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Radionuclide Therapy in Paediatric Patients

Radionuclide therapy uses radioactive substances for the selective delivery of radiation to tumors or target organs, providing a valid alternative to surgery or traditional medical treatments in paediatric patients.
In particular, it combines the advantage of target selectivity and therapeutic strategy with curative intent or for disease control and palliation.

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key points

- Radionuclide therapy is a specialised area of nuclear medicine that uses radioactive compounds able to release high-energy ionizing radiations.
- In paediatric patients, the use of radionuclide therapy is validated, safe and effective for the treatment of several benign and malignant diseases.
- The identification of patients who may benefit from radionuclide therapy is crucial in order to improve outcome and limit radiation exposure.

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Introduction

Nuclear medicine is a branch of medicine based on the administration of radiopharmaceuticals, radioactive compounds able to reproduce biological, cellular or metabolic pathways.
The radioactive isotopes can be used individually or combined with different molecules and, according to their decay properties, may have diagnostic and/or therapeutic applications.
In particular, α- and β-emitters are able to release low-range highly ionizing radiation, allowing for therapeutic effects.

Radionuclide therapy is a specialised area of nuclear medicine that uses radioisotopes for therapeutic purposes and it is widely used for the treatment of several benign and malignant conditions. Radionuclide therapy has been demonstrated to be safe and effective also in paediatric patients.

Children are considered more vulnerable as compared to adults because of their longer life expectancy. Moreover, several malignancies typically show a more aggressive clinical behavior in paediatric patients as compared to adults.
Therefore, the availability of concrete therapeutic options is mandatory in these patients.

Historically, Iodine-131 (131I) is the most widely used radionuclide therapy agent in children. It has the ability to be taken up into well differentiated follicular cells of thyroid epithelium.

This therapy is currently performed for the treatment of benign conditions such as hyperthyroidism or malignant diseases such as differentiated thyroid cancer (DTC).

In children, DTC accounts for 21% of all head and neck tumors, with an increasing incidence rate of approximately 1% per year. Differently from adults, they typically present with more advanced disease at diagnosis, with extensive lymph nodal involvement and distant metastases. Moreover, the rate of recurrence seems to be higher in paediatric patients, leading to frequent re-operations or additional treatments. Despite this evidence, prognosis remain excellent and it seems to be related to several prognostic factors, including tumor type and younger age. In children with DTC, the initial treatment consists of surgery, that can be

radical or more conservative determined by extent of disease. Then, in patients identified as at intermediate-high risk of recurrence, radioactive iodine treatment is recommended. In these patients, DTC are usually highly iodine avid, and show an excellent response to 131I therapy. Several authors reported improved survival, decreased disease progression, and lower recurrence rates in patients with advanced DTC who received postoperative radioactive iodine therapy.

Another validated application of radionuclide therapy in children is the treatment of metastatic or recurrent neuroblastoma not responding to conventional treatment. Neuroblastoma is the most common malignant extracranial solid tumor of childhood, derived from the sympathetic nervous system chain. Meta-iodobenzylguanidine (MIBG) is an analogue of the norepinephrine that, once injected, is taken up by cells rich in sympathetic neurons by an active uptake process, mediated by the norepinephrine transporter.

In order to enable therapeutic effects, MIBG can be labeled with 131I. In children with advanced disease treated with multiple administrations of 131I -MIBG, excellent results in terms of disease control have been achieved. Moreover, this radionuclide therapy seems to be well tolerated and toxicity is limited to hematological side-effects. Currently, 131I -MIBG represent the best palliative treatment in these patients; the combined administration of radionuclides and chemotherapy agents has been proposed as an additional opportunity in paediatric patients with advanced neuroblastoma. However, available data is still limited and further studies are needed.

Radionuclide therapy in paediatric patients can thus be safe, efficient and well tolerated, however several issues still remain to be addressed.

Recently, several radiotracers able to bind to specific targets of disease have been proposed and validated in adults, yet not in paediatric patients as the role of these agents has not yet been elucidated.

Radionuclide therapy in paediatric patients can thus be safe, efficient and well tolerated, however several issues still remain to be addressed

For example, radiolabeled somatostatin analogues currently represent the main therapeutic option in adult patients with gastro-entero-pancreatic neuroendocrine neoplasms. In children, the role of these radiopharmaceuticals has not been fully clarified, but encouraging results emerged from some preliminary data(references maybe?). As mentioned above, it should be considered that paediatric patients represent a very radiosensitive category, due to growing processes and higher life expectancy. Therefore, the optimisation of therapeutic protocols and an accurate selection of paediatric patients who may really benefit from radionuclide therapy is mandatory, in order to improve outcome without significant adverse effects.

Conclusion

In the era of precision medicine in adults, radionuclide therapy may also likely represent a valid, highly-specific therapeutic option in paediatric patients. In the future, the availability of new radioactive agents, the identification of more specific disease targets and the optimisation of administration protocols will contribute to an even more effective treatment of several benign and malignant disease in children.

Conflict of Interest

None. ■

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