

Implementing evidence-based supportive care for patients with skin toxicity associated with epidermal growth factor inhibitors in an ambulatory care setting

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Abstract

Background Epidermal growth factor receptor inhibitors (EGFRI) cause skin toxicity in the majority of patients who receive them. Evidence-based guidelines aim to reduce the severity and duration of skin toxicity which causes physical discomfort and impacts negatively on patients' quality of life.

Methods A pre/post-audit design was utilised at an ambulatory cancer care centre in a tertiary metropolitan hospital. Data were collected and audited from January 2018 to December 2019.

Results Documentation for 16 patients was reviewed against best practice recommendations. Barriers to evidence implementation and strategies to improve supportive care were identified and implemented. A post-implementation audit of 13 patients demonstrated that implementation strategies improved the delivery of supportive care.

Conclusion Targeted nurse education and dermatological toxicity-specific documentation are effective strategies for improving the implementation of evidence-based supportive care for patients with EGFRI skin toxicity.

Background

Epidermal growth factor receptor (EGFR) is essential for normal skin structure and function. It is normally expressed in a variety of epidermal cells such as undifferentiated, proliferating keratinocytes which are found in the basal and suprabasal layers of the epidermis of the skin^{1,2}. The role of EGFR includes stimulation of epidermal growth, inhibition of differentiation and acceleration of wound healing³. EGFR expression is an important feature of normal skin development and assists in the normal function of skin, sebaceous glands, sweat glands, hair and nails⁴. EGFR is known to be over-expressed in many solid tumour cancer cells, including colorectal cancer, head and neck cancers, lung cancer, breast cancer and pancreatic cancers^{2,5-7}.

Epidermal growth factor receptor inhibitors (EGFRIs) target the over-expression of EGFR in specific cancer cells by blocking the normal receptor pathway to reduce tumour growth^{3-6,8}. This blocking mechanism disrupts the normal expression of EGFR causing an inflammatory response and subsequent cutaneous injury; it is the inflammatory response that commonly causes dermatological toxicity in patients receiving EGFRIs^{1,2}. There are two classes of EGFRi, specifically monoclonal antibodies and tyrosine-kinase inhibitors^{2,8}. Monoclonal antibody EGFRi treatments have improved outcomes for advanced cancers with associated progression free survival, particularly in metastatic colon cancer. Two such drugs are commonly administered intravenously in the ambulatory care centre, Cetuximab and

Panitumumab^{2,3,5,9}. Despite the known benefits of this treatment, it is estimated that greater than 80% of patients receiving anti-EGFR therapies experience skin toxicity^{3,5,8,10–13}. Skin toxicity in patients receiving this treatment typically presents as a papulopustular rash, dry skin, pruritus and paronychia and symptoms are severe in 10–20% of patients^{3,5,9}. The intensity of skin toxicity varies between individuals; however, the reason for the significant variability of toxicity is not known⁹.

Due to the impact of skin toxicity, treatment with EGFRIs is frequently modified, discontinued or, in some cases, ceased altogether, thus negatively impacting the efficacy of treatment and potential subsequent progression free survival^{2,5,9,14}. EGFRi skin toxicity also impacts on patients' quality of life and can have a profound psychological impact^{4,9,14–16}. In addition to discomfort and distressing physiological symptoms of pruritus, pain and burning, patients report severe impact on their usual activities of daily living and the avoidance of socialising. Several papers report that poor body image leads to further emotional and psychological symptoms^{2–5,9,17}.

Research has shown preventative, pre-emptive skin care strategies can mitigate the intensity of skin toxicity in some patients and in turn the impacts on their quality of life and psychological wellbeing^{5,16–21}. In 2011 the Multinational Association for Supportive Care in Cancer (MASCC) published evidence-based guidelines for EGFRIs⁶. The guidelines recommend the early implementation of supportive care strategies to delay severe skin toxicity and reduce the need for dose reductions, treatment interruption and discontinuation of treatment^{5,19,22}. Evidence-based recommendations for supportive care in preventing and managing EGFRi skin toxicity include patient education at the initiation of EGFRi treatment, including information about frequent moisturising of the skin throughout treatment and avoidance of sun exposure. Health professional education that facilitates an understanding of EGFRi skin toxicity and related skin assessment and documentation is also recommended^{1,5–7,11–14}.

