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Short report

A randomized crossover trial assessing patient preference for two different types of portable infusion-pump devices

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Summary

Background: A variety of anticancer agents are better tolerated and more effective if given as continuous compared to bolus administration. Portable pump devices are needed to allow outpatient continuous infusion. Different types of portable pumps are available and we tested patient preference in a randomized crossover design.

Patients and methods: Patients on continuous infusion fluorouracil were randomly assigned to start treatment with an elastomeric infusor (Baxter) or a mechanical, electronically controlled pump (CADD-1®, Pharmacia) and crossed over to the alternative model after three weeks. After exposure to both pump types patients were asked to indicate their preferred device.

Results: After 10 patients the study was closed because all study participants preferred the elastomeric pump ($P < 0.01$). Reasons were pump weight (100%), smaller pump size (89%), interference with daily activities (89%), user friendliness (56%), impact on sleep (44%), and lack of technical problems (22%). Although the mechanical pump required more handling time for the first two refillings, the learning curve suggested about equal time requirement thereafter.

Conclusion: In the interest of patient comfort, the disposable elastomeric infusor is an acceptable alternative to the more accurate electronically controlled pumps especially for drugs with a short half-life and a favorable toxicity profile.

Key words: continuous infusion, elastomeric, fluorouracil, mechanical, patient preference, portable pump

Introduction

Theoretical considerations suggest a benefit of continuous infusion over bolus administration or short infusion for various chemotherapeutic agents. Most of these drugs are preferentially effective in specific phases of the cell cycle. However, cancer cells of the most prevalent solid tumors typically have a doubling time of days to weeks and cell division is not synchronous [1, 2]. On this background, it is obvious that active drug levels and sensitive cell cycle phase rarely coincide, if anticancer agents are given as bolus or short infusion. However, the chance of coincidence can be increased by extending the infusion duration. Prolonging the duration of drug administration may also mitigate the toxicities commonly associated with high drug peak levels.

An absolute requirement for the practicability of prolonged drug administration are portable pump systems to avoid hospitalization and to treat patients in an outpatient setting. Different types of portable pump systems are available and it is not known, which pump characteristics are crucial for patient acceptance. Thus, we designed a randomized crossover trial to assess the patient preference for two fundamentally differing pump types, which are frequently used in clinical practice. We examined the CADD-1® device (Pharmacia, Uppsala, Sweden), which is an electronically controlled mechanical pump, and the disposable non-mechanical elastomeric Baxter infusor (Baxter, Volketswil, Switzerland).

Patients and methods

Consecutive outpatients on continuous infusion (200–300 mg/m^2) fluorouracil were randomized to start treatment either using the CADD-1 or the Baxter infusor device. After three weeks of continuous treatment, the alternative pump device was used for another three weeks. At the end of this study period, patients were asked to fill out a patient questionnaire evaluating preference for one of the two devices. The nurse in charge of refilling the pump had to complete a weekly report on pump handling and pump accuracy (nurse questionnaire).

Pump specifications

Electronically controlled portable pump (CADD-1®)
Size 160 × 89 × 28 mm; weight 425 g without drug. The flow rate of the pump was kept constant at 0.5 ml per hour. Cassettes were filled with fluorouracil (50 mg/ml) and 0.9 % saline to a total volume of 96 ml to allow weekly intervals for changing cassettes.

Disposable nonmechanical elastomeric pump (Baxter infusor)
Size 270 × 40 × 40 mm; weight 40 g without drug. The pump provides a constant drug flow of 0.5 ml per hour over seven days. Pumps were filled with fluorouracil (50 mg/ml) and 0.9% saline to a total volume of 84 ml and were changed weekly.

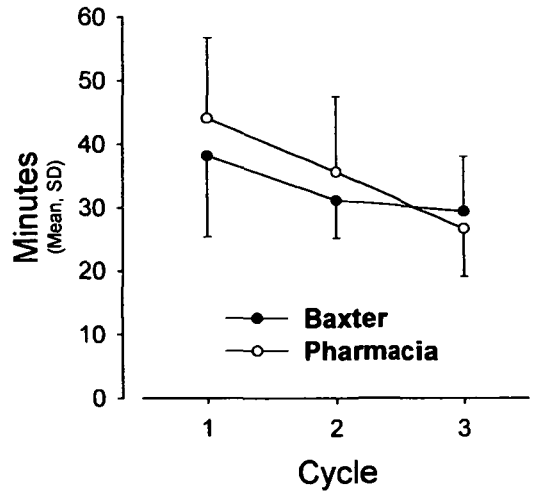

Figure 1 Pump handling time.

