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A Prospective Clinical Pilot Study of Sativex® for Refractory Trigeminal Neuralgia: Patient-Reported Outcomes and Tolerability

Joshua. W Bryan

bryanj4@cardiff.ac.uk

Cardiff University

George Eralil

University Hospital of Wales

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Abstract

Background

Trigeminal neuralgia (TN) is a severe neuropathic pain disorder characterised by paroxysmal, ‘electric shock’ like facial pain, substantial functional impairment and a reduced health-related quality of life. Concerningly, first-line pharmacological treatments, such as carbamazepine, are ineffective or poorly tolerated in up to one-third of patients.

Objectives

To assess the efficacy and tolerability of Sativex® (THC:CBD oromucosal spray) in patients with TN within the constraints of a heavily regulated National Health Service (NHS) in the UK; and to generate preliminary data to inform future larger-scaled studies.

Methods

This prospective, single-centre pilot study included three female patients with refractory TN, all of whom had previously undergone neurosurgical intervention and had trialled at least two pharmacological modalities unsuccessfully. Patients received Sativex and were followed at baseline, 4 weeks, 8 weeks, and 12 weeks. Quantitative outcomes included the Neuropathic Pain Scale (NPS) and Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scores for neuropathic pain and SF-36 total score to assess HrQoL. Analyses were primarily descriptive, with change-from-baseline calculations and exploratory Friedman tests performed for the three principal quantitative measures. Qualitative follow-up data were also reviewed to capture symptom change, functional impact, tolerability, and practical barriers to treatment use for each patient.

Results

Descriptive analyses found higher HrQoL scores at all follow-up timepoints than at baseline, with the greatest numerical increase observed by 8 weeks and broadly maintained at 12 weeks. Mean NPS and LANSS scores were lower than baseline across follow-up, illustrating reduced neuropathic pain levels although these changes were smaller and more heterogeneous. Exploratory Friedman tests were not statistically significant for any of the primary measures. Qualitative review demonstrated extensive heterogeneity in onset and magnitude of response, with functional improvements reported in some patients alongside important tolerability and practical barriers.

Conclusion

These preliminary findings suggest that Sativex may be associated with improvement in HrQoL and a reduction in pain-related symptom burden in some patients with refractory TN, although response was heterogeneous and limited by tolerability and practical treatment barriers. Larger prospective studies are needed to better define clinical effectiveness, durability of response, and meaningful patient-centred outcome measures.

Introduction

Trigeminal neuralgia (TN) is a severe neuropathic pain disorder that is characterised by recurrent, unilateral, paroxysmal facial pain in the distribution of one or more branches of the trigeminal cranial nerve, most commonly resulting from neurovascular compression. Attacks are classically described as brief, 'electric shock-like' episodes triggered by innocuous stimuli such as speaking, teeth brushing, chewing, or simply light touch. According to the International Classification of Headache Disorders, 3rd edition (ICHD-3), TN is defined by characteristic clinical features and exclusion of alternative structural or neurological causes.[1] The condition carries an extensive burden of morbidity, with significant impairment in daily functioning and HrQoL remaining prevalent.

Pharmacological therapy is typically the first-line management of TN, with carbamazepine and oxcarbazepine remaining as the recommended initial treatment in national and international guidelines.[2–4] Despite this, up to one-third of patients experience inadequate control of their symptoms or intolerable side effects, including sedation, cognitive impairment, dizziness, and systemic toxicity.[5,6] Second-line pharmacological agents such as gabapentinoids, baclofen, and lamotrigine have been shown to offer variable benefit. Moreover, surgical interventions such as microvascular decompression (MVD) and ablative procedures have historically been reserved for refractory cases and may be unsuitable for some patients deemed to have high operative risks or due to patient preference.[7,8] As a result of this, there remains a significant unmet clinical need for alternative therapeutic strategies that are both effective and well tolerated for this large subset of unmanaged patients.

More recently, cannabinoid-based medicinal products (CBMPs) have received increasing interest in the management of chronic and resistant neuropathic pain. Nabiximols (Sativex®) is a standardised oromucosal spray containing a 50:50 ratio of Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), and is only licensed in the United Kingdom for the treatment of moderate-to-severe spasticity in multiple sclerosis.[9] Although its use in trigeminal neuralgia is not currently approved, evidence from a series of randomised controlled trials (RCTs) and systematic reviews suggests that cannabinoids may offer analgesic benefit in certain neuropathic pain conditions.[10–13] Despite this evidence, research into the effects of Sativex in patients with TN is limited, with existing data being largely restricted to case reports in situ with inferences from other neuropathic pain syndromes. To date, no RCTs evaluating Sativex in TN patients have been published.

