

## **Benefits of Percutaneous Ethanol Injection in the Palliative Treatment of Advanced Hepatocellular Carcinoma.**

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**Abstract:** Hepatocellular carcinoma (HCC) is a devastating disease in which survival is measured in months rather than years from the time of diagnosis. The aggressive nature of the tumour and the usual background chronic liver disease make the management difficult warranting multidisciplinary cooperation. Percutaneous ethanol injection (PEI) was introduced ten years ago as palliative therapy for patients with inoperable hepatocellular carcinoma. **Objective:** This study was aimed at evaluating the benefits of percutaneous ethanol injection in the management of advanced hepatocellular carcinoma. **Patients and methods:** Consecutive patients who had percutaneous ethanol injection for hepatocellular carcinoma at Adoose specialist hospital from August 2008 to July 2012 were prospectively analysed and formed the basis of this study. **Results:** A total of 32 patients had (PEI) during the study period out of an initial 82 that presented with HCC. The mean age of the study population was 40.4+/- 14.2yrs with age range of 18 to 60yrs. There were 28(87.5%) males and 4(12.5%) females giving a male: female ratio of 7:1. Right hypochondrial pain and mass were the main symptoms seen in 28(87.5%). Pre intervention pain score ranges from 6-8 while post intervention pain score a week after treatment dropped to 1 or 2. The longest survivor at follow up with this treatment is 14months with mean survival duration of 8months. **Conclusion:** Percutaneous ethanol injection significantly reduces the pain of advanced hepatocellular carcinoma and prolongs survival.

**Keywords:** Hepatocellular carcinoma, Percutaneous Ethanol injection, Palliation, Benefit

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### **I. Introduction**

Hepatocellular carcinoma (HCC) is a devastating disease in which survival is measured in months rather than years from the time of diagnosis.(1) The aggressive nature of the tumour and the usual background chronic liver disease make the management difficult warranting multidisciplinary cooperation. There are many treatment options in hepatocellular carcinoma with none of these proven to be superior to the other. The stage of the disease helps in selecting the ideal treatment option for a particular patient with HCC.(2) The incidence of Hepatocellular carcinoma is highest in Asia and Africa, where the high prevalence of hepatitis B and hepatitis C strongly predisposes to the development of chronic liver disease and Hepatocellular carcinoma.(3-4) While HCC is now being diagnosed early in developed countries as a result of routine follow up with screening procedures which allows early interventions geared towards cure, this is still grossly inadequate in developing countries especially Africa.(5-6) In these patients, local ablative therapies, including radiofrequency ablation, chemoembolization, and potentially novel chemotherapeutic agents, may extend life and provide palliation.(7) Ethanol injection though no longer popular is a good option for us in our centre. It is available, cheap and easily administered under ultrasound guidance.(8) Percutaneous ethanol injection(PEI) treatment, introduced ten years ago as palliative therapy for patients with inoperable hepatocellular carcinoma, can now be used with a curative intent to treat small tumours with results comparable to surgical resection.(9) Made possible by sophisticated radiological techniques, percutaneous ethanol injection became the treatment of choice for patients with poor liver function in whom resection is not possible and local control of the disease is desirable for palliation.(10) For patients with large tumours, or in case of recurrence after previous surgical treatment, a therapeutic approach combining transarterial lipiodol chemoembolization and percutaneous ethanol injection has shown promising results. The number of patients seen at our clinic has increased in the last three years. It is worrisome to note that majority of the patients present late and are suitable only for palliative care aimed at extending as well as improving quality of life in these patients. This study was aimed at evaluating the benefits of percutaneous ethanol injection in the management of advanced hepatocellular carcinoma.

### **II. Patients and methods**

Consecutive patients who had percutaneous ethanol injection for hepatocellular carcinoma at Adoose specialist hospital from August 2008 to July 2012 were prospectively analysed and formed the basis of this study. Excluded from this study were patients with jaundice, flapping tremors and those in coma. Procedures were carried out under ultrasound guidance. The ultrasound was used to localize the tumours and ensure correct needle placement into the tumours before injection. 10-50mls of absolute alcohol manufactured by Riedel-de

Haen in Germany was injected percutaneously into the liver tumour(s). The quantity of absolute alcohol injected never exceeded 50mls to prevent intoxication. Injections were repeated fortnightly targeting different parts of the tumour each time in order to achieve symptom control. The site of maximal tenderness was chosen for injection since it represents the point of rapid tumour growth. Information obtained was of the age and sex of the patients, main symptoms and signs at presentation, predisposition to HCC, tumour location and number, stage of the disease, associated paraneoplastic syndromes, Pre and Post-intervention pain scores and survival duration. Data obtained was entered into a proforma and analysed for simple means and percentages using Epi-info version 5.3.2

