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Evaluation of the introduction of buprenorphine-naloxone oro-adhesive film formulation to patients in NHS Lanarkshire

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Summary

Background. A new combination formulation of buprenorphine-naloxone was approved for use in Scotland. This new preparation offered a different treatment option for patients and prescribers, but the service wanted to determine if patients were satisfied with the new formulation as a treatment option and benefits experienced. **Methods.** Patients already on the existing buprenorphine-naloxone preparation were offered the new formulation for their treatment. Those wishing to be prescribed the new formulation were asked to complete a questionnaire after a minimum of 4 weeks of the new formulation. The questionnaire evaluated the satisfaction levels of the new formulation and a number of other psychosocial aspects. The responses were analysed for any benefits or adverse effects reported. **Results.** There were several benefits reported by patients from the new formulation, both medical and psychosocial following the change. The benefits included feeling better controlled, quicker dissolution of the medication, improved relationships with family and attendance for other health related issues. **Conclusions.** The film formulation of buprenorphine-naloxone was well accepted by patients. Patients reported several benefits in comparison to their previous treatment with the sublingual formulation. The film appears to have a welcome role as a new treatment option of opioid use disorder.

Key Words: Buprenorphine/naloxone; film; evaluation

1. Background

Buprenorphine-naloxone combination product has been available as an approved licensed treatment in Scotland for opioid dependency since 2007 **[4]**. The Scottish Medicines Consortium (SMC) approved the combination product for use, and to date, this is the standard against which the SMC compares oral buprenorphine medications **[4]**.

Naloxone was added to buprenorphine as a deterrent aimed at reducing illicit use and diversion **[1-3, 8, 10, 12, 13, 15, 18]**. Buprenorphine is a partial opioid mu receptor agonist with a high affinity for receptors **[9, 17]**. The role of buprenorphine is to replace and block opioids on the receptors due to the high opioid receptor affinity. Buprenorphine has a high oral bioavailability of 35-55% **[3]**. Naloxone, in comparison, has a deficient activity if swallowed (bioavailability is less than 10%) **[3]** and is active only if inhaled (snorted) or injected, which bypasses the first-pass metabolism. Through insufflation of the combination product, the bioavailability of both buprenorphine and naloxone is increased, from buprenorphine 30% sublingual to 48% and naloxone from 10% to 30% **[6]**. The ratio of buprenorphine to naloxone is 4:1, respectively; this ratio was assessed

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based on patient safety and efficacy [14, 16]. The Scottish Medicines Consortium approved the "new" formulation of buprenorphine/naloxone in autumn 2021 [5]. This new formulation was an oro-adhesive film. The film formulation was already available in the US, Australia, and some other European countries and has been prescribed for several years. In some countries, it was the sole preparation of buprenorphine/naloxone available.

The film formulation uses a new delivery vehicle. Still, the medication combined in the preparation is the same, and the doses are the same as the sublingual formulation of buprenorphine/naloxone, already available as a licensed medication for use in treating opioid dependence. Although some evaluations have been previously undertaken in Australia, which were double-blind, randomised trials, this evaluation looked at different patient groups and time scales and concentrated on patient outcomes and feedback. The buprenorphine/naloxone film preparation continues to use the established ratio of 4-part buprenorphine to 1-part naloxone, and the only difference is the formulation. The sublingual tablets are dissolved under the patient's tongue (preferably after rinsing the mouth with water to facilitate dissolution). The tablets, however, leave a small amount of residue. The film adheres to the mucosal membranes of the cheek or under the tongue and dissolves in situ, leaving no residue.

The film formulation in Scotland provided another new treatment option for patients, an alternative to the sublingual preparation, which has been available since 2007. The advantage of the film formulation is that it rapidly adheres to the oral mucosal membranes, reducing the risk of diversion and accelerating the supervised self-administration process, allowing community pharmacies to oversee the process more quickly.

In Scotland, the Medical Assisted Treatment (MAT) standards were being introduced [7] to increase access to treatment, and encourage patients to be more involved in the choice of medication and formulations with other standards of treatment improved, e.g. trauma-informed care, links with primary care, patient advocacy etc. MAT standard 2 focuses on the availability of all licensed treatment options to patients, with patients included in the informed decision-making regarding the choice of medication [7].

As the film had not previously been available in the UK, evidence was examined from international reports regarding the new treatment option. An initial report from Australia provided information on the film compared to sublingual tablets, which provided reassurance on the formulation [11].