In the United Kingdom, the clinical adoption of CBMPs within the NHS is constrained by regulatory, financial, and evidentiary barriers.[14] Despite the amendment of cannabis-based products for medicinal

use in 2018, prescribing still remains very limited, with National Institute for Health and Care Excellence (NICE) guidance only recommending CBMPs for highly specific indications and emphasising the need for further, more thorough research.[15] These systemic constraints highlight the importance of developing studies to produce robust clinical data to inform future policy and clinical decision-making.

In light of these findings, this prospective pilot study aimed to assess the efficacy and tolerability of Sativex in patients with TN had been deemed refractory to standard pharmacological and/or surgical interventions within the NHS setting. By systematically evaluating changes in neuropathic pain measures, HrQoL, and patient-reported functional experience over time, this study aimed to provide preliminary evidence regarding the potential role of Sativex in TN. Our findings may help to inform the design of future prospective studies and contribute to the evolving evidence base for cannabinoid-based therapies in neuropathic facial pain.

Methods

Study Design:

This was a prospective, single-centre exploratory pilot study evaluating the tolerability and patient-reported outcomes of nabiximols (Sativex®) in three female patients with refractory trigeminal neuralgia. Given the exploratory design and very small sample size, the study was not powered for formal hypothesis testing and thus was intended primarily to characterise patterns of change over time with the aim to inform future randomised-controlled trials.

Study Setting and Recruitment:

Patients were recruited from the neurosurgical service at the University Hospital of Wales, Cardiff. Eligible patients were identified from the clinical practice of the treating consultant neurosurgeon.

Recruitment commenced in December 2025 and final data collection was completed in April 2026. All patients were enrolled prospectively following clinical assessment and confirmation of eligibility.

Ethical Approval and Consent

The study received approval from an NHS Research Ethics Committee, and written informed consent was obtained from all patients prior to enrolment.

Participants:

Inclusion Criteria

Participants were eligible for inclusion if they met the following criteria:

- Adults aged 18 years or older.
- A Diagnosis of trigeminal neuralgia in accordance with the International Classification of Headache Disorders, 3rd edition (ICHD-3).
- Persistent symptoms despite sufficient trials of standard pharmacological therapy.
- Previous neurosurgical intervention for TN.
- Capacity to provide informed consent.

Exclusion Criteria

- Secondary TN due to structural lesions requiring urgent surgical intervention.
- Severe psychiatric illness or contraindications to cannabinoid-based therapy.
- Pregnancy or breastfeeding.
- Concurrent use of illicit cannabis or other cannabinoid-based medicinal products.
- Significant medical comorbidity likely to interfere with treatment or assessment.
- A diagnosis of anaesthesia dolorosa.

Intervention:

Sativex was prescribed by the treating neurosurgeon in accordance with UK regulatory requirements. Each dose of the oromucosal spray delivered 2.7 mg Δ9-tetrahydrocannabinol and 2.5 mg cannabidiol. Treatment was initiated at three to four sprays daily and the maximum permitted dose was four sprays daily. Participants were reviewed at four-week intervals and were given contact details for a member of the team if any issues were to arise. Treatment use, tolerability, and any concomitant medication adjustments were reviewed pragmatically during the four-weekly follow-up consultations.

Concomitant Medications:

Participants continued their baseline pharmacological therapies for TN at study entry.

At each follow-up visit, clinical response and tolerability were assessed by the treating neurosurgeon. Adjustments to concomitant medications, including dose reduction or withdrawal, were undertaken pragmatically on a case-by-case basis according to clinical response to Sativex and patient tolerability, rather than through a predefined protocol.

Only one patient had a concomitant drug dose (carbamazepine) where the dose was changed after four weeks.

Outcome Measures:

Quantitative outcomes included Neuropathic Pain Scale (NPS) total score, Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) total score, and SF-36 domain scores recorded at baseline, 4 weeks, 8 weeks, and 12 weeks. For descriptive purposes, an SF-36 total score was calculated as the sum of the recorded SF-36 subscale scores. In addition, qualitative follow-up data was collected through patient interviews to highlight specific symptom patterns, functional impact, tolerability and any practical barriers to Sativex use.

Safety Monitoring:

Adverse effects were reviewed through structured clinical discussion at every follow-up consultation. Treatment discontinuation and serious adverse events were recorded where applicable. No participant permanently discontinued treatment during the reported follow-up period, and no serious adverse events were documented. Patients were also given worsening advice and a contact number should they have had any concerns regarding their treatment.

