LIFE-SAVING ADVANCES IN SKIN CANCER TREATMENT

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ABSTRACT

AIM: This study aims to find out about life-saving advances in skin cancer treatment.

INTRODUCTION: Skin malignant diseases are those that emerge from the skin. They are due to the development of abnormal cells that can invade and spread to different parts of the body there are three types of skin cancer- basal cell carcinoma, squamous cell carcinoma and melanomas. Hereditary factors strongly influence the risk factor of skin disease and malignant growth. Basal cell malignant growth develops gradually and can harm the tissue around it, however, it does not spread to distant areas or result in death. Squamous cell skin disease is bound to spread. Melanomas are the most aggressive. Although hereditary variables may have the least impact on skin management growth, most skin cancers are caused due to exposure to UV radiation.

MATERIALS AND METHODS: Review of various scientific literature was done in preparation of the manuscript. Several databases were searched for relevant articles from pub med and Google scholar. Databases of individual journals were searched for keywords such as skin cancer, sunlight on skin cancer, treatment, advances, prevention etc. The exclusion criteria were case reports, review and studies in other languages.

CONCLUSION: From the review, we can know about many recent advances for the cure of cancer. Personalised vaccines, cell therapy, gene editing and micro-treatment are newer technologies for treating cancer. In future cancer can also become a curable disease.

KEYWORDS - Skin cancer; UV radiation; immunotherapy; chemotherapy; photodynamic therapy; prevention.

INTRODUCTION

Skin malignancies are diseases that emerge from the skin. They are caused due to the development of abnormal cells that can invade and spread to different parts of the body. There are three fundamental sources of skin cancer- basal cell carcinoma, squamous cell carcinoma and melanoma[1]. Basal cell carcinoma and Squamous cell carcinoma are also known as nonmelanoma skin cancer. Basal cell malignant growth develops gradually and can harm the tissue around it, however, it does not spread to distant areas or result in death[2]. It frequently shows up as a painless area on the skin that may be gleaming with little veins running over it or may present as a raised zone with an ulcer. Squamous cell skin disease is bound to spread. It is generally seen as a hard lump with a scaly top but may also form an ulcer[3] Melanomas are the most aggressive; signs incorporate a mole that has changed in size, shape, shade and has unpredictable edges, they have more than one colour, it is itchy or bleeds[4]

Hereditary factors strongly influence the risk of skin malignant growth. Some of the features that individual attributes for getting skin cancer are; having a normal bright complexion tone, light-hued eyes,

blonde or red hair, dysplastic nevi or numerous regular moles, and skin that burns, wrinkles, redness or become painful after too much time in the sun[5]. Having a past analysis or family and history of skin malignant tumour will also increase the risk. Less obvious genetic factors such as gene variants or mutation also play some role in melanoma. Melanocyte, cells found on the basal layer of skin give skin and eyes their shading, and a hereditary factor used to create a particular measure of melanin[6] The measure of melanin or level of pigmentation is contrarily related with the sun which causes skin malignant growth. Melanin retains and disperses radiation from UV light, shielding the epidermal cells from harm[7]

Although hereditary factors may have the best impact on skin malignant growth, all skin cancer are additionally related at any rate to some extent to UV presentation[8]. UV radiation activates the melanocytes to create melanin, which can show up as tanned skin; and causes harm to the skin. Skin cells and DNA; are increasingly exposed and can bring about burn from the sun, indicating cell death. UV radiation is one part of electromagnetic radiation estimating in frequency from 100 to 400 nm[9]. There are three subtypes of UV radiation UVA, UVB, and UVC. UVA beams have the longest frequency, estimating from 315 to 400 nm[10] They are not consumed by the ozone layer and enter profoundly into the skin, through the epidermal intersection where the melanocytes dwell in the basal layer[11]. UVB beams or shorter, estimating from 280 to 315 nm. Both UVA and UVB radiation can bring about a tanned appearance. UVB makes a tan by expanding melanin creation that gives a negligible measure of photoprotection, compared to about an SPF of 3, and shows harm to the skin. Overexposure of UV B radiation causes erythema, swelling and pain, and signs of sunburn[12]

