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Research Article

TREATMENT RESULTS WITH LONG ACTING OCTREOTIDE IN INOPERABLE HEPATOCELLULAR CARCINOMA: REVIEW OF LITERATURE AND LOCAL EXPERIENCE

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Abstract:

Aim: To determine the efficacy of long-acting octreotide (LAR) in the treatment of inoperable to hepatocellular carcinoma; and also assess improvement in quality of life.

Methods: This study was conducted in the Gastroenterology Unit of Allied hospital Faisalabad for six-months duration from December 2019 to May 2020. Patients were recruited after obtaining informed consent. There were 22 patients who decided to take the drug, while 20 patients refused because of socio-economic problems. They served as controls. Patients who agreed to the treatment were administered octreotide 100 mcg subcutaneously three times a day for two weeks. Thereafter, 20 mg of octreotide was administered intramuscularly monthly. Patients were followed for 6 months. Tumor size, alpha-fetoprotein levels and improvement in quality of life (QOL) were monitored during treatment.

Results: 19 patients completed the treatment out of 22 patients, they were all men. The average age at the time of the presentation was 55 years. Tumor size regression was observed in 10 of 22 patients (45.5%). Mean alpha-fetoprotein levels decreased in 11 of 22 (50%) patients. An improvement in the quality of life was observed in 10 out of 22 (45.5%) patients after treatment with long-acting octreotide. In the treatment arm, 14 of 22 (64%) patients were alive at the end of six months compared with 10 of 20 (50%) in the control group.

Conclusion: LAR causes regression of tumor size, lowers AFP levels, and improves quality of life in patients with inoperable hepatocellular carcinoma.

Key Words: Long Acting Octreotide, Inoperable Hepatocellular Carcinoma, Treatment Outcomes.

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INTRODUCTION:

Hepatocellular carcinoma (HCC) is widespread in various geographic regions. Although the prevalence is high in Asia and Africa, the incidence in Western societies is very low¹⁻². The prevalence in Pakistan is 8/100,000 per year, and viral hepatitis has been shown to account for the majority of cases of C HCC. Non-surgical treatment of HCC is not satisfactory and various therapeutic regimens have been tested³⁻⁴. Treatment of inoperable HCC remains unsatisfactory and different therapeutic regimes have been tested. Recently trials with tamoxifen, flutamide and chemoembolisation with lipiodol have been reported. Somatostatin receptors have been detected in various adenocarcinomas, including breast, kidney, colon and ovary⁵⁻⁶. Kouroumalis and colleagues have reported significant reductions in tumor size and AFP levels for the first time, which have long been used effectively long acting octreotide (LAR)⁷⁻⁸. Since HCC patients in Pakistan are very advanced, it is important to determine the optimal treatment strategy for our HCC patients⁹⁻¹⁰. In this context, we decided to determine the effectiveness and long effective security profile of octreotide in the advanced stage of HCC.

PATIENTS AND METHODS:

This observational study was conducted at the Gastroenterology Unit of Allied hospital Faisalabad for six-months duration from December 2019 to May 2020. The study was conducted after approval by the corporate audit committee and the hospital's ethics committee. We recorded 42 patients in the study. In all patients, a detailed history and a physical examination were detected by a consultant gastroenterologist. The diagnosis was made with ultrasound accompanied by a biopsy (USA) or computed tomography (CT) and alpha-fetoprotein (AFP). After diagnosis, the prognosis of the disease was also explained to the sick and family members. We organize patients using the oxuda staging system, which takes into account the size of the tumor, the presence of acid, bilirubin and the average level of albumin. Since we are interested in advanced patients with hepatocellular carcinoma, we only cover patients with stage III Okuda. The prognosis was announced after the diagnosis and

staging of the disease. These patients were referred to a consultant surgeon for possible injury resection. Only if surgical resection is not possible or if the patient is not considered to have any possible benefits, other treatment options have been discussed with the patient. 22 out of 42 patients refused treatment due to financial problems. Therefore, we divide patients into two groups; While the 22 patients who were treated served as patients, 20 patients who could not meet the treatment served as control. The Octreotide administration was just a mitigating measure. After obtaining informed consent, treatment was initiated. The top 100 ocg oxidized were submerged three times a day for two weeks. Then 20 mg of LAR was applied intramuscularly every month for 6 months. To assess the improvement in QOL measurements, 1-5 likert values were assigned to four variables, including pain control, appetite, energy levels and general well-being. Symptoms are evaluated "excellent" (total resolution), "good" (significant improvement), "fair" (minor recovery), "bad" (unchanged), and "very bad" (worst result). Tumor-sized regression was evaluated every 2 months using repeated ultrasound, while alpha-fetoprotein levels reduced by AFP every 3 months were documented. We use a paired T-test to compare the effectiveness of treatment in this subgroup.