Data analysis

Due to the exploratory design and very small sample size (n = 3), analyses were primarily descriptive and were intended to characterise any patterns of change over time rather than estimate treatment effect. Croup level summaries were used to describe overall trends across the three patient while within-patient trajectories were examined quantitatively and narratively to capture the heterogeneity of the responses.

Statistical analyses were performed using Jamovi statistical software[16,17]. For the three primary quantitative outcomes (Neuropathic Pain Scale (NPS) total score, Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) total score, and SF-36 total score), descriptive statistics were calculated at baseline, 4 weeks, 8 weeks, and 12 weeks. Individual SF-36 domain scores were also summarised descriptively across the same four timepoints. For SF-36, higher scores reflected better HrQoL, whereas for NPS and LANSS, lower scores reflected lower neuropathic pain/symptom burden. Full descriptive values for each of the scales and subscales over each of the time points can be found in Supplementary Table 1.

Change-from-baseline values were then calculated for the SF-36 total score, NPS total score, and LANSS total score for each follow-up point. Exploratory Friedman tests were then performed for these three outcomes across the four study timepoints. Because the study was not powered for formal hypothesis testing, inferential analyses were interpreted cautiously and treated as supportive exploratory findings. Qualitative follow-up data collected was reviewed descriptively to provide context regarding symptom change, functional impact, tolerability, and practical barriers to treatment use for each of the patients.

The change from baseline values were then calculated for SF-36 total score, NPS total score, and LANSS total score at each follow-up timepoint to quantify the direction and magnitude of change within the patient cohort. In addition to this, exploratory Friedman tests were performed for these three primary

outcomes, again across the four time points. Because the study included only three patients and was resultantly not powered for formal hypothesis testing, these inferential analyses were interpreted cautiously and treated as supportive exploratory findings rather than confirmatory evidence. Qualitative data collected from each patient at each follow-up were also reviewed descriptively to provide context regarding symptom change, functional impact, tolerability, and practical barriers to treatment use to confer an overall effect of Sativex treatment.

Results

Three female patients aged 42–56 years were included in the analyses. Baseline patient characteristics are summarised in Table 1.

Table 1
Baseline patient characteristics

ID	Gender	Phenotype	Prior Interventions	Baseline medication	Baseline pain
A	Female	Classical trigeminal neuralgia	Previous MVD: multiple peripheral neurolytic procedures (alcohol and botulinum toxin) and pulsed trigeminal ganglion radiofrequency	Amitriptyline 30 mg/day; carbamazepine 1600 mg/day; gabapentin 3600 mg/day; pregabalin 600 mg/day	Single type of pain, intermittently present
B	Female	Classical trigeminal neuralgia with possible coexisting glossopharyngeal neuralgia	Previous MVD: multiple peripheral neurolytic procedures (alcohol and botulinum toxin)	Eslicarbazepine 1200 mg/day; duloxetine 120 mg/day; propranolol 40 mg twice daily; thyroxine 100 micrograms/day	Continuous background pain with breakthrough flares
C	Female	Classical trigeminal neuralgia	Previous MVD: multiple peripheral neurolytic procedures (alcohol and botulinum toxin)	No concomitant medication reported	Continuous background pain with breakthrough flares

Group-level quantitative outcomes

Overall, the SF-36 total scores were higher at follow-up than at baseline for all three patients, suggesting improved HrQoL over time at group level. Furthermore, mean NPS and LANSS total scores were lower than baseline across follow-up suggesting lower neuropathic pain and symptom burden scores over the 12-week observation period. The largest group-level change in SF-36 total score was observed by 8 weeks and was broadly maintained at 12 weeks. By comparison, reductions in NPS and LANSS were

present at each follow-up timepoint but were smaller and much less uniform than the change seen for SF-36. Full descriptive statistics are presented in Table 2.