Cancer has likely been around as long as humans have. However, throughout the years our capacity to test for the illness and treat it has incredibly improved. More individuals who get the disease are living longer[13]. Some are being relieved. Our immune system hunts down and kills invaders like bacteria and viruses. It additionally searches out and destroys cancer as they form[14]. But cancer has developed ways to hide from your immune system. It can develop even if our body tries to stop it[15]. Immunotherapy enables our immune system to assault malignant growth. It prevents cancer from hiding, it boosts the immune system against cancer. Checkpoint inhibitors, our immune system has contenders called T cells [16]. They look for and decimate outside cells, including malignant growth. Monoclonal antibodies, our immune system makes proteins called antibodies to help it spot invaders like bacteria and viruses. Each antibody seeks out another protein, called an antigen, on the surface of an invading cell[17]. Adoptive cell transfer, this technique utilises our immune cells to treat cancer. Specialists take a cell from keratinocyte derived tumours such as basal cell carcinoma and squamous cell carcinoma[18]. Other tumour types are Kaposi Carcinoma and cutaneous T lymphoma. The clinical contrast between basal cell carcinoma and squamous cell carcinoma could not be more striking[19]. NMSC is one of the commonest malignancies, among all the other cancers, morbidity and mortality are low, and therapy is usually straightforward and effective[20]. Whereas in melanoma incidence is one to two orders of magnitude lower, but case fatality is 25% and treatment of all but the earliest lesions is dismal[21]. However the two types of tumours have things in common, both are related to sun exposure and the necessary diagnostic suspicion almost entirely on clinical trials[22].

Way of life changed during the previous five decades, with an expansion in the exposure to daylight due to open-air exercise and Sunbathing regularly brings about skin cancer[23]. Chronic UV exposure, skin ageing, wrinkles, uneven skin pigment, loss of skin elasticity and disturbance of skin barrier junction causes changes in tumour[24]. Previously our team had conducted numerous clinical trials[25,26][27–31] and lab animal studies[32–36] and in vitro studies[37–39] over the past five years. Now due to global warming and erratic climate change, the incidence of skin cancer is on the rise. So the idea of this review

is to highlight the various treatment modalities available for the treatment of skin cancer in today's advancing medical field. .The idea for this review stemmed from the current interest in our community.

MATERIALS AND METHODS

Review of the scientific literature was done in preparation of the manuscript. The system and databases were searched for relevant articles from pub med and Google scholar. Databases of individual journals were searched for keywords such as skin cancer, sunlight on skin cancer, treatment, advances, prevention etc. The exclusion criteria were case reports, review and studies in other languages.

DISCUSSION

Skin cancers are classified into two based on their biological and clinical differences as melanoma skin cancer and non-melanoma skin cancer [40]. The majority of nonmelanoma skin cancer causes changes in the skin that superimpose the alteration of chronological ageing. The development of SCCs, BCCs and threatening melanoma are regularly connected with sunburns[41]. Chronic exposure to UV rays is known as the most significant hazards factor for the advancement of actinic keratoses. Exposure to UV radiation during adolescence and puberty causes a future for the development of skin cancer. The epidemiology implicating UV exposure as a cause of melanoma is further supported by biological evidence by the damage caused by UV radiation, particularly damage to DNA, plays a central role in the development of melanoma. UV exposure patterns have been associated with the improvement of various sorts of skin Malignant growth and at different anatomical distribution patterns.[42] Chronic cumulative exposure including occupational outdoor exposure has been related all the more regularly with BCC and SCC skin cancer[43]The distribution of BCC by anatomical site varies by histological type with nodular BCC most commonly appearing on the head and superficial BCC most commonly occurring on the trunk[27]. SCC skin cancer, melanoma is generally associated with intermittent exposure and a history of sunburn[44].

Photodynamic treatment is a non-invasive technique that includes photosensitising medication, and its ensuring indication by light to deliver receptive oxygen species that explicitly obliterate target cells. As of late photodynamic therapy has been broadly utilised in treating nonmelanoma skin malignancies[45]. The photosensitisers regularly utilized are 5 aminolevulinic (ALA) and it's esterified subordinate methyl 5 aminolevulinate which are for runners of the endogenous photosensitizers protoporphyrin 9. After treatment with ALA or methyl 5 aminolevulinate, protoporphyrin 9 especially collects in the injury region of different skin ailments which permits PDT, as well as fluorescence finding with ALA, instigated porphyrins[46]. Photodynamic therapy requires the presence of three key elements: light, photosensitizers and oxygen. After exposure to a specific wavelength of light, the photosensitizers are emitted from a grounded state(S0) to an excited state (S1)[47]. Then it undergoes an intersystem crossing to a long-lived excited droplet state(T1). The photosensitizers at T1 state can undergo two types of reactions; either a type 1 reaction through hydrogen or electron transfer with the production of free radicals or a type 2 reaction through energy transfer to oxygen. The singlet oxygen damage occurs at the site of a generation and it affects all intracellular components like proteins, lipids and DNA[48]