### III. Results

A total of 32 patients had (PEI) during the study period out of an initial 82 that presented with HCC. The mean age of the study population was 40.4+/- 14.2yrs with age range of 18 to 60yrs. There were 28(87.5%) males and 4(12.5%) females giving a male: female ratio of 7:1. Right hypochondrial pain and mass were the main symptoms seen in 28(87.5%) patients while 4 (12.5%) had only a mass. The main signs at presentation were tender liver mass in 24(75%) patients, ascites in 2(6.2%) and anaemia in another 2(6.2%). Twenty four (75%) patients had hepatitis B related HCC, 7 (21.9%) had hepatitis C associated HCC while one (3.1%) patient had cryptogenic HCC. Using ultrasound scan, tumours were seen in the right lobe in 20(62.5%) patients, left lobe in 10( 31.3% ) while 2(6.2% )had centrally located tumours. Multiple tumours were seen in 22 (68.8%) patients and solitary in 10(31.3%). Mean tumour size was 8.7cm with a range of 7.5 to 21cm. 24 (75%)patients had Okuda stage 2 tumours while 8(25%) had stage 3. Sixteen patients (50%) had no paraneoplastic manifestations while 8(25%) had polycythaemia and 4(12.5%) had hypoglycemia while another 4(12%) had skin pigmentation. Pre intervention pain score ranges from 6-8 while post intervention pain score a week after treatment dropped to 1 or 2 (see Table1).

No. of Patients	Pre-intervention Pain Score	Post-intervention Pain Score
20	8	2
2	8	2
7	7	2
3	6	1
32		

Table 1 shows the Pain Scores before PEI and one week after PEI

Supplemental systemic analgesia was required in 2( 6.2%) patients post intervention. Longest survivor at follow up with this treatment is 14months with mean survival duration of 8months.

### IV. Discussion

The main finding of this study was the significant reduction in pain score by 5-6 points on the Visual Analogue Scale (VAS) noticed in 93.8% which occurred a week after treatment. This is in agreement with the finding by Lin et al who reported relief of abdominal discomfort in all patients with Hepatocellular carcinoma treated with PEI.(11) Bearing in mind that majority of our patients had severe right hypochondria pain associated with a mass as main symptoms at presentation, there is no doubt that PEI is an important modality in the management of advanced Hepatocellular carcinoma.(12) This study also reveals that all the patients presented late as evidenced by the advanced Okuda stage at presentation. This finding is supported by most reported works in Africa and other developing nations.(12-15). This late presentation is not surprising since most developing nations do not have dedicated screening programs for HCC. The mean age at presentation in this study was 40yrs; this is a decade earlier than what was reported by Olubuyide 20 years ago in the same country. This may suggest a changing trend in the age of development of HCC in line with the global observation of cancers generally occurring in younger patients.(16-17) More males appear to be affected in this study than females. This was in agreement with what is generally known about the disease.(18) The mean survival duration in this study was 8 months with the longest survivor so far at his 14<sup>th</sup> month of life. This is much better than the 6.3 months reported by Manterola et al.(19) the average survival at diagnosis of hepatocellular carcinoma is six months without intervention. This treatment option appears to prolong survival though marginally. Half of the patients in this study had associated paraneoplastic syndromes which is in consonance with that reported by Teniola et al.(20) This implies that paraneoplastic syndromes are common in patients with HCC and should be sought in the management of these patients. We conclude that percutaneous ethanol injection significantly reduces the pain of advanced hepatocellular carcinoma and prolongs survival. We strongly recommend establishment of dedicated screening centres for early detection of Hepatocellular carcinoma.

### V. Conclusion

Percutaneous ethanol injection significantly reduces the pain of advanced hepatocellular carcinoma and prolongs survival.