Table 2
Primary outcomes for HrQoL and neuropathic pain scores over time

Timepoint	SF-36 total, mean (SD)	NPS total, mean (SD)	LANSS total, mean (SD)
Baseline	141.7 (54.5)	68.3 (15.5)	17.67 (7.09)
4 Weeks	293.0 (86.9)	38.7 (31.9)	15.33 (6.35)
8 Weeks	409.0 (33.5)	43.7 (16.4)	13.33 (7.37)
12 Weeks	405.0 (101.3)	38.7 (29.2)	13.67 (5.51)

Note - *values are presented as mean (standard deviation). SF-36 total score is an exploratory sum of all of the eight recorded SF-36 domain scores.*

SF-36 domain patterns

When looking within the eight domains of the SF-36 scale, the clearest numerical changes occurred in physical functioning, energy and fatigue, emotional wellbeing, social functioning, pain, and general health. These domains were higher at follow-up than at baseline, consistent with improvement across physical, psychosocial, and pain-related aspects of HrQoL. In contrast, the role limitation domains were more variable over time, particularly role limitations due to emotional problems, which did not show a clear sustained pattern of improvement. Full subscale values are presented in Table 3

Table 3
SF-36 domain scores across the duration of the study

SF-36 domain	Baseline mean (SD)	4 weeks mean (SD)	8 weeks mean (SD)	12 weeks mean (SD)
Physical functioning	51.7 (33.3)	60.0 (26.0)	88.3 (7.64)	85.0 (13.2)
Role limitations due to physical health	0.0 (0.0)	0.0 (0.0)	16.7 (28.9)	41.7 (52.0)
Role limitations due to emotional problems	11.0 (19.1)	33.3 (57.7)	33.3 (33.5)	0.0 (0.0)
Energy and fatigue	11.7 (7.64)	40.0 (13.2)	50.0 (5.00)	41.7 (5.77)
Emotional wellbeing	28.0 (14.4)	56.0 (8.00)	74.7 (12.9)	65.3 (6.11)
Social functioning	4.33 (7.51)	33.7 (7.51)	41.7 (14.4)	50.3 (21.9)
Pain	3.33 (5.77)	30.0 (26.0)	52.7 (22.5)	59.3 (35.7)
General health	31.7 (5.77)	40.0 (13.2)	51.7 (10.4)	61.7 (12.6)

Note - values represent mean (standard deviation). Higher SF-36 scores indicate a better HrQoL within the corresponding domain; the maximum score for each domain is 100.

Change from baseline analysis of the primary outcomes

A change from baseline analysis was also conducted which supported the same overall pattern seen in the descriptive summaries. SF-36 total scores increased from baseline at each follow-up timepoint, with the greatest mean increase being seen at 8 weeks alongside a similarly elevated value at 12 weeks. Contrastingly, NPS and LANSS total scores were numerically lower than baseline at all follow-up timepoints, suggestive of reduced neuropathic pain and symptom burden. This highlights how pain-related measures remained below baseline throughout follow-up. These findings provide a clearer estimate of the direction and magnitude of change and can be found in Table 4.

Table 4
Change from baseline analysis of HrQoL and neuropathic pain

Outcome	4 weeks, mean change (SD)	8 weeks, mean change (SD)	12 weeks, mean change (SD)
SF-36 total	+ 151.0 (140.0)	+ 267.0 (56.1)	+ 263.0 (107.0)
NPS total	−29.7 (18.1)	−24.7 (7.09)	−29.7 (14.4)
LANSS total	−2.33 (2.52)	−4.33 (1.15)	−4.00 (5.29)

Note - *Positive change in SF-36 score indicates a higher HrQoL relative to the baseline assessment. Negative change in NPS and LANSS total scores indicates lower neuropathic pain or symptom burden relative to baseline.*

Within-patient quantitative trajectories

While expected, a review of individual trajectories showed that changes in HrQoL and neuropathic pain were not uniform across the patients. All three patients demonstrated a higher SF-36 total score at follow-up than at baseline, although the extent of improvement differed between patients. Patient A showed the most marked and progressive increase in SF-36 total score across the full follow-up period. Moreover, patient B demonstrated an early rise in SF-36 total score that was not fully maintained by 12 weeks, although values did remain substantially above baseline. Patient C showed relatively limited change at 4 weeks, followed by a larger increase at 8 weeks that persisted (although to a lesser degree at 12 weeks).

Pain-related measures showed greater heterogeneity. Patient A demonstrated notably lower NPS and LANSS values than baseline across follow-up. Patient B showed some reduction in NPS at follow-up, but LANSS remained largely unchanged by 12 weeks, potentially suggesting a more mixed pattern. Patient C demonstrated more modest reductions in NPS over time, while LANSS was lower than baseline by follow-up, particularly at 12 weeks. These patient-level findings are illustrated in Fig. 1.

