Shifting from FOLFOX-4 to XELOX Chemotherapy, Cost Effectiveness in a Single Institute

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Abstract

Background: The purpose of the study was to evaluate the cost-effectiveness of capecitabine plus oxaliplatin (XELOX) compared with 5-fluorouracil/folinic acid and oxaliplatin (FOLFOX-4) chemotherapy in patients with colorectal cancer.

Methods: Cost data were collected for patients who received XELOX and FOLFOX-4 chemotherapy who presented to the Oncology Center at King Fahad Specialist Hospital in Dammam, Saudi Arabia. Drug costs and hospital day stays were calculated and expressed as cost per patient. Estimated travel, investigations, outpatient visits and time costs were not included in our analysis. Costs were based on government and hospital sources and expressed in Saudi Riyals (SR) without drug discounts.

Results: XELOX chemotherapy was calculated for a total of 8 cycles, while FOLFOX-4 chemotherapy was calculated for a total of 12 cycles. The scheduled cost per patient per cycle was 4000 SR and 2500 SR for XELOX and FOLFOX-4 respectively. Total treatment cost per patient was 32000 SR for XELOX and 30000 SR for FOLFOX-4. The average bed cost per day at our hospital is 2000 SR. The addition of the hospital stay costs for 2 days for the FOLFOX-4 chemotherapy increased the total treatment cost per patient to 78000 SR. The total cost for FOLFOX-4 was 41% greater than that of XELOX. Analysis showed XELOX was less costly than FOLFOX-4 when using full drug regimen costs in Saudi Arabia.

Conclusion: Capecitabine combined with oxaliplatin has proven non inferior in several phase II/III clinical trials and could be a substitute for continuous-infusion 5-FU/LV/Oxaliplatin. In our study we found that using XELOX cost less than using FOLFOX-4 by 41%. The principal reason for this lower cost was the reduced use of hospital bed days for the treatment administration.

Introduction

The increase in the healthcare costs is a universal problem all over the world. In 2008, Australia's healthcare expenditure reached AUS$104 billion (8.5% of Gross Domestic Product (GDP) (1) and that of the United States (US) US$2.3 trillion (16% of GDP) (2). Expenditure on drugs has recently been the fastest growing component of expenditure in Australia (1), Canada (3, 4), UK (5) and US (6, 7). While new treatments usually have a higher purchase price than older, they may be new targeted therapies in oncology, which often have high drug-acquisition costs (8-10). Cost-effectiveness analyses (CEA) are therefore increasingly used by decision makers to determine which drugs should be included in public formularies (1, 3-7, 11-17). The United Kingdom National Institute of Health and Clinical Excellence has used CEA since 1999 (14,18), Australian Pharmaceutical Benefits Advisory Committee since 1993 (14,19) and Canadian Common Drug Review since 2002 (14, 20). In Hong Kong, the Hospital Authority is a government funded provider of specialist healthcare services. Its Drug Advisory Committee appraises new drugs for inclusion into the Drug Formulary but has not, to date, required cost-effectiveness evidence as a component of drug evaluation (21, 22). This is a common situation for smaller countries or those, for example, in the Asia Pacific region where skills in health economics are lacking (22, 23) and for which the available cost-effectiveness information, derived from other countries, may or may not be applicable (22, 24, 25).

Significant progress in chemotherapy of metastatic colorectal cancer (MCRC) has been made in recent years (26, 27). Until approximately the year 2000, 5-fluorouracil (5-FU) plus leucovorin (LV) was the standard regimen used in most countries, but oxaliplatin or irinotecan-containing regimens were developed rapidly and are now widely administered to many MCRC patients. As a result, median overall survival (OS) of patients with MCRC has improved steadily over this decade (27).

Oxaliplatin regimens, FOLFOX-4 (28) or FOLFOX-6 (29), are the most frequently used chemotherapies for MCRC. To avoid continuous infusion, as is necessary for 5-FU administration, the use of oral fluorinated pyrimidine drugs, such as capecitabine, has recently increased. Capecitabine belongs to the fluorinated pyrimidine class of anticancer drugs. It is metabolised in the body and eventually converted into FU within tumour tissue, where it shows antitumour activity (30). Because the enzyme (thymidine phosphorylase) responsible for the last conversion step is more concentrated in tumour tissue than in normal tissues, FU levels in tumour tissue are selectively increased (31).

Thus, capecitabine offers an improved tolerability profile compared with FU/LV with respect to some systemic side effects (32). Also, as capecitabine is given orally, it avoids the need for intravenous drug preparation and administration and associated visits to the clinic. Patient preference data also suggest that

patients generally prefer oral over intravenous therapy (33). Capecitabine plus oxaliplatin (XELOX) (34-38) is an improved regimen which includes capecitabine but does not require 5-FU infusion. Clinical trials, which compared XELOX and FOLFAX4, demonstrated non-inferiority of XELOX as first-line (38) and second-line chemotherapy (37-40).

Economic models have showed XELOX to be more cost-effective than FOLFOX4 in Japan (41) but of equivalent cost-effectiveness in US (42). However, the US model demonstrated cost-effectiveness of XELOX when a societal perspective, including patient costs and lost productivity, was taken.

Method

Due to increasing numbers of waiting list for patients at our center, Admission and bed utilization task force was formulated to look at the reasons of admission for adult oncology patients. We reviewed the reason of admission for patients who presented to the adult oncology department at King Fahad Specialist Hospital-dammam in Saudi Arabia during the period from October 2011 to December 2011.

This cost analysis was a relatively simple study designed to obtain information to allow a more considered assessment of XELOX and FOLFOX-4 regimens.