RESULTS:

The average age of the examined group was 52.5 years (45-60 years). All patients were male, and 15 (68%) of the treated patients had hepatitis C as the cause of HCC, 5 (23%) of hepatitis B, and in 2 (9%) of the patients the cause of HCC was unknown. Treatment was discontinued in three because of adverse events. Nineteen patients continued treatment for six months. As our study was based on multifocal tumors, we measured the size of the lesion with the largest size; marked as an indicator tumor. Among the patients undergoing treatment, the average tumor size at the initial presentation was 5.0 + 1.0 cm, while the average AFP levels at the time of the first presentation were 15000 + 1000 IU / L. However, the tumor size index and AFP levels in patients serving as the group.

Table 1. Tumor size and AFP levels before and after treatment with LAR in HCC (n=22).

	Before treatment	After treatment (mean score)	p-value
Tumor size (cms)	5.00 ± 1.00	3.0 ± 1.00	0.05
AFP levels (IU/L)	15000 ± 1000	8000 ± 1000	0.04

The controls were 4.5 + 1.5 and 14500 + 750 IU / L, respectively. A decrease in tumor size greater than 25% was observed in 10 of 22 (45.5%) treated patients. At the end of treatment, the average tumor size in these patients was 3.5 cm. AFP levels were reduced in 11 of 22 (50%) treated patients. AFP levels decreased in 11 of

22 (50%) treated patients. In this subgroup, mean AFP levels at the end of treatment were 8,000 IU / L. (Table 1) QOL rates for pain control, appetite, energy level and general well-being improved in 10 out of 22 (45.5%) patients with a mean score of 2 to mean score 4 (Table 2).

Table 2. Likert Scale for assessing quality of life pre-treatment and post -treatment (n=22).

Before treatment (mean score)	After treatment (mean score)	p-value	
Pain control	2	4	0.004
Appetite	2	4	0.003
Energy level	2	4	0.003
Overall wellbeing	2	4	0.001

Of the 22 patients, 14 (64%) were alive at the end of the 6-month follow-up period, while 10 of the 20 (50%) control patients had died at the end of the 6-month follow-up period. No serious side effects were observed in any of the patients who continued treatment. However, two patients developed diarrhea and discontinued treatment.

DISCUSSION:

The most common HCC etiology in the patient population was hepatitis C. This has been confirmed by other studies in Pakistan. In our observation, long-acting octreotide led to a decrease in tumor size and a decrease in THE AFP level 3-6 months after treatment in patients with hepatocellular carcinoma, which cannot be supported. Since there is currently no long-term follow-up to the harassment of these patients, it is not possible to determine the effectiveness of the regime in terms of average survival growth¹¹. However, when the median survival of patients with advanced disease between 2-4 months is reported in untreated patients, it is important to note that 64% of patients live at the end of 6 months of treatment. Improving quality of life, considered an important variable evaluated in the study population. The Likert scale was used to assess the quality of life of patients undergoing treatment¹². About 45% of patients showed an improvement in the quality of life index. There are conflicting reports about the effectiveness of long-acting octreotide in the hepatocellular mulch. In a cohort of 63 patients in Germany, partial tumor remission was achieved in only two patients (3.17%)¹⁴. However, after three months of treatment, these patients have a median survival without any difference. Similarly, researchers in Hong Kong found no difference in cumulative life, tumor-sized regression, decreased AFP and quality of life among groups treated in LAR and untreated groups. On the contrary, Greek scientists showed a significant difference in average survival time and a significant improvement in quality of life. However, there was no decrease in AFP levels or a decrease in tumor weight. Studies in Pakistan have shown a significant decrease in the level of AFP high oxidized doses and results in improved quality of life of treated patients¹⁵. While we don't have enough evidence if LAR increases the long-term

survival of HCC patients, a significant improvement in quality of life is an important variable to consider. This certainly means means of palliative care in patients with terminal illnesses.

Limitations

Some of the significant limitations of the study include a non-random experiment. In addition, the lack of long-term follow-up at this stage and the basis of this study to one center are other factors to consider.

CONCLUSION:

Long-acting octreotide improves the quality of life of patients and tumor regression. However, multi-centered, controlled and randomized trials are required with proper follow-up to adopt or refute this idea.

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