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Safety and feasibility of home-based chemotherapy

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ABSTRACT

INTRODUCTION: The purpose of this study was to evaluate the safety and feasibility of home-based chemotherapy and to compare chemotherapy given at home with chemotherapy given as an outpatient treatment in relation to toxicity, quality of life and patient's preference.

METHODS: Patients who had undergone radical surgery for colon cancer and who were eligible to receive adjuvant treatment with capecitabine and oxaliplatin could be included. To ensure patient safety, the first infusion was given at an outpatient clinic. Patients with adverse events graded ≤ 2 on the Common Terminology Criteria for Adverse Events version 3.0 were randomised to either group A continuing with four treatments at home followed by three in an outpatient clinic, or to group B continuing with three treatments in an outpatient clinic followed by four at home. To assess quality of life, the EuroQol-5 Domain was used at baseline and before each treatment. Preference cards were used at baseline and at end of treatment.

RESULTS: A total of 51 patients were included between 2007 and 2010. Forty-two patients continued in either group A or B. The nurse found that the treatment was safe and acceptable in all cases. In 145 cycles (99.3%), patients answered that they felt secure; only one patient answered: "Do not know". The highest-ranking preferences for patients were transportation time followed by waiting time.

CONCLUSIONS: Our study demonstrates that home-based chemotherapy is feasible and safe and that it might be a valuable alternative to treatment at an outpatient clinic.

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TRIAL REGISTRATION: not relevant.

The number of cancer patients is increasing steadily worldwide due to a growing population with a larger proportion of elderly people and an increased prevalence of established risk factors such as smoking, overweight and physical inactivity [1, 2]. Along with more treatment options, these factors have increased pressure on the healthcare system, making alternative ways to administer treatments an interesting topic.

Many antineoplastic treatment regimens must be administered at hospitals as they require qualified staff and equipment in order to monitor patients during treatment. One way of freeing up resources for complex treatments may be to move less complex treatments out of hospital and into patients' homes or to smaller primary healthcare centres. Furthermore, patients will benefit from this as they avoid transportation and waiting time at the hospital. Despite the potential benefits of home-based chemotherapy, such treatment has never been established as standard treatment in Denmark. The results from trials with home-based chemotherapy have been summarised in reviews [3, 4]. In general, results support home-based chemotherapy as far as patients' satisfaction, quality of life (QoL) and compliance are concerned. However, not all patients favour home-based chemotherapy. Therefore, we need further exploration and additional evidence to identify which treatments and which patient groups may benefit from home-based chemotherapy [4].

We here focus on the feasibility and safety of home-based adjuvant chemotherapy for patients having undergone colon cancer surgery. Adjuvant treatment for six months with 5-fluorouracil/leucovorin or capecitabine together with oxaliplatin was the current worldwide standard treatment for patients with stage III and high-risk stage II colon cancer when the study was conducted. Furthermore, we evaluated possible differences in toxicity, QoL and patients' preference between home-based and outpatient treatment.

METHODS

Design

This was a randomised crossover study that used patients as their own controls. As severity of adverse events, particularly neurotoxicity, might increase during treatment, half of the patients started treatment at home and half in an outpatient clinic in order to reduce bias. All patients received the first treatment in the outpatient clinic to ensure that it was well tolerated. Only patients with ≤ grade 2 adverse events after their first treatment who were willing to continue and who had an initial computed tomography without metastatic disease continued in the study. Patients were randomised in a 1:1 ratio to continue the next seven treatments in either group A, with four cycles at home followed by three cycles in the outpatient clinic, or to treatment in group B with three cycles in the outpatient clinic followed by four cycles at home; in total eight cycles.

The primary endpoints were safety and feasibility. Secondary endpoints were toxicity, QoL and patient preference on selected topics. The treatment regimen

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TABLE 1

Items and examples of preference cards.