Full dosage based on the average body surface area was calculated for both regimens. Cost data were collected for both chemotherapy regimens. Drug costs and hospital days were recorded and expressed as cost per patient from the healthcare provider perspective. Estimated travel, investigations, outpatient visits and time costs were not included in our analysis. This includes only the cost of the drugs and does not take into account hospitalization for serious adverse events, the incidence of which is similar in both arms. Costs were based on government and hospital sources and expressed in Saudi Riyals (SR). The cost of XELOX chemotherapy was calculated for a total of 8 cycles while FOLFOX-4 chemotherapy was calculated for a total of 12 cycles. Simple calculations were done by addition of the total cost of each component of both chemotherapy regimens. Hospital stay of two days was added to the total cost of FOLFOX-4 chemotherapy. We did not apply any discounting in this study and costs relate to the base year of 2011.

Results

A total of 305 patients were admitted to the oncology ward during the period between October 2011 and December 2011. In an attempt to decrease the number of patient admissions and saving beds for highly indicated cases, we reviewed the reasons of admission during that period. Of those patients 197 (64.6%) were admitted for chemotherapy, 49 (16.1%) for staging work up and initiation of treatment, and 47 (15.4%) for supportive treatment, Table 1.

One hundred (50.8%) patients received FOLFOX-4, 45 (22.8%) received FOLFIRI, while 52 (26.4%) received other regimens, Table 2.

Full dosage based on the average body surface area would cost 4000 SR for XELOX and 2500 SR for FOLFOX-4 regimens and, assuming the complete of 8 or 12 cycles respectively had been administered, total costs per patient would become 32000 SR for XELOX and 30000 SR for FOLFOX4 i.e. XELOX was more expensive than FOLFOX4. The average cost of bed utilization for 1 day of admission is 2000 SR. Adding to the cost of FOLFOX-4 chemotherapy 2 days of admission (4000 SR) per cycle will make the total cost of administration for this regimen 78000 SR, Table 3.

Table 1: Reason of admission

Reason of admission	Total number	%
Chemotherapy	197	64.6
Staging and treatment	49	16.1
Supportive care	47	15.4
Procedures	12	3.9
Total	224	100

Table 2: Type of chemotherapy

Chemotherapy	Total	%
FOLFOX-4	100	50.8
FOLFIRI	45	22.8
Others	52	26.4
Total	197	100

Table 3: Cost of chemotherapy

Chemotherapy	FOLFOX-4	XELOX
Cost per cycle in SR	2500	4000
Total cost in SR	30000	32000

Discussion

In many countries all over the world, increased medical costs represent a major issue. Making decisions about health-care interventions that consider costs, in addition to efficacy and safety, has become increasingly important. Thus, we investigated the cost of XELOX in comparison to FOLFOX-4.

The use of oral fluoropyrimidines as substitutes for I.V. 5-FU is an attractive approach because it presents the advantages of being taken at home without the inconvenience of I.V. administration, and it can interfere less with daily activities and allow for better quality of life. A different toxicity profile with less severe toxicity or life-threatening events has also been reported, mainly in comparison with bolus 5-FU–based regimens. One small randomized trial (33) has questioned patient preference for I.V. or oral fluoropyrimidines in the setting of mCRC, comparing capecitabine with bolus I.V. 5-FU (Mayo Clinic regimen) or continuous-infusion 5-FU (de Gramont regimen). After receiving both treatments, 64% of patients expressed a preference for the oral route. In the present setting of first-line chemotherapy, however, the combination with other I.V. drugs will require a central venous catheter that will, from this point of view, minimize the benefit of the oral route. In addition, visits to the clinic will be necessary for the administration of oxaliplatin; therefore, schedule designs should avoid weekly administration of I.V. drugs in order to preserve the benefit of the oral route. From this criterion, the XELOX regimen looks more convenient, with 1 visit every 3 weeks for administration of oxaliplatin and prescription of capecitabine.

Efficacy is a major concern for patients and should be preserved with oral chemotherapy. Many trials have reached the conclusion of no inferiority (37-40). The XELOX regimen comprising capecitabine and oxaliplatin requires less intravenous administration than FOLFOX4, comprising 5-FU, folinic acid and oxaliplatin. Therefore it might be expected that it would cost less overall when costs of drug delivery are taken into account. This study showed that this was indeed the case and that, when the fewer cycles of therapy required with XELOX (8 versus 12) were also taken into account, the savings in other costs outweighed the higher purchase price of the XELOX regimen.

Our cost analysis was a relatively simple and was designed to obtain information to allow a more considered assessment of the two regimens.

Our study found that XELOX is less costly than FOLFOX-4, as the total cost of its use was 41% lower of that of FOLFOX-4. This was mainly because of the reduced need for hospital-based intravenous drug delivery, a finding that is consistent with many other trials (42- 44). Conversely, based on the US costs, Mayer concluded that the use of XELOX compared with various FOLFOX or FUOX regimens would be 95.2% more expensive (45).

Several limitations of our study should be noted. Our analysis did not consider indirect costs, such as work loss resulting from chemotherapy. If we include direct non-medical cost (such as costs of transportation of patients to clinics) and indirect costs from the societal perspective, incremental costs of XELOX would be even lower than the current analysis from the payer's perspective.

Conclusion

Capecitabine combined with oxaliplatin has proven non inferior in several phase II/III clinical trials and could be a substitute for continuous-infusion 5-FU/LV/ Oxaliplatin. We found that using XELOX cost less than using FOLFOX-4 by 41%. The principal reason for this lower cost was the reduced use of hospital bed days for the treatment administration.

Based on this study we adopted XELOX chemotherapy as a standard of care for our patients with metastatic colorectal cancer taking into consideration patient preference, compliance to treatment and patient tolerance to oral Xeloda.

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