Novel treatment (new drug/intervention; established drug/procedure in new situation)

Observations and hypothesis on an individual patient topically treated for capecitabine-induced Palmar-Plantar syndrome

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Summary

Palmar-Plantar syndrome (PPS) is a common side effect of oral capecitabine—a chemotherapeutic agent used as an adjuvant treatment for colorectal cancer. A 66-year-old man suffering from grade II PPS described how Germolene New Skin, a topical healing agent, provided relief from the pain associated with this syndrome and a return to normal function. The patient's observations form the basis for some interesting hypotheses regarding the natural progression of PPS and the potential of New Skin to alleviate pain. Caution must be exercised at this stage as these are single case observations; however, they may be worthy of further exploration in a randomised controlled clinical trial.

BACKGROUND

Palmar-Plantar (PPS) is a well-documented side effect of oral capecitabine. A recent randomised controlled trial (RCT) reported that 44% of patients suffered from grade II or III PPS while receiving treatment.¹ Current recommendations state that chemotherapy should be terminated until the symptoms of this syndrome stop. In a single case, New Skin (New Skin product ingredients: ethyl acetate, alcohol denat, nitrocellulose, *Ricinus communis*, isopropyl alcohol, amyl acetate, isobutyl alcohol, camphor, parfum (includes benzyl alcohol, citronellol)) appeared to allow alleviation of pain associated with PPS while continuing a course of chemotherapy. The patient did not seek further medical advice during the treatment cycle due to the beneficial effects of New Skin application and, therefore, treatment dose remained unchanged. Clearly, these observations are limited to the experiences of a single patient and may not be representative of a wider patient cohort. A controlled clinical trial would establish whether the benefits observed are transferable to other patients on capecitabine. This would also address any potential concerns over capecitabine toxicity secondary to maintaining dosage.

CASE PRESENTATION

The patient, a 66-year-old Caucasian man, presented with a 2-week history of rectal bleeding associated with an increased frequency of bowel motions. Colonoscopy showed a sigmoid tumour at 18–21cm and histology confirmed a moderately differentiated adenocarcinoma subsequently staged as a pT4 N0 M0 with anterior perforation. Anterior resection of the rectum was followed up by adjuvant chemotherapy. He received eight cycles of oral capecitabine, 1250 mg m² twice daily for 14 days and repeated every 21 days. At follow-up clinic, after his third cycle, PPS had developed, which was recorded as grade I. These symp-

toms advanced to grade II by his fifth cycle where he described them as extremely debilitating and limiting to his normal manual activities. Pyridoxine 50 mg three times a day was prescribed to address these symptoms in an attempt to maintain treatment dosage but was stopped by the sixth cycle as it had been ineffective. At this time, the patient reported the beneficial effects of New Skin for alleviating pain. This had resulted in full compliance with dosage without the patient seeking further medical advice midcycle. He described a reduction in pain that was secondary to an apparent healing of the fissures and which allowed a return to normal function. No analgesics were prescribed or used by the patient during the eight cycles of capecitabine.

A pain score was conducted by the patient as an appropriate method for objectively scoring this improvement during his seventh cycle. The pattern was further confirmed by detailed observations made in the eighth cycle. The patient's observations reveal some interesting insights into the natural progression of PPS and create a hypothesis for the possible beneficial effects of New Skin application.

OUTCOME AND FOLLOW-UP

The patient experienced fissuring in his fingertips during the seventh and eighth cycles. These symptoms corresponded to grade II of the National Cancer Institute grading system.² He recorded the pain that resulted on a 0–10 basis throughout the 2 weeks on chemotherapy and the following treatment-free week (see figure 1).

His pain rating showed a similar pattern during both cycles. This involved pain preceding the appearance of fissures by 2 days and subsiding during the treatment period. Fissures were also noted during the treatment-free week, which were less painful and tended to subside more quickly.

Figure 1 Patient-rated pain score during the seventh cycle of capecitabine. The treatment was continued for 14 days (1–14) with a rest week before the next cycle (15–21). First two fissures occurred on day 7 on the left hand and were treated with New Skin. A further fissure occurred on day 9 and New Skin was applied. Symptoms resolved by day 14. A further, less severe, fissure arose in the treatment-free week, which resolved by day 21.

DISCUSSION

Our results suggest two novel findings regarding the natural history of PPS and the use of New Skin.

Our patient demonstrated a trend whereby pain was perceived at the site of the fissures before their physical appearance. This has not been described elsewhere. It appears from speaking to other patients that this is a common finding and would be worthy of further investigation.

The patient's pain score decreased to 0 within 4 days of the most severe rating. While previous treatment cycles had resulted in considerable loss of function due to PPS, the application of New Skin coincided with return to normal activities secondary to the relief of pain. Recent studies have reported termination of capecitabine until grade II fissures had healed.^{1 3 4} Where treatment had continued, fissures progressed resulting in skin breakdown, desquamation, bullous formation and secondary infection.^{3 5} In severe cases there have even been reports of palmoplantar keratoderma.⁶ Our patient continued treatment at the same dose without requesting medical advice and suffered none of these sequelae. There is no published evidence to date that suggests that patients are able to continue with capecitabine despite grade II PPS without the mentioned complications. Indeed, all recommendations suggest termination of chemotherapy until the fissures have healed.¹ This difference is possibly attributable to the effect of New Skin protecting the wound from mechanical damage and promoting healing.

New Skin is a product of Germolene (Bayer plc, Leverkusen, Germany) and is advertised as providing 'a waterproof and germproof barrier to protect minor skin wounds'. The observation of pain relief could be considered an unexpected positive outcome of the treatment. There are no apparent contraindications to its use alongside capecitabine. A number of other therapeutic agents have been cited

for the relief of PPS of which pyridoxine appears to be the most popular.⁷ However, the data are far from convincing and show little apparent benefit both in its use prophylactically and for symptomatic relief.^{8 9}

The patient's observations suggest that New Skin may alleviate the pain caused by PPS. We hypothesise that this may result from the provision of a mechanical barrier, which may also promote healing. These findings may warrant further investigation in a RCT. This could determine whether New Skin has a role to play in providing symptomatic relief from PPS. Furthermore, it would address any concerns over potential toxicity that could arise from maintaining capecitabine dose regimen.

Learning points

- A recent RCT reported that 44% of patients suffered from grade II or III PPS while on oral capecitabine.¹ This indicates a requirement for an agent that will effectively address this common side effect.
- The observations regarding New Skin have come to light as a result of a patient's initiative to actively control his symptoms. An exploratory trial among other patients could determine whether these observations are common enough to pursue a RCT. This would also address the potential risks of toxicity associated with continuing treatment.
- The application of robust clinical criteria could determine whether New Skin permits safe continuation of chemotherapy without dose reduction.

Competing interests None.

Patient consent Obtained.

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