Patients voluntarily chose to change from sublingual tablets to try the oro-adhesive film. The formulation strengths are equal, and there is no need to change the dose. Patients' care and support were not disadvantaged if they wanted to continue with the sublingual tablets or change to the oral film.

Aim: The paper aims to evaluate and get a "real-time" evaluation of patients' perspectives on the new film formulation of buprenorphine/naloxone.

The goal is to demonstrate patients' satisfaction with the new film formulation of buprenorphine/naloxone and identify any benefits associated with the preparation over the sublingual tablet formulation.

2. Methods

All patients currently being prescribed buprenorphine/naloxone sublingual were identified using the search function on the Vision prescribing system.

All staff were educated on the film formulation, how to use it, and its potential benefits, as identified in the published article from Australia [7]. It was essential to educate staff as the film formulation differs from the sublingual tablet formulation, and they needed to be able to advise patients on how to use the formulation correctly.

Staff were encouraged to offer the film formulation to the patients currently prescribed buprenorphine/naloxone sublingual tablets at their next clinic appointment, advising them of the new formulation and its associated benefits. Patients were then offered to opt-in for the transfer or continue with the sublingual tablets, i.e. this was a voluntary opt-in to try the film with no negative consequences should they not wish to try it.

This acted as patient consent to the change, and they were reassured that if they felt disadvantages or adverse reactions from the film formulation, they would revert to the sublingual tablet preparation at any point without any changes to their treatment journey. As the film and sublingual tablet formulations were equivalent, there was no requirement to alter the dose, and the transfer between formulations would be a direct swap. Patients who want to try the film preparation will be prescribed this at the next appointment.

During the period between agreeing to try the new formulation and the first prescription, the community pharmacy that dispensed the patient's medication was contacted and advised of the forthcoming change in the patient's prescription. This allowed the community pharmacy to order the film formulation for stock and have it ready to be dispensed to the patient when they presented with their new prescription. The community pharmacies were advised of the differences in the formulations and how patients were to use the medication to ensure patients were administering the formulation correctly.

After a minimum of 4 weeks (28 days) on the film preparation, patients were asked to complete an assisted semi-structured evaluation form (Appendix A) at their next appointment with the keyworker. The

evaluation form looked at several criteria relating to substance use and other biosocial aspects to assess how patients had adapted to the new preparation. It also asked what they felt the benefits of the film preparation were as patients and any negatives they perceived/experienced.

Ethical approval was not required as this was determined as a service evaluation to determine patients' views on a new treatment option and, hence, whether the product should be offered as a choice.

3. Results

The data collection period ran from October 2021 to May 2022.

The Vision (prescribing system) used by the prescribers for patients in the service was searched, and 44 patients were currently being prescribed sublingual buprenorphine/naloxone. All 44 patients were offered an opportunity to try the new film formulation or stay on the current sublingual formulation. There was no change to treatment if patients declined to try the new formulation, and their treatment journey continued as it had been.

Twenty-three patients (52.3%) opted to try the film preparation and evaluate the treatment. From the initial cohort of 23 patients, three failed to commence treatment with the film – 2 lapsed out of treatment and one due to initial stock issues at the community pharmacy. The pharmacy had sublingual tablets but could not get films for the same day that the patient accessed treatment. After commencing the sublingual tablets, the patient no longer wanted to try the film as he were content with the treatment option provided by the sublingual tablets.

Of the 20 remaining patients prescribed the film formulation, 14 evaluations were completed (return rate of 70%) and returned for analysis.

The length of time the patients had been prescribed the film formulation was analysed, and the duration varied from 1 month (28 days) to 5 months. The average time for patients responding in the evaluation was 2.69 months (11 weeks). The daily dose of buprenorphine prescribed to the patients varied from 4 mg to 24 mg, with an average dose of 12.57 mg.

The patients reported several differences in comparison to sublingual tablets. These included the speed of dissolution being much quicker, reported by 42.9% (n=6) patients. 28.6% (n=4) of patients reported being "held better" and "getting more" from the film. Five patients (35.7%) completing the evaluation reported stopping heroin use whilst on the film, whilst 50% (n=7) of patients completing the evaluation reported reduced illicit substance use (including non-opioid substances, benzodiazepines, cocaine, and cannabis).

In response to the questions relating to possible diversion, two patients (14.3%) reported that the film formulation was harder to divert than the tablets. One of these patients reporting that diversion was harder also disclosed that they had been "snorting" the sublingual tablets previously, which they could not do with the film preparation. They had tried to "snort" the film preparation unsuccessfully.