Item	Options	Example
Transportation time	0, 3 or 6 h	3 h
Waiting time	0, 2 or 4 h	0 h
Time with doctor	0 and 10 min.	10 min.
Time with nurse	10 min. together with other patients or 30 min. alone	10 min. together with other patients
Safety	High vs low	High
Surroundings	Private or in presence of others	In presence of others
Contact with relatives	Private or in the presence of other	In the presence of other

consisted of eight cycles of oxaliplatin 130 mg/m^2, every three weeks and oral capecitabine 1,000 mg/m^2 twice a day during two weeks, followed by a one-week pause. Oxaliplatin is normally prescribed to be given over two hours, but can also be given as an infusion over 30 min. [5]. Our study used 30-min. infusions. To avoid nausea, the patients were pretreated with prednisolone 50 mg and ondansetrone 8 mg. If these drugs proved insufficient, palonosetrone or aprepitant were prescribed. Diarrhoea was treated with loperamide.

Participants and procedures

The study participants had to be more than 18 years old and to have been operated for stage III or high-risk stage II colon cancer. The exclusion criteria were patients living more than 30 km from the hospital or receiving anticoagulation treatment. Home-based treatment was administered by a study nurse with extensive oncological nursing experience. She carried a mobile phone allowing her to contact the hospital for medical advice or to call for emergency assistance in case of severe reactions. She also carried all the equipment needed for the treatment, administration and handling of any potentially severe reactions, including oxygen, portable suction, and emergency medication to treat allergic reactions. The set up allowed for three daily treatments. Before each treatment, the nurse was asked to evaluate whether it was considered safe and acceptable to administer the treatment as home-based chemotherapy. Before each treatment, adverse events were scored according to the Common Terminology Criteria for Adverse Events version 3.0. For home-based treatments, this was done by the same nurse every time. The nurse made telephone interview the day before the planned treatment. For treatment in the outpatient clinic, the adverse event scoring was done by an oncologist, but not necessarily by the same person each time. The same work sheets for scoring adverse events were used in both settings.

TABLE 2

Patient characteristics.

	Treatment A (N = 21)	Treatment B (N = 21)
Age, median (range), yrs	64 (44-76)	67 (34-80)
Gender, n (%)		
Male	14 (66.7)	10 (47.6)
Female	7 (33.3)	11 (52.4)
Performance status, n (%)		
0	18 (85.7)	19 (90.5)
1	3 (14.3)	2 (9.5)
Disease stage, n		
Stage 2	4	6
Stage 3	17	15
Distance from hospital, median (range), km	11.2 (1.9-23.0)	10.2 (3.8-32.5)
Civil status, n (%)		
Married	17 (81.0)	15 (71.4)
Living alone	4 (19.0)	6 (28.6)
Get to work, n (%)		
Yes	10 (47.6)	9 (42.9)
No	11 (52.4)	12 (57.1)

After each treatment, the patient was asked if the treatment was given as expected and if he or she had felt secure. Furthermore, the patients completed the EuroQol-5 Domain Health-Related Quality of Life Questionnaire at baseline and before each treatment. Patients' preferences on seven topics were examined in a conjoint analysis. Ten preference cards were prepared, each with the seven topics in varying order. Patients were asked to sort the preference cards from 1 (most preferable) to 10 (least preferable) at baseline and at the final cycle (**Table 1**). They were not asked specific questions, but had to rank the following seven topics: transportation time, waiting time, time with doctor, time with nurse, safety, surroundings and contact with relatives.

This study was approved by the Regional Committee on Health Research Ethics in the Capital Region of Denmark (record no. H-A-2007-0078). The study was presented to the Danish Medicines Agency, but approval was not deemed necessary by the Agency. Furthermore, approval from the Danish Data Protection Agency was granted (record no. 2007-41-1002). All patients provided their written informed consent.

Statistics

Data on toxicity was analysed using Fisher's exact test (non-parametric). We assumed that the average summarised side effect in outpatients would be of grade 2. In order to detect a difference between treatments, the true difference between treatments should be 1.25. The sample size was calculated using the Chow & Wang formula [6]. The parameters provided to the formula were: significance level (adjusted for sidedness) = 0.025, stand-

ard deviation within patients' side effects = 2.0, power 0.8 and minimal detectable difference in mean side effects = 1.25. A total of 43 patients will enter this two-treatment crossover study. The probability is 80% that the study will detect a difference at a two-sided 0.05 significance level.

A generalised linear model was used to analyse the collected health scores. The variables included were course of treatment, period and the interaction between course of treatment and period.

A linear mixed model including both fixed and random effects adjusted for gender and age was used to test the patients' preferences.

