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Research Article

Report of Objective Responses of Breast Cancer Patients to Pharmaceutical Grade Synthetic Cannabidiol

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ABSTRACT

This report is an observational study of objective responses of Breast Cancer patients to Pharmaceutical Grade Synthetic Cannabidiol. There were 29 total cases out of which 27 showed a clinical response.

1. Introduction

The use of a whole variety of cannabis oils of questionable quality, none of which were pharmaceutical grade, and all bought on the Internet has been a matter of routine by cancer patients, especially breast cancer patients. No anticancer effect of these oils has been noted [1-3]. Currently, it is illegal to buy cannabis oil on the internet as the Medicines and Health Regulatory Agency has defined CBD as a medicinal product, which can only be prescribed under the Pharmaceutical Specials scheme, as it is not currently a licensed medicinal product [4]. Cannabidiol targets CB1 and CB2 receptors, which have increased expression in breast cancer as compared to normal breast tissue [5], generally speaking, CB1 and CB2 receptors are upregulated in tumor tissue [6, 7]. Cannabidiol targets CB1 and CB2 cannabinoid receptors.

The phytocannabinoids are a group of chemicals extracted from the cannabis plant. A number of them are able to impede cancer cell growth, induce apoptosis and autophagy, and inhibit angiogenesis. The most widely known phytocannabinoid is Δ9-tetrahydrocannabinol (THC), and although it possesses these anticancer effects, it is also psychoactive, which has arguably hampered its clinical development. It is thought that these actions are mediated, in part, by binding to cannabinoid receptors that are expressed on a number of tissue types [8]. As one type of the receptor is found exclusively on brain cells, studies using THC have focused on this tissue type. *In vitro* data were promising and, in 2016, a pilot clinical study in patients with glioblastoma multiforme indicated THC was safe; however, no clear activity was reported [9]. The dosages were possibly on the conservative side, to minimise psychoactivity that would naturally restrict the use of THC as drug.

Of the 80+ phytocannabinoids, THC is possibly the only one to exhibit this psychoactivity. More recently, studies have diverted away from THC and focussed on other cannabinoids. The next most abundant compound is cannabidiol (CBD), which has a low affinity for the canonical cannabinoid receptors. In contrast to THC, in its pure state, according to the World Health Organisation, CBD did not have abuse potential and caused no harm [10]. Studies have shown that in addition to being able to induce cell death directly, it is also capable of interfering with intracellular signalling [11]. Alterations to pathways such as the PI3K/AKT/mTOR and the ERK suggests that CBD can modify the way certain cancer cells react to other treatments.

Indeed, studies have shown that combining CBD with conventional chemotherapy such as cytarabine and vincristine can lead to enhanced anticancer activity through modifications to these signalling pathways [12, 13]. Furthermore, the sequence in which these drugs are administered can also influence overall activity. Studies have also indicated that in certain leukaemia cell lines, CBD can increase the expression of the cyclin-dependent kinase inhibitor p21 [13]. This increased level appears to be maintained by CBD, which inadvertently impedes cell death. Cytotoxicity could be restored in these cells if the treatment regimen was altered to allow for a temporary cessation of exposure to CBD. Thus, the general efficacy of CBD may also be altered by adapting treatment protocols that include “drug-free” phases [13].

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The findings from a number of studies designed to examine the role of cannabinoids in the management of cancer symptoms varied [14]. The most recent prospective analysis of nearly 3,000 patients using medical marijuana showed that a large proportion of patients reported improvement in their condition [15]. Patients often feel that conventional therapies are not working for them, and so they search the internet for alternative medicines. It is here that they find stories about cannabis working in patients with cancer, and understandably feel it is a route for them. The cannabis products they use vary and can be in the form of whole-plant extracts or purified oils; however, whatever the source, they self-prescribe dosages. A number of anecdotal positive responses have been reported, which sustains the interest in this type of medication.

We have previously reported on objective clinical responses in a variety of cancer patients using pharmaceutical grade synthetic cannabidiol [16]. Over five years ago, we decided to assess the potential use of pharmaceutical grade synthetic cannabidiol in breast cancer patients. Some of the cases reported here were presented in our previous paper [16].