Adoptive cell therapy. It's a promising type of immunotherapy which misuses the antitumor properties of lymphocytes to eradicate essential and metastatic tumours cells. Lymphocytes are isolated from patients' peripheral blood tumours draining lymph nodes or tumour tissues, expanded en Vivo and rein-fused back into the patient.[49]. This procedure would, in principle go around the confounding obligation of breaking tolerance of tumour antigen and produce a large amount of high avidity effector T cells. To be sure, in the course of the last few decades, autologous T cell treatments have shown their capabilities to accurate sensational clinical reactions[50]. ACT with tumour infiltrating lymphocytes is a methodology where T cells, by and large blends of CD 8+ and CD4+ T cells developed from respected metastatic tumours stores are collected and extended before transfer. This approach attempts to reverse the functional impairment of

the tumour specific T cells that reside within the tumour and caused by the immune suppression tumour microenvironment, by growing them before their reinfusion of various cytokines[51]. Ongoing efforts in not only at improving TIL therapy but also on broadening TIL to fight against malignancies. Advances in T cell culturing methods and genetic T-cell engineering ensures that clinically relevant numbers of tumour-specific T cells can be generated and delivered as therapy [52]

The UV radiation from indoor tanning beds is a gathering cancer-causing agent, in a similar class as tobacco or asbestos. Preventing cancer-causing exposures can bring about forestalling malignant growth[53]. Indoor tanning is evaluated as the cause of over 45,000 new skin malignant growths, including more than 1000 melanomas, each year. Despite significant interest in prevention efforts are taken by putting up several well-designed campaigns by the centres of disease control and prevention and foundation focused on skin cancer prevention. Established effective strategies for skin cancer prevention are also underused. Comprehensive sun protection programmes that emphasise shade and sun-protective clothing should be implemented widely[54]. Shade structures in the playground and giving free sunscreen dispenses outside are innovative ideas that should be evaluated[55]. Physicians and the public should remain alert about the indoor tanning industries which use the same technique used by the tobacco industry, paying to bring doubt to the evidence, making false advertising about the health benefits of training, and undermining the scientific consequences on the adverse health effects of indoor tanning should be done [56].

Basic pharmacological therapy. Although the gold standard treatment for NMSC is surgical excision, topically applied 5- fluorouracil and Imiquimod can also be used for the treatment for BCC. Morbidity and mortality have significantly decreased by the introduction of newer drugs that regulate some key receptors and the immune response[57]. For treating malignant melanoma drugs like dacarbazine, temozolomide or carboplatin/paclitaxel can be used. Vismodegib is the first oral selective inhibitor of the Hedgehog signal pathway. It binds to the transmembrane proteins and inhibits the pathway and also inhibits tumour growth[58].

Nanotechnological therapy. Many different types of nanoparticles have been studied for treating skin cancer, some of them are liposomes, dendrimers, polymersomes, carbon-based nanoparticles, inorganic nanoparticles, and protein-based nanoparticles[59]. Recently many studies have been discussing the different new possibilities of combining pharmacological agents and diagnostic procedures[60]. Most of the conventional drug systems are accompanied by unwanted side effects that are mainly attributable to their nonspecific redistribution and uncontrollable drug-releasing characteristics. However, nanomaterials can increase the target specificity as well as the uptake and selective accumulation near a tumour due to the enhanced permeability and retention effect. This in turn leads to lower drug doses and reduces unwanted side effects on healthy tissues[61]. These systems because of their size and circumvent filtration through the kidneys allow them to stay for a longer period in the bloodstream[62].

Vaccines for treating cancer. Cutaneous papillomaviruses are associated with specific skin diseases, such as extensive wart formation and the development of non-melanoma skin cancer (NMSC), especially in immunosuppressed patients. Human papilloma vaccines confer type-restricted protection against HPV types 6, 11, 16 and 18, responsible for 90% of genital warts and 70% of cervical cancers, respectively[63]. However, they do not protect against less prevalent high-risk types of cutaneous HPVs. Over the past few years, several studies explored the potential of developing vaccines targeting cutaneous papillomaviruses. These vaccines showed to be immunogenic and prevent skin tumour formation in certain animal models.

Vaccines are made from cancer cells. One such vaccine is sipuleucel T (Provenge) it treats prostate cancer that spreads[64]

CONCLUSION

From this review, we can know about many recent advances for the cure of cancer. And they are life-saving treatment. The research can be further continued to know more about cancer and its recent development. Researchers have been done to tame the immune system to fight against cancer and get as close to a future where cancer can become a curable disease. Personalised vaccines, cell therapy, gene editing and micro treatment are some of the newer technologies for treating cancers. In future cancer can also become a curable disease.

AUTHOR CONTRIBUTION

Yazhlini P contributed to the data acquisition and drafting of the manuscript. Dr Jayalakshmi Somasundaram contributed to the design, editing and critical revision of the manuscript.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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