This evidence implementation project was instigated following a patient report about receiving conflicting advice from members of the multidisciplinary team regarding optimal management of their EGFRi skin toxicity. The patient reported receiving limited education about optimal skin care strategies, despite reporting that her skin toxicity had negatively impacted her quality of life and had increased her distress.

Aim

The aim of the project was to implement evidence-based supportive care for patients with skin toxicity associated with EGFRIs in an ambulatory care setting.

Methods

Design

This evidence implementation project was conducted using a pre/post-audit design. The project was conducted from January 2018 to December 2019.

Setting

The project was undertaken in the ambulatory cancer centre of a large metropolitan hospital in Queensland, Australia. The ambulatory cancer centre has 40 treatment chairs and delivers cancer treatments to around 70–100 adult patients per day. Within this setting approximately 50 patients receive EGFRIs as part of their treatment regimen per year.

Ethical considerations

A submission was made to the hospital Human Research Ethics Committee (HREC) requesting ethical exemption on the basis that the project was directly related to routine patient care and posed no additional risks to standard care. Ethical exemption was granted as well as local governance and privacy office approvals to ensure the project was performed within a safety and quality framework.

Sample

Eligible patients that met the project inclusion criteria were identified from a report generated by the patient integrated management system used in the department. The sample for the baseline audit was all patients receiving EGFRi therapies during the period January – June 2018. The initial report generated 30 patients which included oral and intravenous EGFRi therapies; however, a significant issue was identified in the patient group receiving oral therapy which required separate education and attention, therefore only patients receiving intravenous EGFRi therapies were included (n=16). The sample for the post-implementation audit was patients receiving intravenous EGFRi therapies during the period June – December 2019 (n=13). Some patients were receiving EGFRi therapy for both data collection periods; however, the post-implementation sample excluded patients who were included in the pre-implementation sample as data regarding EGFRi supportive care had previously been collected. The nursing documentation of all identified patients was reviewed using the audit tool developed for the project.

Development of an evidence-based audit tool

The Multinational Association for Supportive Care in Cancer (MASCC) Clinical Guidelines for the prevention and treatment of EGFRi toxicity⁶ are evidence-based guidelines identified as the optimal benchmark and standard of care to underpin the project. The MASCC guidelines and supporting evidence were used to develop the audit tool for this project (Table 1).

Data collection

All data for the audit was collected from the patients' healthcare records. Questions 1, 2 and 3 of the audit collected data on whether patients received education and written information about skin toxicity and skin care strategies prior to receiving EGFRi therapy. Questions 4, 5 and 6 collected data on the presence of skin toxicity, use of relevant terminology, and documented skin assessment.

Identifying barriers and strategies to change practice

Findings from the pre-implementation audit informed the identification of barriers preventing the implementation of evidence-based supportive care. The implementation phase included the identification and implementation of strategies to overcome these barriers. The post-implementation audit, using the same criteria as the pre-implementation audit, was carried out to determine the success of the implementation strategies on improving evidence-based supportive care for patients receiving EGFRi with skin toxicity.

Results

Patient characteristics

The pre-implementation audit included 16 patients; 10 were male and six female with an age range from 34–73 years. The post-implementation audit included 13 patients; eight were male and five female with an age range from 35–78 years. All patients in both the pre- and post-audit data analysis had received intravenous Cetuximab for either metastatic colorectal cancer (n=24) or head and neck squamous cell carcinoma (n=5).

Pre-implementation audit

The pre-implementation audit demonstrated limited compliance with the recommended clinical guidelines, revealing that only 13% (n=2) of patients receiving EGFRi therapies had received specific education and information about skin toxicity and recommended skin care strategies. Skin toxicity was reported in 69% of patients (n=11). For these 11 patients, the use of

terminology to describe their skin was poor, with the term 'rash' used consistently in all patient records. Specific EGFRi skin toxicity manifestations were reported in 25% (n=4) of all records where skin toxicity was reported. The generic skin toxicity assessment tool within the hospital's documentation system was completed for 50% (n=8) of the pre-implementation group but documentation failed to provide detail of the type of skin manifestation present.