2. Materials and Methods

Patients were given synthetic pharmaceutical grade synthetic cannabidiol (PGSC) (STI Pharmaceuticals), under the Pharmaceutical Specials scheme in oily drops at 5% (w/v) in 20ml bottles. Each drop contains 1mg of synthetic CBD in neutral oil. This was prescribed on an informed consent basis. Of the 32 patients described here in this observational study, every patient in this study signed an informed consent allowing anonymous use of their data. Medicinal use of synthetic cannabinoids has been extensively reviewed in a recent paper [17]. CBD was administered on a three days on and three days off basis, which clinically is found to be more effective than giving it as a continuous dose. The average dose was 10mg twice a day. For increased tumor mass, the dose was increased, in some cases up to 30 drops (30mg). We clearly demonstrated that there is a dose-response relationship in the treatment of cancer using pharmaceutical grade synthetic cannabidiol. In a number of cases where there was stable disease, the dose was reduced to 5 drops (5mg) twice a day. We assessed the majority of patients using circulating tumor cells tests [18, 19]; some decided not to have this.

TABLE 1: Outcomes-breast cancer.

Tumour Free	5
Stable Disease	8
Circulating Tumour Cells Tests	8
Extended Median Survival	12
Died	8
No effect	2
CBD Only	29
Surgery	6
Radiotherapy	6
Total Cases	29

3. Results

The results for our breast cancer cohort treated with PGSC is reported here in significantly more detail than in our previously published study [16]. This has been in response to many requests for more details on outcomes. The results are shown in (Tables 1 & 2). PGSC, as there was an absence of significant side effects. The only noted side effects were some degree of drowsiness in those patients who received a dose of 20mg twice a day or above. This side effect did not persist. The majority of cases showed a response either in circulating tumor cells [15, 16], in those who had this test done or in extended median survival.

TABLE 2 : Breast Cancer- a detailed list of patients included in this study.

Age	Diagnosis	Standard Treatments	CBD only treatment?	Circulating Tumour Cell Test	
F 93 (B1)	Recurrent Metastatic Breast Cancer	None	✓	Not done	This patient was diagnosed with Recurrent Metastatic Breast Cancer with Lung Secondaries, a subsequent Pleural Effusion and a local recurrence. Expected survival when we first saw her was three months. She refused standard treatments. We put her on PGSC 5% 10 drops twice a day (20mg daily), three days on and three days off in October 2015. By June 2016 the Pleural Effusion had cleared up, as had the local recurrence. We saw her again at the end of 2018 and she had no recurrence of Breast Cancer. As of October 2019, she was still alive and well.
F 70 (B2)	Breast cancer	Radiotherapy	✓	May 2016 3.4/7.5ml April 2017 3.7/7.5ml Aug. 2019 2.2/7.5ml	We first saw this patient in November 2015, she had a large left-sided Breast Cancer 5cm in diameter. She refused all standard treatments. We started her on PGSC 10% 10 drops twice a day (40mg daily), three days on and three days off from November 2015. She had a half standard-length series of Radiotherapy treatments in March 2017. We carried out a Circulating Tumour Cell Test in May 2016, this showed 3.4 cells per 7.5ml. By December 2017 there was no tumour present clinically.
F 63 (B3)		None	✓	Not done	This patient had a recurrent left-sided Breast Cancer. She refused all standard treatments. The recurrent Breast Cancer measured 5cm in diameter. She started on PGSC 5% 10 drops twice a day (20mg