Exploratory non-parametric repeated-measures analysis

Exploratory Friedman tests were performed for SF-36 total score, NPS total score, and LANSS total score across baseline, 4 weeks, 8 weeks, and 12 weeks. From this analysis no statistically significant

difference across timepoints was identified for SF-36 total score, $\chi^2(3) = 5.80$, $p = 0.122$, NPS total score, $\chi^2(3) = 5.40$, $p = 0.145$, or LANSS total score, $\chi^2(3) = 5.63$, $p = 0.131$. It is, however, very important to consider that given the inclusion of only three participants and the heterogeneity between them, these findings should be interpreted as exploratory only.

Qualitative Summary

A review of the qualitative comments made by each patient at each follow-up provided a very important context for the quantitative findings obtained from the questionnaires. Across the three patients, response to Sativex was heterogeneous in onset, magnitude, and durability (at least within the constraints of the follow-up period).

Patient A:

Patient A demonstrated the most clinically favourable trajectory in both quantitative and qualitative aspects. At baseline, her symptoms were described as a severe 'electric-shock-like' pains that were 10/10 in severity and occurred multiple times a day, limiting her ability to work, socialise and function, particularly in both moderate and vigorous activity, walking more than a block and with bathing and dressing. By the first follow-up, however, the qualitative change was already notable. Despite patient A reporting that symptoms had initially remained similar for the first 2 to 3 weeks after commencing treatment with Sativex, she then described an abrupt and complete cessation of pain. Specifically, her physical limitations were significantly improved alongside an improvement in social functioning and overall emotional wellbeing.

Importantly, this was not just presented as a reduction in discomfort but as a restoration of typical daily activities. She reported being able to brush her teeth, eat, walk and attend hair appointments without provoking pain. She had started to resume her university work. She was no longer relying on an analgesic oral gel, suggesting reduced need for rescue self-management strategies. By 8 weeks, this improvement appeared to be sustained, with no breakthrough pain and no ongoing uncomfortable pain, although she continued to describe altered sensation and increased sensitivity on the affected side of the face, particularly in colder weather. Her qualitative course was reflective of the strong numerical rise in SF-36 total scores and the reduction in neuropathic pain-related scores, while also showing that 'improvement' in TN does not necessarily imply complete sensory normalisation, but an improvement in physical and emotional functioning.

Patient B:

Patient B's course was much more mixed. At 4 weeks, she continued to experience persistent background trigeminal pain with intermittent exacerbations, however, she felt that Sativex helped her to relax and tolerate her symptoms more easily. Despite this, however, she reported prominent nausea and vomiting, raising concerns about dose-related tolerability and potential interference with nutrition and adherence. She also stated that Sativex did not appear to improve any aspect of the unique glossopharyngeal component of her pain.

By the 12-week review, patient B's progress had become more complicated. She had stopped taking Sativex for a period because she felt unwell yet also reported that pain had become substantially worse after discontinuation and that overall her symptoms had been more tolerable at previous follow-ups. Moreover, she was describing a new severe pain associated with eating and swallowing, with sharp attacks radiating towards the occipital area of the head, restricted eating, and new sensory symptoms including pins and needles in the jaw and abnormal post-auricular sensation. These features imply an unstable and evolving pain phenotype rather and are likely as a result of her concurrent glossopharyngeal neuralgia rather than TN.

Patient C:

Patient C demonstrated a more delayed and modest qualitative response pattern, with her suggesting that any benefit from Sativex, if present, emerged gradually and was strongly influenced by practical treatment barriers. At 4 weeks, she reported essentially no meaningful symptomatic change and described Sativex as unpleasant to use, specifically citing burning of the mouth and back of the throat during administration as key side effects. Unlike patient B, however, she report no systemic adverse effects, but the route of administration itself was clearly problematic. In addition, she described difficulty using the medication during the working day because of storage constraints (with it needing to be refrigerated) and expressed apprehension about the stigma associated with taking a cannabis-based medicine at work.

By 8 weeks, patient C's experience with Sativex had become much more positive. Despite still reporting 'bad days', she felt that the medication 'might be helping', with some pain-free days emerging, background pain becoming less severe, and her classic 'electric shock-like' pains becoming much less frequent and severe. She also described the pain as more bearable overall and stated that she had not needed time off work, suggesting a very positive functional benefit even in the absence of complete symptom resolution. She felt more positive with her condition at this stage, mirroring the observed rise in HrQoL seen in seven of the eight SF-36 subscales. By 12 weeks, however, her progress appeared to plateau. After an experience of being hit in the face at work, her symptoms worsened again. Whilst resulting in an increase in pain and discomfort, it represents an external and unavoidable event. Independent to this, however, she continued to experience more good days, despite the perseverance of her persistent background pain and breakthrough attacks. Overall, her HrQoL was substantially improved based on the SF-36 and whilst her pain had not been completely eliminated, Sativex had moderated an improvement in physical functioning, social functioning and overall pain scores from baseline.