Implementation phase

Further to a review of the findings of the pre-implementation audit, barriers to implementing evidence-based practice were determined and strategies to improve the implementation of EGFRi supportive care were identified. The lack of education and information provided to patients about skin toxicity and the use of a generic skin assessment tool were considered to be fundamental barriers to evidence implementation.

Implementation strategies were developed and delivered over a period of 12 months comprising two approaches – the delivery of education and training to nursing staff, and the creation and implementation of a specific assessment document to record EGFRi skin toxicity. Education sessions were delivered by a cancer care coordinator who had received education about EGFRi skin toxicity management and principles of oncology. Evidence-based learning materials were used to deliver EGFRi toxicity education to chemotherapy nurses. Four face-to-face small group education sessions were integrated into the existing education schedule in the department, with between four to six nurses attending each session. Six nurses from the department also attended an external comprehensive education event on EGFRi skin toxicity management facilitated by an external drug company that manufactures EGFRi therapy; 14 out of 19 nurses (74%) attended at least one of these events.

The project lead (CK) collaborated with hospital personnel responsible for the patient integrated management system (where nursing documentation is recorded), to create and

Table 1. EGFRi skin toxicity evidence implementation project audit criteria

Audit criteria (pre/post-implementation)	
1	Is there documented evidence that the patient received education about the specific skin toxicity side effects associated with EGFRi treatment?
2	Is there documented evidence that the patient received written information relating to specific skin toxicity side effects associated with EGFRi treatment?
3	Is there documented evidence that the patient received written information outlining the recommended self-care skin care strategies?
4	Is there documented evidence that the patient experienced skin toxicity related to EGFRi?
5	Is there documented evidence of any of the following? <input type="checkbox"/> papulopustular / acneiform / follicular rash <input type="checkbox"/> hair changes / trichomegally <input type="checkbox"/> dry skin / xerosis <input type="checkbox"/> paronychia
6	Was the skin toxicity tool completed?

implement a new and specific EGFRi nursing assessment document within the existing system. The MASCC EGFRi Skin Toxicity Tool (MESTT)²³ was used to inform the content for the specific EGFRi nursing documentation.

Post-implementation audit

The post-implementation audit (n=13) demonstrated improved compliance with evidence-based guidelines with an improvement in all audit measures. Figure 1 illustrates the difference in compliance with evidence-based supportive care between the pre- and post-data collection periods.

In the post-implementation audit 85% (n=11) of patients received education regarding EGFRi skin toxicity compared to only 13% (n=2) in the pre-implementation audit. An improvement from the pre-audit was also evident in the provision of written information to patients regarding skin toxicity from 13% (n=2) pre-implementation to 69% (n=9) post-implementation. Similar outcomes were evident in regards to the provision of written directions about skin care strategies. Interestingly, skin toxicity was reported in 100% of patients in the post-implementation audit and had been more accurately described using specific terminology, e.g. ‘papulopustular rash’ rather than ‘rash’.

The newly created EGFRi dermatological nursing assessment had been completed for 92% (n=12) of patients in the post-

implementation audit. Although there was a record of skin manifestation in the pre-audit, Figure 2 illustrates the lack of specific terminology documented in the pre-audit compared to use of accurate terminology in the post-audit. Documentation of terminology had improved after the implementation strategies, with all patient records including an appropriate description of the skin manifestation in addition to the use of correct terminology to describe conditions of trichomegally, xerosis and paronychia.

Discussion

The overall project results demonstrate an improvement in the supportive care of patients with skin toxicity associated with EGFRi. The initial pre-implementation findings support a previous systematic review that suggested that, despite availability of good evidence to prevent and manage EGFRi skin toxicity, the implementation of guidelines frequently failed to reach clinical practice¹⁵.