	Recurrent Breast Cancer				daily), three days on and three days off from June 2015. In August 2015 the left-sided breast tumour was 4cm in diameter. She continues to be alive.
F 63 (B4)	Metastatic Lobular Breast Cancer	None	✓	Not done	We saw this patient in August 2019 with an expected survival of three months. We put her on PGSC 10% 10 drops twice a day (40mg daily), three days on and three days off from August 2019. She was alive and well in September 2019 and continues on the CBD alone.
F 73 (B5)	Recurrent Breast Cancer	None	✓	July 2018 3.2/7.5ml Jan. 2019 3.5/7.5ml June 2019 2.5/7.5ml	We started her on PGSC 10% at 10 drops twice a day (40mg daily), three days on and three days off in November 2017. In July 2018 Circulating Tumour Cell Test showed 3.2 cells per 7.5ml, in January 2019 this was 3.5 cells per 7.5ml and in June 2019 this had gone down to 2.5 cells per 7.5ml.
F 69 (B6)	Lobular Breast Cancer	None	✓	Oct. 2014 9.3/7.5ml Sept 2015 7.5/7.5ml March 2016 6.8/7.5ml March 2017 3.0/7.5ml	We started this patient on PGSC in October 2014, 5% at 10 drops twice a day (20mg daily), three days on and three days off. Expected survival at that time unknown. All standard clinical examinations and scans have been normal since 2016. She is still alive and well.
F 77 (B7)	Breast Cancer	Lumpectomy Radiotherapy	×	Not done	We gave this patient PGSC 5%, 10 drops twice a day (20mg daily), three days on and three days off from when we saw her in March 2015. She is still alive and well.
F 42 (B8)	Metastatic Triple Negative Breast Cancer	Chemotherapy Radiotherapy	×	Feb 2019 5.2/7.5ml July 2019 4.6/7.5ml	We first saw this patient in November 2018 with Triple Negative breast Cancer with Lung Metastases. We carried out Sono and Photodynamic Therapy on her [17] We started her on PGSC 5% 10 drops twice a day (20mg daily), three days on and three days off. Her expected survival when we first saw her was six months. At the time of writing, she is still alive and has stable disease.
F 49 (B9)	Metastatic Breast Cancer	None	✓	Not done	We first saw this patient in November 2015, we started her on PGSC 5% 20 drops twice a day (40mg daily), three days on and three days off. Expected survival at that time was six months. She was still alive and clinically stable in May 2016. Since then, we have lost contact.
F 63 (B10)	Metastatic Breast Cancer	Radiotherapy	✓	Not done	We saw this patient in March 2017, with Metastatic Breast Cancer, she had an expected survival of six months. We started her on PGSC 5%, 15 drops twice a day (30mg daily) on a three-days on and three days off basis. She had significant pain due to bone metastases and in June 2017 the pain was significantly better. She was also taking oral Morphine. Her weight also had increased and we know that she was alive and well in the last half of 2018.
F 64 (B11)	Metastatic Breast Cancer	None	✓	March 2014 11.0/7.5ml Oct. 2014 10.4/7.5ml July 2015 7.3/7.5ml Oct 2015 6.8/7.5ml June 2016 6.6/7.6ml May 2017 7.6/7.6ml Oct 2017	We saw this patient for the first time in March 2014 and started her on PGSC 5% 10 drops twice a day (20mg daily), three days on and three days off for Metastatic Breast Cancer with lung secondaries, mediastinal nodes and a single bone metastasis. At that time, her expected survival was six months. We also carried out Sono and Photodynamic Therapy on her [17]. She remains clinically well

				3.9/7.5ml Aug 2018 2.5/7.5ml July 2019 2.3/7.5ml	
F 65 (B12)	Recurrent Breast Cancer	None	✓	Oct 2018 2.4/7.5ml	We started treatment with this lady with PGSC 5% in November 2018 at 10 drops twice a day (20mg daily), three days on and three days off. She remains clinically well and on standard investigations she is tumour free.
F 61 (B13)	Metastatic Breast Cancer	None	✓	Not done.	We first saw this patient on 15th January 2015 with Metastatic Breast Cancer. We put her on PGSC 5% 10 drops twice a day (20mg daily) on a pulsing basis, three days on and three days off. She continues to be alive and well and is working full time.
F 73 (B14)	Metastatic Breast Cancer	Radiotherapy	✓	Not done	We started her on PGSC 5% at a dose of 10 drops twice a day (20mg daily), three days on and three days off in January 2015. all subsequent scans show stable disease.
F 48 (B15)	Breast Cancer	Pre-operative Chemotherapy Mastectomy Radiotherapy	✓	Not done	We first saw this patient in June 2016, post standard treatments. We started her on PGSC 5% at 10 drops twice a day (20mg daily), three days on and three days off. She continues to be alive and well.
F 47 (B16)	Triple Negative breast Cancer	None	✓	Not done	We first saw this patient in January 2019. She has refused standard treatments. We started her on PGSC 5% at 10 drops twice a day (20mg daily), three days on and three days off. At the time of writing, she is alive and clinically stable.
F 79 (B17)	Metastatic Breast Cancer	None	✓	Not done	We saw this patient with Metastatic Breast Cancer on 13th August 2019. Expected survival was two months. We started her on Pharmaceutical Grade Synthetic Cannabidiol (PGSC) 5 drops twice a day (10mg daily) on a pulsing basis, three days on and three days off. She died in September 2019.
F 75 (B18)	Metastatic Breast cancer	None	✓	Jan 2019 8.1/7.5ml May 2019 5.6/7.5	This patient refused standard treatments. Expected survival when we first saw her was three months. We started her on PGSC 5% 10 drops twice a day (20mg daily), three days on and three days off. She died in July 2019.
F 49 (B19)	Metastatic Breast Cancer	None	✓	Not done	We saw this patient in May 2017 with Metastatic Breast Cancer. We started her on PGSC 5% at 10 drops twice a day (20mg daily), three days on and three days off. This patient was still alive and clinically well in July 2018.
F 59 (B20)	Metastatic Breast Cancer	None	✓	Not done	We first saw this patient on 2nd November 2015 with recurrent Metastatic Breast Cancer. We put her on PGSC 5% 10 drops twice a day (20mg daily) on a pulsing basis, three days on and three days off in October 2015. At the time of seeing her, expected survival was six months. We presumed she died in April 2016, so no result.
F 56 (B21)	Breast cancer	Surgery Radiotherapy	✓	Not done	We started her on PGSC, 5% 10 drops twice a day (20mg daily), three days on and three days off when we saw her in December 2015. She is still alive and well.
F 67 (B22)	Recurrent Breast Cancer	Surgery Radiotherapy	✓	Dec 2016 6.9/7.5ml June 2017 4.5/7.5ml Nov 2017 2.4/7.5ml June 2018 3.1/7.5ml Jan 2019 3.7/7.5ml Oct 2019	We first saw this patient in March 2016. After standard treatments she has been on PGSC 5% at a dose of 10 drops twice a day (20mg daily) three days on and three days off as the only treatment.