Discussion

This prospective pilot study provides clear preliminary evidence to suggest that Sativex may be associated with an improvement in patient-reported outcomes in some patients with refractory trigeminal neuralgia. Across the 12-week follow-up period, we found the most consistent quantitative improvement to be an increase in SF-36 total score and improvement across several HrQoL domains, while NPS and LANSS scores were numerically lower than baseline but overall changed less uniformly.

Subsequently, exploratory Friedman testing did not identify any statistically significant differences across any of the timepoints for either SF-36, NPS or LANSS total scores, which is unsurprising given the very small sample size and the resultant fact that the study was not adequately powered for confirmatory hypothesis testing. The findings are therefore best interpreted as descriptive and hypothesis generating, with the most meaningful insights emerging from the combined quantitative and qualitative review of patient trajectories, which will be discussed in more detail.

A key finding of this study was the radial patient-reported improvements in HrQoL rather than a marked movement in neuropathic pain scale scores (LANSS and NPS). Moreover, for the patients who reported an improvement in HrQoL, this benefit was not expressed solely as less pain burden but as restoration of ordinary daily activities and improved confidence in engaging with day-to-day living. Some of the more marked improvements reported included being able to eat with less/no pain, brushing teeth without issue, walking, returning to university work, and remaining in employment with less disruption. In patients with trigeminal neuralgia, disability often arises as much from anticipatory fear, behavioural avoidance, and disruption of routine as from pain intensity and burden alone. Resultantly, these gains are clinically meaningful and have produced marked functional improvements in some of the patients.

The qualitative findings we obtained also suggest that any perceived benefit, when present, was not necessarily immediate and did not necessarily equate to complete pain cessation. Patient A described little meaningful change early on in the study, although experience marked improvement before the first follow up. Contrastingly, patient C also appeared to experience benefit only after the second follow-up. Importantly, our patients often described the most benefit to be in terms of greater tolerability, reduced intrusiveness of symptoms, fewer disruptive attacks, and recovery of valued activities rather than complete symptom absence (which was only the case in patient A). Furthermore, it suggests that a patient's interpretation of clinically meaningful improvement may be better reflected by function and tolerability than by neuropathic pain intensity alone. In a real-world cohort with refractory disease this may be particularly relevant when evaluating therapies where the benefit elicited is partial, delayed, or shaped by the evolving and unpredictable pressures of daily life.

A key issue we identified in our study is the mismatch between some of the quantitative pain measures and the overall patient-reported experience. Both the NPS and LANSS appeared useful in describing and monitoring neuropathic pain burden and showing directional change. Despite this (and specifically with the LANSS), they were less able to capture several features repeatedly emphasised by the patients, including reduced breakthrough pain frequency, less intense background pain and more pain-free intervals. These aspects are particularly relevant in TN, whereby symptoms are often paroxysmal, trigger-dependent and holistically disruptive in ways that cannot be entirely reflected by generic neuropathic pain tools. Conversely, we noted the SF-36 to be a lot more sensitive to broader changes in patient function and wellbeing, but again it is not specific to trigeminal neuralgia and may be influenced by factors unrelated to the condition itself. Overall, these findings promote the need for a TN-specific outcome measure that is capable of integrating symptom severity, attack frequency, trigger sensitivity, neuropathic pain characteristics, functional limitation, and HrQoL within a single validated instrument.

This is in keeping with published literature that has highlighted limited psychometric evidence for currently used patient-reported outcome measures in TN and calling for better validated TN-specific tools.[18]

The heterogeneity we observed between patients is also important and likely to be multifactorial. Baseline treatment regimens differed substantially across the patient cohort and one patient had coexisting glossopharyngeal neuralgia, introducing additional clinical complexity and making interpretation of symptom change less straightforward. Furthermore, treatment exposure was not uniform in practice: one patient temporarily stopped Sativex due to illness, while others experienced practical barriers to use. These differences could have perhaps contributed to the variable extent and timing of response. Overall, the apparent treatment effect is likely to be mediated not only by the pharmacological properties of the Sativex itself, but also by prior treatment burden, concurrent medication use, overlapping pain syndromes, and the feasibility of sustained real-world use, headlining the point that, as in several neurological pain conditions, treatment response should be expected to vary in speed and efficacy.