Questionnaires

Patient questionnaire
At the end of the study period, patients had to indicate their preference for one of the two pump types and the reasons for the choice.

Nurse questionnaire
After each weekly cassette or infusor change parameters of pump handling were evaluated and premature stop of the infusion and other complications during the previous treatment period were assessed.

Statistical analyses

Sample size calculations
Based on the *a priori* hypothesis of equal preference for both pumps and setting the clinical relevance for a difference in preference at 40% (i.e., 90% of patients prefer one pump model), it was calculated that a sample size of 20 patients was required to detect this difference with a power of 80% [3]. An interim analysis was planned after 10 evaluable patients. Exact confidence intervals for proportions were calculated according to Miettinen [4]. The time spent by the nurses on preparing the infusion pumps was analyzed by repeated measures analysis of variance using the software package Statview 4.5 for Windows.

Results

Four female and six male patients with a median age of 61 years (range 46–81) entered this study. Patients were treated for pancreatic (five), breast (two), rectum, stomach, and neuroendocrine cancer of unknown primary (one each). No patient had previous experience with portable pumps. Two additional patients starting with the Pharmacia and one patient starting with the Baxter pump went off treatment before crossover was possible because of disease deterioration. All study subjects had a good performance status at treatment start without limitations for the use of a portable pump. The study was closed after the first ten patients were crossed over, since there was a statistically highly significant preference for the disposable nonmechanical infusor ($P < 0.01$). The reasons for this preference were lower pump weight in 100%, smaller pump size in 89%, less interference with daily activities in 89%, user friendliness in 56%, less impact on sleep in 44%, and lack of technical problems in 22% of the study participants.

Due to its elastomeric mechanism without electronic control or external source of energy, the disposable perfusor was less accurate than the electronically controlled CADD-1® pump. Two patients experienced stop of infusion eight and twelve hours earlier than planned due to premature emptying of the elastic reservoir.

The time spent by the nurses to handle the pump decreased significantly from the first to the third treatment cycle ($P < 0.001$; Figure 1). This learning effect appeared to be more pronounced for the technically more demanding mechanical pump. However, this difference levelled out after two treatment cycles. This could be partially due to the more cumbersome filling process typical for the elastomeric pump [5], which cannot be optimized beyond a certain degree. The time spent per treatment cycle and the handling time was not significantly different between both pump types.

Discussion

This study unequivocally shows, that cancer patients prefer the disposable elastomeric infusor device over an electronically controlled mechanical pump for the continuous infusion of fluorouracil. This choice was mainly affected by the factors size and weight, which have a strong impact on the visibility of the pump and patient convenience. The importance of these 'comfort' factors is underlined by the fact, that even the two patients, who had to contact the hospital during the night because of premature emptying of the elastic reservoir, still preferred this device over the mechanical pump. Thus, even this clear evidence for inaccuracy of the flow rate had no negative impact on patient preference.

Looking at pharmacokinetic parameters, Vokes et al. did not detect a significant difference in the mean steady state plasma fluorouracil levels achieved with elastomeric compared to mechanical pumps [6]. Others have shown that the effective flow rate of disposable pumps deviates considerably from the intended flow rate. The pumps typically infuse at a higher than expected rate at the beginning of the infusion and after the first three to six hours a steady decline of the flow rate can be observed [5]. These pump characteristics can be potentially dangerous for drugs with a narrow therapeutic window and a long elimination half-life. However, in the case of drugs with a short half-life such as fluorouracil, the impact of intermittent flow changes on the steady state concentration is short-lived and does not lead to drug accumulation. This suggests, that the pharmacodynamic effect of continuous infusion fluorouracil should not be affected by transient flow irregularities.

The question of the optimal portable pump device might lose relevance in view of the increasing availability of oral fluorouracil prodrugs such as UFT or capecitabine [7, 8]. The hope is, that oral forms of fluorouracil will be able to replace continuous infusion fluorouracil.

However, the available clinical data suggest that continuous infusion fluorouracil and oral prodrugs exhibit differing toxicity profiles [7, 8]. Since it is well known for fluorouracil, that the schedule of administration has a strong pharmacodynamic impact on toxicity and efficacy [9], it will have to be shown in randomized trials, whether all continuous administration modi are interchangeable. It is possible, that the availability of oral fluorouracil prodrugs adds a new dimension to the pharmacodynamics of fluorouracil rather than replacing continuous infusion.

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