				2.2/7.5ml	
F 61 (B23)	Triple Negative Breast Cancer	None	✓	Not done	We saw this patient in June 2015, expected survival was six months. We put her on PGSC 5% 10 drops twice a day (20mg daily), three days on and three days off. She died in June 2016.
F 64 (B24)	Triple Negative Metastatic Breast Cancer	Radiotherapy Chemotherapy	✓	Not done	We first saw this patient in November 2014 after standard treatments for Metastatic Triple Negative Breast Cancer. We started her on PGSC 5% at 10 drops twice a day (20mg daily), three days on and three days off. Standard investigations in July 2016 showed that she was tumour free. She is still on the PGSC .
F 62 (B25)	Metastatic Breast Cancer	Radiotherapy	✓	Not done	We started her on PGSC 5% in February 2015 at 10 drops twice a day (20mg daily), three days on and three days off. Expected survival was three months, she died in August 2015.
F 42 (B26)	Breast Cancer	None	✓	Not done	We first saw this patient with Metastatic Breast Cancer in June 2015. Expected survival was three months. She died in December 2015.
F 44 (B27)	Metastatic Breast Cancer	None	✓	Not done	We saw this patient in March 2016, expected survival was three months. We started her on PGSC 20 drops twice a day (40mg daily), three days on and three days off. She died in December 2016.
F 75 (B28)	Metastatic Breast Cancer	None	✓	Not done	We saw this patient in September 2016, expected survival was three months. We put her on PGSC 5% 20 drops twice a day (40mg daily), three days on and three days off. She died in March 2017.
F 43 (B29)	Inflammatory Metastatic Breast Cancer	None	✓	Not done	Diagnosed in July 2019 with left-sided Inflammatory Breast Cancer with nodal involvement. Also, four liver metastases detected on MRI. Tumour is oestrogen and progesterone negative, HER2 positive. We first saw this patient in July 2019, she had been offered pre-operative Chemotherapy, followed by left mastectomy and axillary node clearance on the left side, followed by Radiotherapy. She turned down standard treatments. We started her on PGSC 10% 5 drops twice a day (20mg daily), three days on and three days off. When we first saw her the tumour in the left breast was 9cm in diameter. On seeing her again in November 2019 the tumour in the left breast had reduced to 5cm in diameter, left axillary nodes were no longer palpable. On seeing her for another appointment at the end of February 2020, the tumour in the left breast had reduced to 4.5cm in diameter, and left axillary nodes were no longer palpable.

4. Discussion

PGSC in breast cancer is shown in this paper to have significant anticancer effects. This study is an observational study and prospective randomised control studies are worth doing using this approach, as it is free from side effects. The weakness of this study is that it is an observational study.

5. Conclusion

PGSC has an objective anticancer effect in breast cancer patients. To elucidate this further, then further studies addressing the weakness of this particular study are worth carrying out.

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Conflicts of Interest

None.

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