Trial registration: not relevant.

RESULTS

In total, 51 patients initiated treatment between November 2007 and November 2010. Nine patients were excluded after the first treatment. Three were excluded because the initial computed tomography showed metastatic disease and six due to > grade 2 adverse events (abdominal pain, laryngeal spasm, intestinal thrombosis, diarrhoea, infection and sudden death). A total of 42 patients continued in the study as planned. Age, performance status, tumour stage, civil status and employment status were similar in the two groups (**Table 2**).

Safety and feasibility

A total of 146 cycles were planed and given as home-based treatment. In all cases, the study nurse found it safe and acceptable to administer the treatment in the patient's home. One grade 2 allergic reaction was reported in relation to treatments administered in the patients' homes. Furthermore, one patient experienced an allergic reaction of grade 2 after the nurse had left, and was referred to hospital. In 16 cycles (11%), inserting a peripheral intravenous catheter proved to be difficult, but it was successfully inserted in all cases. Ten (6.9 %) patients had to be seen in the outpatient clinic for toxicity scoring as telephone interviews were inconclusive. In one case, the planned treatment had to be omitted as the patient suffered from palmar-plantar erythrodysaesthesia that was incorrectly scored in the telephone interview. In regimen A, starting with home-based chemotherapy, four patients withdrew from the study before cross-over, one due to non-compliance, one due to relapse, one due to a grade 2 allergic reaction and one due to grade 3 abdominal pain. Among patients receiving regimen B and starting chemotherapy in the outpatient clinic, one patient withdrew due to grade 2 cardiotoxicity. No patients chose to voluntarily withdraw from the study. In 145 (99.3%) of treatments given at home, patients felt secure, with only one answering "Do not know".

TABLE 3

Toxicity for the 42 patients who continued treatment after cycle one. The most severe reported adverse event from each patient was registered, Common Terminology Criteria for Adverse Events version 3.0. The values are number of patients (%).

	Home-based treatment (21 patients, 146 cycles)		Out-patient treatment (21 patients, 158 cycles)	
	toxicity grade 2	toxicity grade 3	toxicity grade 2	toxicity grade 3
Neutropenia	5 (25)	1 (5)	2 (10)	
Neurotoxicity	10 (50)	1 (5)	5 (25)	2 (10)
Diarrhoea	6 (30)	1 (5)	1 (5)	1 (5)
Palmar-plantar erythrodysaesthesia	6 (30)	-	2 (10)	-
Hand-foot-syndrome	4 (20)	-	-	-
Fatigue	2 (10)	-	2 (10)	-
Nausea	2 (10)	-	2 (10)	-
Vomiting	2 (10)	-	-	-
Infection	-	-	1 (5)	-
Obstipation	1 (5)	-	1 (5)	-
Allergic reaction	1 (5)	-	-	-
Abdominal pain	-	1 (5)	-	-
Cardiotoxicity	-	-	1 (5)	-
Pulmonary embolism	-	1 (5)	-	1 (5)

TABLE 4

Patient preferences: the variance explained by the different items. The values are %.

	Baseline		End of treatment	
Significant attribute	group A	group B	group A	group B
Transportation time	39	39	44	63
Waiting time	14	14	3	10
Time with doctor	1	5	-	1
Time with nurse	1	1	2	-
Safety	-	-	-	1
Surroundings: private/hospital	-	-	-	-
Relatives: private/hospital	-	-	-	-

Toxicity

The severest reported adverse event from each patient was registered. The treatment was generally well tolerated with only nine patients (five in home-based and four in out-patient treatment) reporting grade 3 adverse events. There was a trend of more reported grade 2 toxicity in home-based treatment than in outpatient treatment. The most frequent adverse event was neurotoxicity which was managed by reduction or discontinuation of oxaliplatin. Other adverse events observed in more than 10% were neutropenia, diarrhoea, palmar-plantar erythrodysaesthesia and hand-food syndrome (**Table 3**). No significant difference was observed between the regimens (p = 0.34).

Quality of life

In total, 286 of 304 (94%) of the questionnaires given to the patients were completed and returned. QoL scores


Nurse making a telephone interview with a patient.


Patient treated at home.

during home treatment and outpatient treatment did not show significant differences.

