

Incidence of Skin Cancer – A Long Term Outcome of Immunosuppression in Renal Transplant Recipients Associated With The Usage of Azathioprine

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Background: The main cause of mortality in Kidney Transplant Recipient's is malignancy. The cancer incidence is increased by treating with immunosuppressive agents and longer grafts survival of kidney. Multiple studies have indicated that there is an increased incidence of melanoma and non-melanoma skin cancer in immunosuppressed Kidney Transplant Recipient's(KTRs).

Methods: This is a long term retrospective single centre study to evaluate the incidence of skin cancer, comprising of about 941 patients who had transplants between 1998 to 2018 at University Hospital Coventry and Warwickshire NHS Trust (UHCW) with a follow up period of 1 to 20 years. The average dose of immunosuppressant Azathioprine administered to study subjects was calculated with the range of 6 months, 1, 5, 10, 15 and 20 years respectively. The standard maintenance dose of Azathioprine was 50-125mg daily by clinical guidelines of UHCW NHS Trust. As per clinical guidelines by UHCW, KTRs who received standard dose i.e. 25-100mg were included in low dose group and the dose greater than or equal to 100mg were under high dose group. The demographic and clinical characteristics of patients (such as gender, age at transplantation, ethnic group and type of transplant) and biopsy results of the KTR's were obtained from the Clinical Results Reporting System (CRRS) and Proton; and patients with histologically proven skin cancers and pre cancers as well as post-transplant lymphoproliferative disorder (PTLD) and other skin disorders were identified. A Chi- Square test of independence was used to compare the association of skin cancer incidence with high and low dose of Azathioprine in KTRs with characteristics of patients such as gender, ethnic group, type and transplant and age of transplant.

Results: Out of 941 patients, KTRs excluded from the study were 77 (KTRs) with incomplete data or no data, 10 had pre-transplant skin cancer diagnosis [these includes Actinic Keratosis (AK) and Bowen's Disease (BD)] and 425 KTRs who did not receive immunosuppression therapy with Azathioprine at any point and 170 KTRs who received a combination of Azathioprine and Mycophenolate Mofetil at some point during the follow up period. As a result, 259 KTRs who received immunosuppression therapy with Azathioprine alone were included in the study. While a total of 34 patients were diagnosed with skin malignancies of which Basal Cell Carcinoma (BCC) (8), Squamous Cell Carcinoma (SCC) (8), Kaposi Sarcoma (1), patients with both BCC and SCC (7), Post Transplant Lymphoproliferative Disorder (PTLD) (2) and Pre-cancers (8). Among the KTRs with confirmed skin cancer diagnosis, 28 received Azathioprine low dose [25-100mg] and 6 received Azathioprine high dose [\geq 100mg].

Conclusion: Based on the findings it concludes that Azathioprine was associated with a significant risk in the incidence of skin cancer. The immunosuppressive regimens which were widely used in earlier years carry out risks for carcinogenicity after kidney transplantation. Long-term follow up and patients on Azathioprine after transplantation resulted in significant impact on the incidence of skin cancer.