Cancer nurses routinely deliver patient education about treatment-related side effects and are responsible for ensuring tailored education and information is provided to patients and their families prior to and throughout their treatment and cancer care trajectory²⁴. Nurses also play a significant role in the management of skin care, which is regarded as a fundamental element of nursing practice²⁵, therefore their role in the delivery

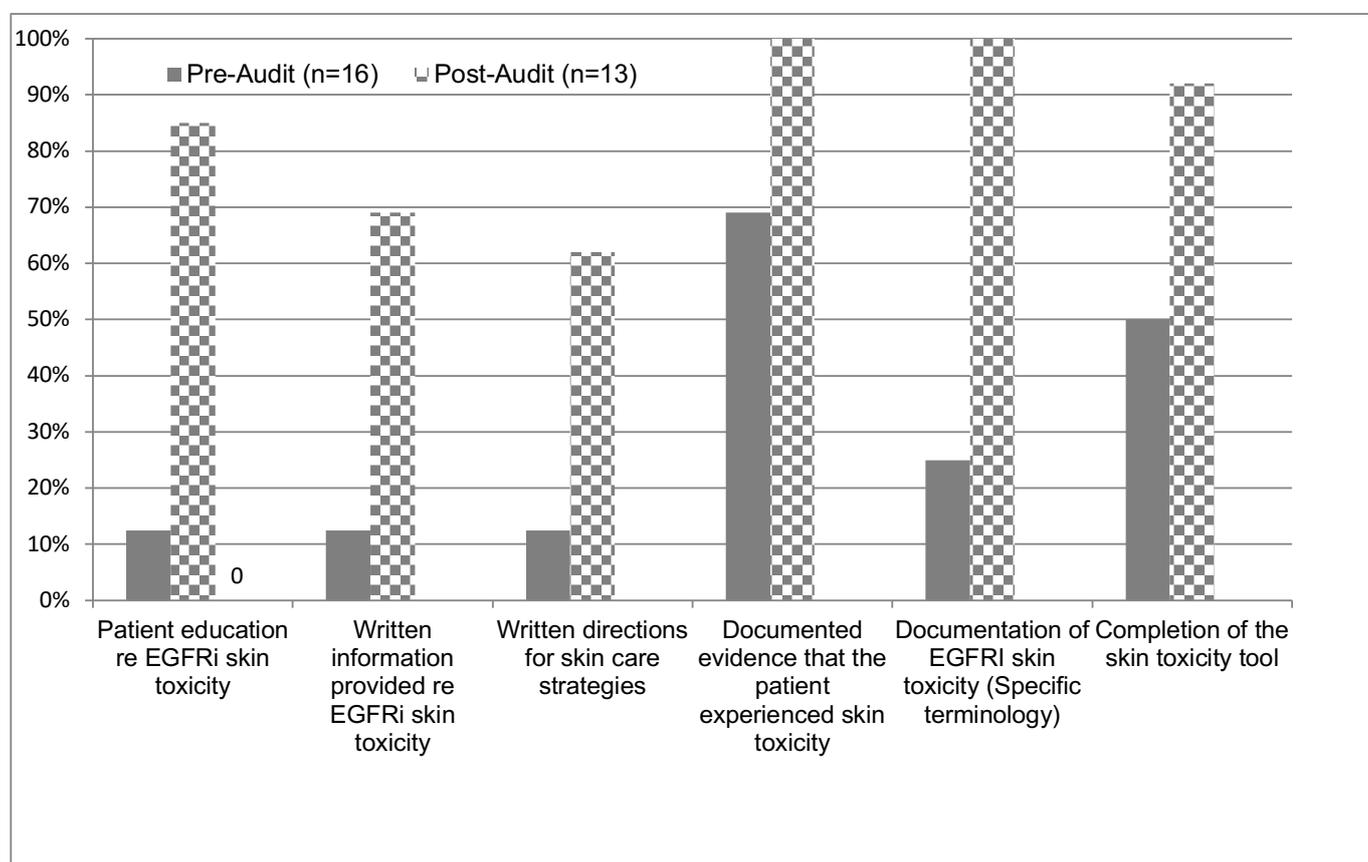


Figure 1. Compliance with evidence-based supportive care for EGFRi

of supportive care for EGFR skin toxicity is appropriate and important. Cancer nurses are well positioned within the team to play a central role in delivering tailored patient education and supportive care to minimise the impact of EGFR skin toxicity^{7,22}; however, nurses may lack confidence in applying evidence-based practice in dermatological care²⁵. The results of this project are similar to an implementation project undertaken in China which demonstrated that education of clinicians and patients in regards to EGFR skin toxicity did not occur routinely and was greatly improved through the implementation of nurse education¹¹.