Preferences

We found no significant difference between patient preferences in the two groups. The highest-ranking preference of the patients was transportation time, both at the start of treatment and at the end of treatment (**Table 4**).

DISCUSSION

Patients with cancer who require treatment with chemotherapy often experience major changes in lifestyle and overall well-being. Going to hospital can be time-consuming and inconvenient, why alternative ways of administering treatment are interesting and relevant. While some chemotherapy regimens are complex and do require visits to the hospital, others are less complex and may be administered outside the hospital. However, guidelines are lacking in most European countries [7]. Treatment with capecitabine and oxaliplatin is simple and easily administered, and our study also confirms that it is feasible and safe to give these treatments at home. Both nurses and patients felt comfortable when treatments were administered in the patient's home, and no severe reactions or complications were observed. These results are similar to those reported from a Spanish study which found home-based treatment to be a safe alternative to outpatient treatment [8]. Our study used telephone interviews to score treatment toxicity. Approximately 7% of the patients had to be seen in an outpatient clinic for toxicity scoring as telephone interviews were inconclusive, and in one case planned home-based treatment was postponed due to an incorrect score. Other studies have also found telephone-based toxicity scoring to be a feasible option for patients receiving chemotherapy [9, 10]. However, as we observed some cases of erroneous toxicity scoring, we hypothesise that video conferencing, based on Skype or FaceTime, may be a way of improving remote toxicity scoring in future trials.

There was no difference in grade 3 toxicity, but a trend of higher grade 2 toxicity in home-based chemotherapy was observed. The toxicity scoring in home-based chemotherapy was achieved through a telephone interview performed by a nurse, while toxicity scoring in the outpatient clinic was done by a doctor. We believe that this trend towards a higher grade 2 toxicity in home-based chemotherapy was due to more exact toxicity scoring by the nurse at home than by the doctors at the hospital and that it did not reflect a real difference. The absence of any difference in toxicity is in accordance with a review by Bazian Ltd [4]. Further, we found no significant difference in the amount of discontinued treatments due to toxicity between home-based and outpatient treatment, which is in accordance with a previous study [8]. The present study detected no differences in QoL between home-based treatment and treatment in the outpatient clinic, which is in agreement with two previous randomised studies [8, 11]. It should be pointed out that our study has a very small population, which makes it difficult to detect any differences. Our patients considered transportation and waiting time more important, which is in accordance with a Danish [12], and an Australian study [13]. The patients in our study ranked security and time with the doctor/nurse low, which is in line with a study by Lüthi et al [14], but in contrast to a study by Kelly et al [15]. It should be emphasised that the patients in our study could only choose selected combinations and were not allowed to choose freely. Like other investigations of home-based chemotherapy, our study was not designed to detect differences in efficacy.

As the financial resources in healthcare continue to be an issue, the financial aspects of home-based treatment need to be evaluated. Several studies have attempted to address this question; but, the results have been ambiguous. Some studies demonstrate a higher

cost [11], while others found no significant difference [16]. Home-based treatment may be resource intensive, with a lower throughput of patients due to transportation time and lack of ability to parallelise treatment. In our study, the nurse was able to administer three treatments per day, which is less than in the outpatient clinic. A more economically viable treatment option could be to move treatment away from the hospitals and into healthcare centres. This could reduce waiting and transportation time for the patients as these healthcare centres are often closer to patients' homes than the larger centralised hospitals [17]. Alternatively, home-based treatment could be limited to patients were this is warranted by their physical and/or social situation. We expect that our findings will apply to many of the patients receiving commonly administered chemotherapy regimens, although individual factors such as patient performance status, comorbidity and the toxicities of a specific chemotherapy regimen should be taken into account.

This study has demonstrated that home-based chemotherapy with capecitabine and oxaliplatin is feasible and safe. However, the study has some limitations. It is too small to tell if there could be real a difference in the quality of life or toxicity between outpatient and home-based chemotherapy. Furthermore, the study cannot establish any financial aspects.

CONCLUSIONS

Our study demonstrates that home-based chemotherapy is feasible and safe and that it might be a valuable alternative to treatment at an outpatient clinic. Further, patients reported that minimum transportation and waiting time were their most important preferences.

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