Interpretation of the HrQoL findings also requires consideration of psychosocial context beyond trigeminal neuralgia itself. Some of the patients within the study experienced significant life stressors during follow-up, including job loss and relationship breakdown, which may plausibly have influenced SF-36 domains such as emotional wellbeing, social functioning, energy and fatigue and role limitations due to emotional problems independently of TN severity or the effects of Sativex. In addition, trigeminal neuralgia is known to be associated with substantial psychosocial burden, including anxiety, depressive symptoms, and marked disruption of daily living, all of which may contribute to very low baseline HrQoL scores and complicate interpretation of subsequent change. These contextual factors do not undermine the observed HrQoL improvements but do reinforce the need for caution when interpreting broad quality-of-life measures in small, clinically complex cohorts.

Tolerability and practicality emerged as major determinants of the overall treatment experience. The key issues faced included nausea (n = 1), oral and throat burning (n = 3), difficulty using the medication during the working day (n = 1) and concerns about stigma associated with a cannabis-based medicine (n = 1). These observations are particularly important because they reflect the reality of using a cannabinoid-based treatment outside a controlled trial setting. Even where symptom improvement is present, route of administration, side-effect burden, occupational context and importantly, social acceptability may all influence adherence and continuation in a wider population. This mirrors recent cannabinoid literature which suggests that benefit in neuropathic pain are often accompanied by important concerns around tolerability, acceptability and the consistency of real-world use[12].

Limitations:

This study has several important limitations to consider. The most obvious is the very small sample size which significantly limits generalisability across a wider TN population and makes any inferential

analysis exploratory only. Moreover, there was no control group, no blinding, and no formal monitoring of dosing adherence, meaning that inconsistent exposure, placebo effects, regression to the mean alongside the influence of concomitant medication changes cannot be excluded or evaluated in sufficient detail. Further, pain in itself as well as its reporting is inherently subjective, and the quantitative tools used were not developed specifically or formally evaluated for trigeminal neuralgia. It is important to consider that these limitations should not negate the descriptive value of the findings we have obtained but suggest that the study should be interpreted as an exploratory clinical signal rather than evidence of efficacy. Further real-world, dose withdrawal trials and studies are pressingly needed to elucidate these effects more formally.

Strengths:

Despite obvious limitations, the study also has notable strengths. It was prospective, used repeated follow-up over a defined period and combined validated quantitative measures with detailed patient-level qualitative review. This mixed approach is of particular value in a sample of this size as it correlates score to qualitative improvements. In this study, the qualitative data were not merely supplementary; they were essential to understanding why patients with similar diagnoses could experience very different trajectories in benefit, burden, and tolerability when undertaking Sativex treatment. The findings therefore support continued use of patient-level narrative alongside quantitative outcomes in future TN research.

Future Directions:

Future work should build directly on these observations. Larger prospective studies are needed to clarify whether the HrQoL improvements seen here are reproducible and how transient these effects are over a longer follow-up period. Future research would benefit from a more standardised dose titration, prospective monitoring of adherence, the presence of a placebo (or controlled dose withdrawal of existing medications) and most importantly, a much more diverse sample. Moreover, there is a strong case for development or validation of a TN-specific patient-reported outcome measure that can quantify pain severity, frequency, burden, functional limitation, and HrQoL within a single clinically meaningful framework.

Conclusions

In conclusion, Sativex was associated with numerical improvement in HrQoL and reduction in pain-related scores in some patients with refractory TN. Despite this, the pattern of response was heterogeneous and strongly shaped by tolerability, practical barriers, concurrent clinical complexity, and wider psychosocial context. The clearest apparent benefit in this cohort was not lower neuropathic pain scores but improved daily functioning and global improvements in HrQoL. Moving forward, larger prospective studies are now needed to determine which patients are most likely to benefit from Sativex, how durable any benefit may be and which patient-centred outcomes most meaningfully capture treatment response.

Abbreviations

CBD
Cannabidiol
CBMPs
Cannabis–based medicinal products
HrQoL
Health–related quality of life
ICHD
3–International Classification of Headache Disorders, 3rd edition
LANSS
Leeds Assessment of Neuropathic Symptoms and Signs
MVD
Microvascular decompression
NHS
National Health Service
NICE
National Institute for Health and Care Excellence
NPS
Neuropathic Pain Scale
RCTs
Randomised controlled trials
SF
36–36–Item Short Form Health Survey
THC
Delta–9–tetrahydrocannabinol
TN
Trigeminal neuralgia
UK
United Kingdom

Declarations

Ethics approval and consent to participate

Sativex was prescribed as part of routine clinical care, with treatment decisions and clinical management undertaken by the treating consultant neurosurgeon. Formal research ethics approval was not obtained. Written informed consent was obtained from all participants.