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### **References**

- [1]. Tanaka K, Nakamura S, Numata K, Okazaki H, Endo O, Inoue S, et al. Hepatocellular carcinoma: treatment with percutaneous ethanol injection and transcatheter arterial embolization. *Radiology*. 1992 Nov;185(2):457-60.
- [2]. Ramsey WH, Wu GY. Hepatocellular carcinoma: update on diagnosis and treatment. *Dig Dis*. 1995 Mar-Apr;13(2):81-91.
- [3]. Enwezor CJ. Sixty cases of primary hepatocellular carcinoma in one year. A preliminary appraisal. *Int Surg*. 1992 Oct-Dec;77(4):277-9.
- [4]. Olubuyide IO, Aliyu B, Olaleye OA, Ola SO, Olawuyi F, Malabu UH, et al. Hepatitis B and C virus and hepatocellular carcinoma. *Trans R Soc Trop Med Hyg*. 1997 Jan-Feb;91(1):38-41.
- [5]. Seleye-Fubara D, Jebbin NJ. Hepatocellular carcinoma in Port Harcourt, Nigeria: clinicopathologic study of 75 cases. *Ann Afr Med*. 2007 Jun;6(2):54-7.
- [6]. Paul SB, Manjunatha YC, Acharya SK. Palliative treatment in advanced hepatocellular carcinoma: has it made any difference? *Trop Gastroenterol*. 2009 Jul-Sep;30(3):125-34.
- [7]. Dubel GJ, Soares GM. Regional infusion-radioembolization. *Surg Oncol Clin N Am*. 2008 Oct;17(4):957-85, xii.
- [8]. Di Stasi M, Buscarini L, Livraghi T, Giorgio A, Salmi A, De Sio I, et al. Percutaneous ethanol injection in the treatment of hepatocellular carcinoma. A multicenter survey of evaluation practices and complication rates. *Scand J Gastroenterol*. 1997 Nov;32(11):1168-73.
- [9]. Rustemovic N, Vucelic B, Opacic M, Ostojic R, Pulanic R, Petroveckii M, et al. Palliative treatment of hepatocellular carcinoma with percutaneous ethanol injection using tumor's feeding artery occlusion under the ultrasonic color Doppler guidance. *Coll Antropol*. 2004 Dec;28(2):781-91.
- [10]. Livraghi T, Giorgio A, Marin G, Salmi A, de Sio I, Bolondi L, et al. Hepatocellular carcinoma and cirrhosis in 746 patients: long-term results of percutaneous ethanol injection. *Radiology*. 1995 Oct;197(1):101-8.
- [11]. Lin ZY, Wang JH, Hsieh MY, Yu ML, Chen SC, Chuang WL, et al. Percutaneous ethanol injection of the supplying artery to hepatocellular carcinoma that is not amenable to conventional treatment. *Br J Radiol*. 2000 Aug;73(872):833-9.
- [12]. Mondragon Sanchez R, Ochoa Carrillo FJ, Ruiz Molina JM, Herrera Goepfer R, Onate Ocana LF, Aiello Crocifoglio V. [Hepatocellular carcinoma. Experience at the Instituto Nacional de Cancerologia]. *Rev Gastroenterol Mex*. 1997 Jan-Mar;62(1):34-40.
- [13]. Olubuyide IO. The natural history of primary liver cell carcinoma: a study of 89 untreated adult Nigerians. *Cent Afr J Med*. 1992 Jan;38(1):25-30.
- [14]. Akinyinka OO, Falade AG, Ogunbiyi O, Johnson AO. Hepatocellular carcinoma in Nigerian children. *Ann Trop Paediatr*. 2001 Jun;21(2):165-8.
- [15]. Abdel-Wahab M, el-Enein AA, Abou-Zeid M, el-Fiky A, Abdallah T, Fawzy M, et al. Hepatocellular carcinoma in Mansoura-Egypt: experience of 385 patients at a single center. *Hepatogastroenterology*. 2000 May-Jun;47(33):663-8.
- [16]. Dusheiko GM. Hepatocellular carcinoma in Africans. *Ital J Gastroenterol*. 1992 Mar-Apr;24(3):146-7.
- [17]. Echejoh GO, Tanko MN, Manasseh AN, Ogala-Echejoh S, Ugoya SO, Mandong BM. Hepatocellular carcinoma in Jos, Nigeria. *Niger J Med*. 2008 Apr-Jun;17(2):210-3.
- [18]. el-Zayadi AR, Badran HM, Barakat EM, Attia Mel D, Shawky S, Mohamed MK, et al. Hepatocellular carcinoma in Egypt: a single center study over a decade. *World J Gastroenterol*. 2005 Sep 7;11(33):5193-8.
- [19]. Manterola C, Munoz S, Araya JC, Calderon C, Barroso MS. [Carcinoma hepatocellular. Description of verified clinical characteristics in a region of Southern Chile]. *Rev Med Chil*. 2000 Aug;128(8):887-95.
- [20]. Teniola SO, Ogunleye IO. Paraneoplastic syndromes in primary liver cell carcinoma in Nigeria. *Trop Geogr Med*. 1994;46(1):20-2.