Targeted alpha therapy for thyroid cancer: Radiation-induced toxicity of $^{211}$At$\text{NaAt}$ in mice\(^1\)

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Radioactive iodine (RAI) therapy is used for the treatment of patients with differentiated thyroid cancer.\(^1,2\) However, a percentage of patients shows insufficient $^{131}$I accumulation\(^3\) or low therapeutic effect even with enough $^{131}$I accumulation, and some patients suffer from recurrence or metastases and become RAI-refractory during follow-up.\(^4,5\) For these patients, a more effective treatment is required.

Astatine ($^{211}$At) is a halogen with chemical properties similar to those of iodine, but it emits alpha particles, and we have found that the radiochemical purity of astatide dramatically improves upon treatment with 1% ascorbic acid. Consequently, the uptake of $^{211}$At increases in the thyroid gland and thyroid cancer cells.\(^6\) In this study, we evaluated the radiation-induced toxicity of different doses of $^{211}$At$\text{NaAt}$ solution at different time points to estimate its time-dependent toxicity.

**Methods**

The biodistribution of $^{211}$At$\text{NaAt}$ was measured in normal ICR mice ($n = 12$) and the absorbed doses in major organs were calculated.

Groups of ICR mice ($n = 60$) were injected with 0.1 MBq or 1 MBq of $^{211}$At$\text{NaAt}$ using saline as the control group ($n = 30$). Their body weight and food intake were followed up for 60 days. The blood cell count and serum level of biochemical parameters were measured 3, 7, 15, 29, and 60 days after injection. Histological analyses of major organs with hematoxylin and eosin staining were performed.

**Results**

Figure 1 revealed a high-absorbed dose in the thyroid gland, stomach, bladder, heart, lungs, spleen, kidneys, and testes. The 0.1 MBq group showed no abnormalities. The 1 MBq group showed decreased body weight and food intake. Figure 2 showed that hematological toxicity was mild and transient. The total cholesterol, albumin, and total protein increased with no signs of recovery, which can be attributed to hypothyroidism. Figure 3 showed atrophy and fibrosis in the thyroid gland and a transient hypospermagenesis was found in the testis of one mouse on day 29.

**Conclusion**

High-dose administration of $^{211}$At$\text{NaAt}$ showed transient toxicity in the white blood cells and testis without severe hematological or renal toxicity, suggesting its tolerable safety as targeted alpha-therapy for differentiated thyroid cancer in the 1 MBq group.

**References**


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