All patients (100%, n=14) would recommend the film to others, with three patients (21.4%) stating this was the formulation they found the best "if you want to stop using". Most patients (n=13, 92.9%) reported having no complaints about the film formulation. The single patient who raised a complaint was dissatisfied with the taste of the film formulation; however, despite his complaint, the patient rationalised this and his continuation of the film by stating the sublingual tablets had a worse taste.

Patients reported other health-related benefits following the change to the film formulation, with five patients (35.7%) reporting to have engaged with other health services, e.g., attending dieticians, attending a General Practitioner regarding anxiety, seeking care for the treatment of a leg ulcer, and attending behavioural therapy.

There were additional benefits in social arrangements for patients, with two patients (14.3%) reporting positive changes to living arrangements (e.g., partner moving in with patient, patient moving in with parent to care for their parent) and six patients (42.9%) completing the questionnaire reporting improved relationships with families, partners, and friends.

Despite the evaluation being optimistic about the acceptability and the outcomes from the film formulation, two negative issues were mentioned: taste (as mentioned previously) and increased constipation. With respect to the increased constipation, this was reported by a single patient (7.1%). Although reporting constipation as a side effect, the same patient had additionally reported that the film preparation was giving him better control of their substance misuse and, as such, did not want to change.

Finally, the questionnaire looked for any recommendations from patients when using the film formulation. Six patients (42.9%) recommended putting the film on the inside of the cheek (which is suitable after the initial dose), while two (14.3%) suggested they found placing the film under the tongue was better for them. Two patients reported that you must avoid plates and dentures as the film would readily adhere to them, but adsorption could have been more effective.

4. Discussion

These discussions add local experience from Lanarkshire comparing with the report from Australia **[11]**, with similar findings.

There were few clinical differences between film and sublingual tablets. However, there were practical

improvements; the patients felt the film dissolved quicker, and no tablet residue remained, indicating a complete dissolution and dosing (it is thought that up to 40% of the sublingual dose may be swallowed as part of a tablet; thus, this percentage is ineffective).

As reported by patients, it is harder to divert. Once the film has adhered, it is very hard to remove from the site, reducing the potential to divert, and the film formulation cannot be snorted.

The film formulation facilitates the process of supervised consumption in community pharmacies easier than the sublingual tablets, and this may help reduce treatment stigma as the process is more discreet and quicker while decreasing the potential for diversion. It is reported that the tablet formulations can take between five and eight minutes to dissolve, whilst the films are reported to be quicker. The potential benefit from this faster dissolution time could be an essential factor in times of pandemic risks, etc., where we seek to reduce the exposure time of patients to potential viruses or where there can be capacity issues for the supervised self-administration of buprenorphine by patients.

It is interesting to note the reduction reported in illicit substance use, which extends further than the opioids to include benzodiazepines, cocaine and cannabis reportedly, but at this point, we cannot be sure if this has been a result of reduced exposure to dealers as not requiring opioids and not "topping up" as the film provides a more significant dose than the sublingual tablets or if this is an effect of a better dose consumption (i.e. no swallowing of residual tablets remains).

With only one side effect from the medication reported, i.e. constipation, it was interesting to note the patient reported his opioid control had improved, and this raises the consideration that the side effect may have been experienced as the patient is absorbing more buprenorphine from the film formulation in comparison to the sublingual tablets.

Patients have reported several benefits (as above), and these are, in the main, very positive. The benefits reported are not solely addiction-related, but also extend into social aspects, including relationships and wider health issues.

Limitations. This is a small study that only included existing patients prescribed buprenorphine/naloxone sublingual tablets. For a fuller evaluation, a repeat of the evaluation should be conducted after it has been used more widely on all patient groups

5. Conclusions

Buprenorphine/naloxone film has a role as a treatment option for patients who are prescribed buprenorphine. The formulation has advantages and benefits, such as those reported by the patients participating in the evaluation, e.g., quicker dissolution time and better control of symptoms. This is a valuable addition to the opioid agonist treatments available for treating opioid use disorders. However, prescribers and services must be aware that not every patient will want this formulation, nor will it suit all patients. Offering the film as a treatment option, where clinically appropriate to the patient, agrees with the recommendations of Standard 2 of MAT standards in Scotland **[7]**.

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Conflict of interest

Author declared no conflict of interest.

Ethics

Ethical approval was not required as this was determined as a service evaluation to determine patients' views on a new treatment option and, hence, whether the product should be offered as a choice.

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