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Editorial

Is 5-Fluorouracil Cream Chemoprevention for Actinic Keratoses

According to the National Population-Based Cancer Registry, skin cancer accounted for 2.5% of all malignancies in Indonesia between 2013 and 2017. Non-melanoma skin cancer (NMSC) is more common than melanoma.[1] Sunscreen is essential for preventing skin cancer as a primary chemopreventive measure, while secondary chemoprevention helps suppress and reverse carcinogenesis (agents could be administered topically or systemically). Tertiary chemoprevention aims to reduce recurrence and metastasis.[2]

Actinic keratosis (AK) is a very common neoplastic intraepidermal squamous proliferative lesion associated with ultraviolet radiation exposure and characterized by squamous dysplasia. AKs may remain stable, regress spontaneously, or progress to invasive squamous cell carcinoma (SCC). According to the ICD-O coding of skin tumours, AK is a premalignant keratosis and a precursor of skin tumours.[3] Currently, topical 5-fluorouracil (5-FU) cream, diclofenac sodium gel, imiquimod cream, ingenol mebutate gel, and tirbanibulin have been approved by the FDA for the treatment of AK.[2]

Compared with other targets of secondary chemoprevention, the skin is easily accessible. 5-FU is a chemotherapeutic drug that acts as a pyrimidine analogue by being misincorporated into RNA and DNA in place of uracil or thymine, thereby causing the death of rapidly proliferating cells. The topical use of fluorouracil has a selective cytotoxic effect on actinically damaged skin, while normal skin is relatively unaffected.[4] Walker JL et al. (2017) found that topical 5-FU for AKs remained effective after treatment was discontinued, with more than a 60% decrease in the number of new AKs on the face and ears at 6 months, and the effect persisted for at least 2 years.[5] Weinstock MA et al. (2018) conducted a study of 5-FU treatment for AKs on the face and ears and found that it reduced the need for surgery for SCC for 1 year without significantly increasing the risk of BCC.[6]

Further studies are needed to provide evidence that 5-FU could be used as chemoprevention for AK, since 5-FU is efficacious, inexpensive, practical, and has manageable adverse effects. Therefore, any treatment that reduces the development of SCC or other keratinocyte carcinomas could be cost-effective and decrease the tumour burden.

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