Nurse education

Nurses require knowledge about general and specific side effects of cancer treatments if patients are to receive optimal evidence-based care. Cancer nurses are typically not trained in oncodermatology principles, resulting in a lack of knowledge about appropriate skin care, limited dermatological assessment skills, and limited understanding of dermatological terminology¹¹. The field of oncodermatology within cancer nursing is an increasingly important area with the growing prevalence of dermatological symptoms in cancer care settings beyond anti-EGFR therapy, particularly with the increased use of immunotherapy²⁶. Indeed, in their review of adverse events from immunotherapies and novel therapies, Ciccolini et al.²⁷ report on the necessity of nurses to be skilled in both dermatological assessment and accurate grading of dermatological adverse events. Their findings reinforce the importance of cancer nurses acquiring and advancing dermatological knowledge and skills

in an environment where an increasing number of novel cancer therapies are delivered. Given the increase in the delivery of immune-related therapies which have a dermatological toxicity profile of up to 50%^{26,28}, cancer nursing education programs should equip nurses to further develop their knowledge and skills in dermatological assessment, related supportive care strategies, and documentation utilising appropriate grading tools.

Nursing documentation and assessment

This project found that the current generic nursing documentation and assessment tool in use was limited in its specificity and capacity to record and monitor EGFR-specific skin toxicities. Our findings support previous studies which found that the development of specific and focused assessment tools would ensure more accurate monitoring of EGFR toxicities and implementation and evaluation of related supportive care measures^{14,16,29}. Further work was published during the conduct of this project describing the development of a comprehensive skin assessment instrument that extends beyond a single therapy and considers the impact of skin toxicity on quality of life¹⁴.

The lack of appropriate documentation for reporting EGFR skin toxicity in this setting appears to have led to the frequent use of generic terms. This project highlighted that the use of the term 'rash' in routine nursing practice prevents ongoing accurate assessment of the skin, lacks detail of the type of skin manifestation, and prevents the systematic evaluation of implemented supportive care strategies and treatment. The

