Capecitabine is an oral pro-drug of 5-fluorouracil (5-FU) used in the treatment of breast and colorectal cancer. Hand-foot syndrome (HFS) or palmar-plantar erythrodysesthesia (PPE) is one of the most common adverse events associated with capecitabine, which is rarely serious and never life-threatening. The mechanism is suggested to be due to drug accumulation in skin. This study was conducted to determine the frequency of hand foot syndrome (HFS) associated with capecitabine as a single agent and in combination with oxaliplatin in local population to guide local physician in selecting the starting dose of capecitabine.

This was a cross-sectional retrospective study conducted at Advanced Medical and Dental Institute (AMDI), Penang, Malaysia. Data of 43 consecutive patients, with diagnosed colorectal carcinoma planned for capecitabine based chemotherapy, was collected from patient records between June till December 2008. Patients on palliative care were excluded. SPSS was used for the application of chi-square test, by keeping the level of significance as p < 0.05. Fifteen (34.9%) patients developed HFS, 10 in the single-agent and 5 in the combination group. No significant association of HFS with either regimens was noted (p=0.876).

Capecitabine dose of 1.25 gm/m² was used as single agent twice daily, two weekly with one week rest for total 8 cycles in adjuvant setting. A total of 28 patients studied. Combination regimen (XELOX) consisted of oxaliplatin130 mg/m² on day one (D1) and capecitabine with dose of 1 gm/m² twice daily for 2 weeks and cycle repeated every 3 weeks till disease progression. A total of 15 patients belonged to this group. Patients had been followed for any side effect of HFS on these two regimens and grade of HFS was noted (grade 1-3). Dose adjustments were made for patients developing grade 2-3 HFS.

Data analyzed with SPSS for frequency of HFS and for any association of HFS with any particular regimen. Chi-square test was used for assessment of any association and p < 0.5 set for any significance.

Adult patients aged between 35-70 years were treated in this study. The results showed an overall high frequency of HFS (34.9%) in both treated groups combined, but no significant association with any regimen (p=.876) was seen with chi-square analysis (Table I). A higher percentage of patients (35.7%) developed HFS in single agent chemotherapy group, but it was not statistically significant.

Scheithauer et al. reported around 15-20% frequency of hand foot syndrome. This study had higher overall frequency of 34.9% combined all grades of HFS. In this study combination of capecitabine with oxaliplatin had slightly less frequency (33.3%) of HFS compared to single agent capecitabine most likely due to comparatively low dose of capecitabine in combination regimen. However, small sample size could be a reason for statistical non-significance.

Most of the patients required dose modification; however, a high frequency of HFS in this study with standard doses of capecitabine as a single agent and in combination warrants a review of stating dose of capecitabine in the studied population with a larger sample size. Dose interruption strategy with restarting capecitabine with a lower dose was adopted at our centre and led to the completion of treatment in all the cases.

The important question being raised now is whether the starting dose of capecitabine is correct or not. Since most patients who develop hand foot syndrome ultimately
go on compromise dose. Dose interruption/reduction does not affect the overall anti-tumour efficacy of capecitabine so starting with a safer dose may be a reasonable option.5

Usually the manifestations of HFS are classified into 3 grades according to their severity in terms of skin damage.6 Grade 1, HFS is described as erythema of the lateral aspects of the fingers that progress to the thenar and hypothenar eminences with swelling, numbness, dysesthesia/paresthesia and tingling, especially over the pads of the distal phalanges. The same manifestations occur on the soles, but less frequently on the dorsal aspects of the hands and feet. Grade 2 to grade 3 is the superimposition of blistering, moist desquamation and ulceration, coupled with severe pain,6 most patients and physicians will stop drug at this point.

In this study grade 2 to grade 3 changes required dose adjustment in recurrent cases and all patients successfully completed treatment with certain delays in treatment schedules. None of the patients proceeded to grade 3 changes as dose adjustments or drug interruption strategy was adapted in time.

More studies from various regions are needed for recommendation of starting dose of capecitabine for local population. At our centre, the starting dose of capecitabine in adjuvant treatment for colorectal cancer is moving from 1.25 gm/m² twice daily to 1 gm/m² twice daily for most patients, especially elderly population as over experience with the drug has shown higher frequency of HFS.

**REFERENCES**