Consent for publication

Informed consent for publication was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

J.B. was responsible for the statistical analysis and writing the whole manuscript text.G.E. was responsible for overseeing the prescribing and medical care of the patients and the design of the study.Both authors reviewed the manuscript collaboratively.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

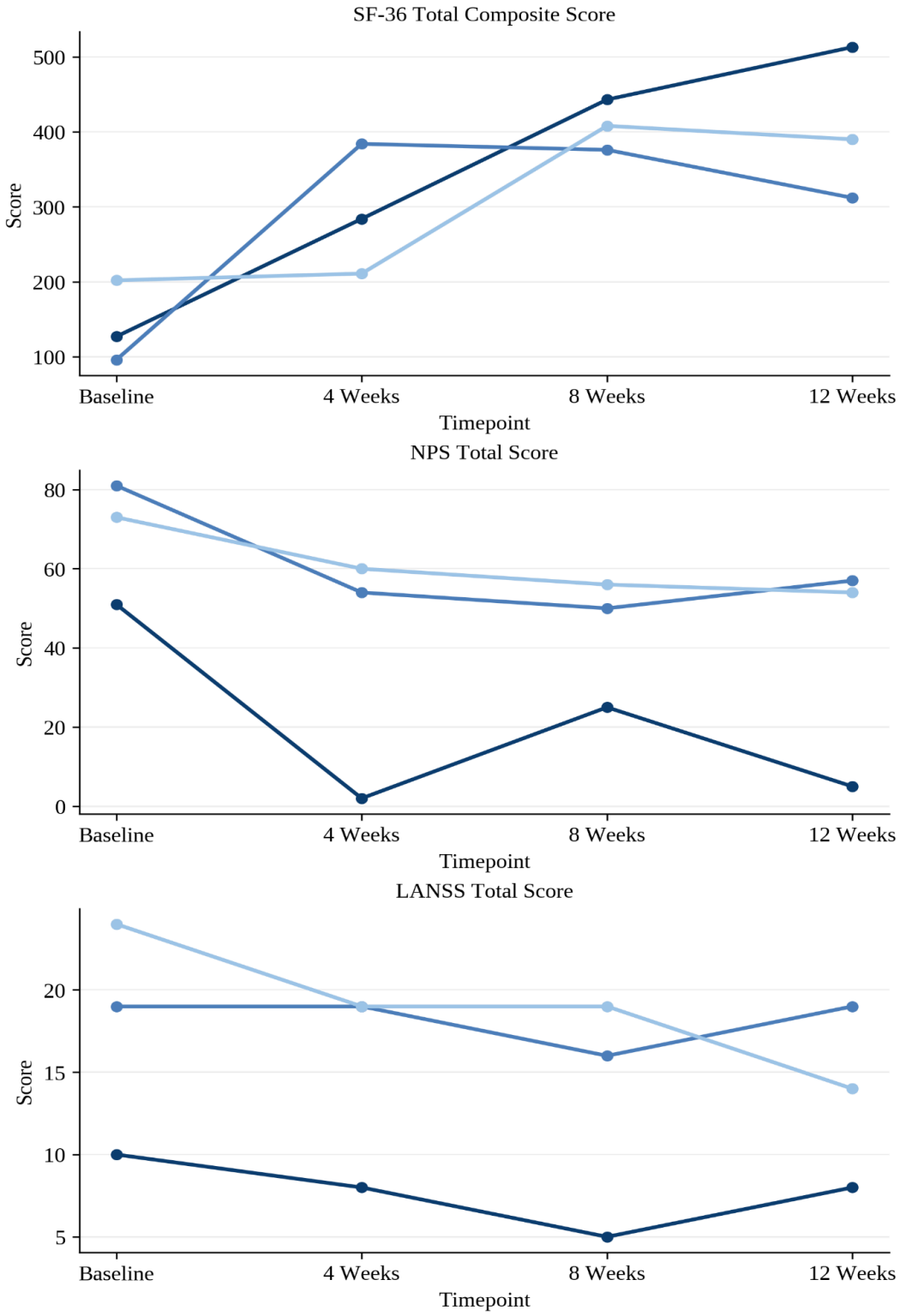


Figure 1

Individual patient trajectories across the 12-week follow-up period. The lines represent the three patients (A, B, C). Higher SF-36 total score indicates better HrQoL, whereas lower NPS and LANSS scores indicate lower neuropathic pain and symptom burden.