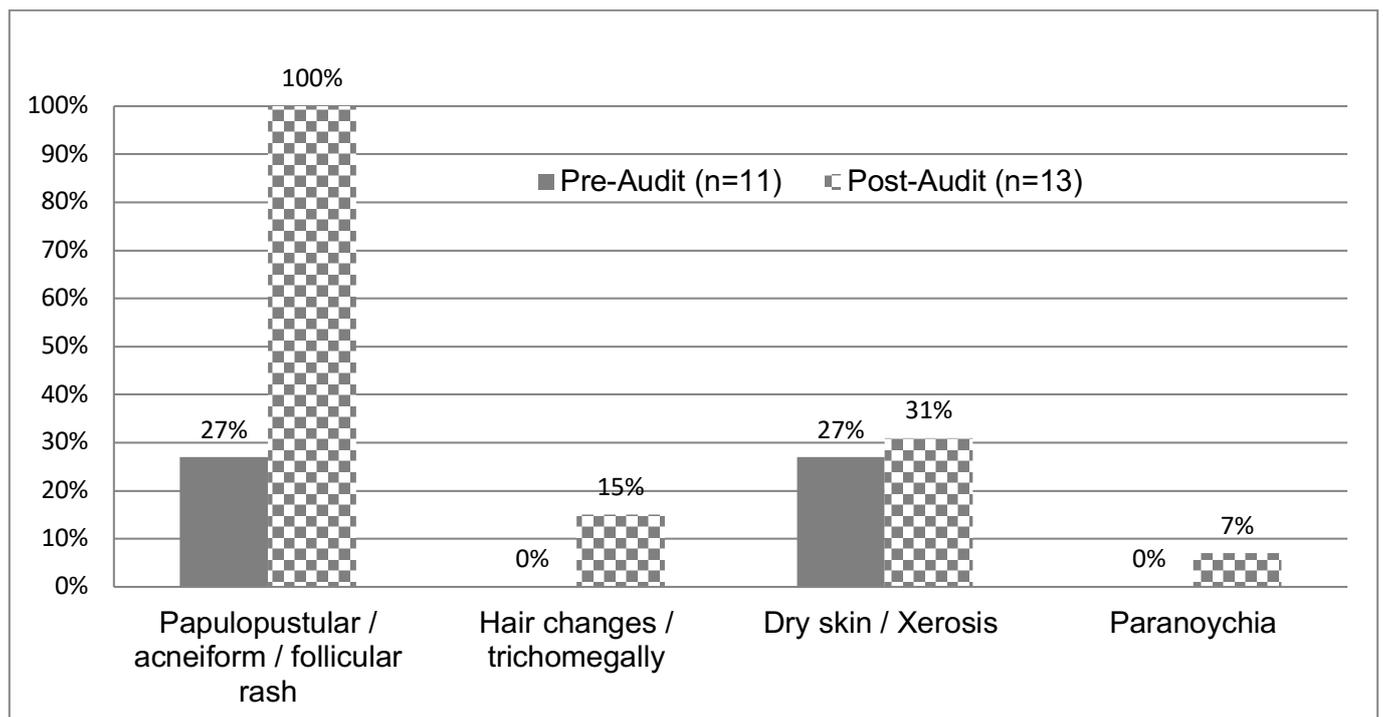


Figure 2. Documented terminology of skin toxicity

importance of accurate terminology in monitoring EGFRi toxicity has previously been reported as a crucial factor in optimal evaluation of adverse events and management²⁹. Consistency in education, evaluation and use of terminology is essential when caring for patients with skin toxicity and supports patient perspectives of being well cared for. Educating nurses on the importance of correct and specific terminology resulted in significant improvements in patient documentation in our context and such education strategies could be implemented in other settings.

A significant limitation of this project was identified during the pre-audit data collection process whereby a consistent and significant gap was noted in the implementation of nursing assessment for all patients receiving oral cancer therapies. Significant disparities between the supportive care of patients receiving oral EGFRi compared to those receiving intravenous EGFRi were evident. A decision was made to exclude patients receiving oral EGFRi therapy from this project, with further work to address the needs of this specific group to be undertaken by the clinical department. This finding is an important learning outcome that may be relevant in other settings where disparities in access to supportive care may exist between patients receiving oral and intravenous cancer therapies; acknowledgement of disparities should be addressed to ensure the delivery of high quality evidence-based care for all patients, irrespective of their cancer therapy.

This project demonstrated the importance of listening and responding to the unique patient experience and how this approach can assist health service providers to identify areas of improvement that lead to optimal patient outcomes. In acknowledging the diverse role of the patient in contemporary health services, consideration should be given to accurately monitoring skin toxicity in cancer patients and understanding the real impact on patients and their functional, social, psychological and physical wellbeing^{15,21}.

Conclusions

Skin toxicity is a significant problem for most patients receiving EGFRi treatments and, although supportive care strategies can reduce the severity and duration of these toxicities, they are not routinely implemented. Patients receiving intravenous EGFRi require information about skin toxicity and recommended skin care strategies. Cancer nurses are ideally placed to deliver this care but require specific education in dermatological toxicity. Further education and training in the principles of oncodermatology is recommended as a core competency for cancer nurses and especially for those delivering EGFRi and newly emerging therapies in the ambulatory cancer care setting. Cancer therapy documentation systems and processes should incorporate assessments and grading tools that are specific to the therapies being given to ensure toxicity is closely monitored and appropriate and timely supportive care is delivered.

Conflict of Interest

The authors declare no conflicts of interest.

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