breast cancer treatment preferences has demonstrated the impact of side-effects on quality of life and adherence [9, 22]. When patients were asked to imagine a scenario where injections would result in fewer hot flushes, the proportion of women opting for the injection option increased considerably and preferences for tablets decreased. Although not life-threatening, hot flushes remain an important problem for women treated for breast cancer [23].

When patients were asked to express a preference based on the scenario that two injections (one in each buttock) would be better at controlling the cancer, the percentages opting for injections increased considerably. This finding may be of importance should further research demonstrate a benefit with higher doses of endocrine treatment that would necessitate the administration of two injections. In another study patients with incurable cancer were asked about hypothetical preferences for oral or intravenous palliative chemotherapy; patients were generally not willing to sacrifice efficacy for their preference [10].

Why patients choose a particular treatment is often poorly understood by the health-care professionals treating them [9]. We asked the clinicians and nurses from the six centres treating women in the study which route of administration they thought their patients would prefer and reasons for these preferences. The health-care professionals correctly assumed that the majority of patients would prefer tablets to injections, that convenience and adherence would affect patient choice and that a preference for injections would increase if this method caused fewer side-effects or was more efficacious (even if it necessitated two monthly injections rather than one). However, estimates varied widely even between health-care professionals working within the same clinic with the same patients.

The individual preferences shown here emphasise the importance of good communication concerning available treatment options. If different routes of administration exist, then these merit appropriate discussion and consideration alongside other clinical benefits. Finally, adherence to an oral regimen cannot be assumed even when prescribed for patients with life-threatening diseases.

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