I-131 THERAPY

i) HYPERTHYROIDISM

ii) THYROID CANCER

Tc-99M

I-123

I-131
• **I-131 THERAPY FOR HYPERTHYROID PATIENTS**

• **IODINE RADIO-ISOTOPES FOR THERAPEUTIC USE**

• **HOW DOES THIS WORKS??**

• **FACTORS THAT INFLUENCE THE EFFICACY OF THE RA I-131 DOSE**

• **AIM OF THE TREATMENT**

• **COMPLICATIONS AND RISK FACTORS**

• **DOSAGE AND MEASUREMENT UNITS**

• **THERAPY PROCEDURE AND INFORMED CONSENT**

• **WHAT HAPPENS TO THE PATIENT AFTER THE THERAPY WAS GIVEN??**

• **FOLLOW UP AND ADJUVANT TREATMENT eg B BLOCKERS, ANTI-THYROID MEDICATION**
IODINE RADIO-ISOTOPES:

- For therapy the I-131 is the agent of choice,
- with both Beta and Gamma rays that are being emitted.
- The Beta particles causes ionizing effects by a path length of 2 mm,
- allowing a localized irradiation of the thyroid tissues alone.
- Practically no effects on the surrounding tissues.
I-131:

- Half-life = 8.02 days, the physical half life is long enough for uptake and organification by the Follicular thyroid cells.
- Beta emission energy is 0.61MeV, this energy from the path length of 1-2mm B-ray, is enough to destroy the follicular cell.
- It’s high energy Gamma radiation results in poor images, contributes to the whole body radiation burden and adds to the radiation dose delivered to staff and relatives.
• It is a halogen that evaporates, causing ingestion by staff dispensing the dose and contamination of the atmosphere. This risk can be minimized by using the I-131 capsules.
• Is a cheap radionuclide, also readily available and the liquid form makes oral administration simple.
• Since 1940 this has become the most common treatment for thyrotoxic adults, it is safe and effective, but may require more than one dose.
• Regular checks of thyroid uptake and personal dose meters are essential in those workers regularly administrating I-131.
Dietary Iodine**

- Is essential for the synthesis of thyroid hormones.
- ** Sources of Dietary Iodine: egg seafood, fresh water fish, fresh vegetables and fruits except spinach), cereal grains, meats, milk, eggs, sea salt, iodized table salt, red food coloring agents like erythrosine, kelp or algae products and cod liver oil)
- ##The normal human daily requirement is 76-150 micrograms
**RAI TREATMENT**

- When the RAI treatment is administrated orally to thyrotoxic patients, the RAI is metabolic incorporated into the follicular thyroid cells,
- resulting in the intra-cellular delivery of Beta-radiation doses to
- this metabolic overactive follicular thyroid cells
- --- with their subsequent destruction.
- The physical quantity of the iodine in RAI is very low ±1 microgram##
- Side effects of this amount of iodine are very rare!!!!
- Seldom headache, vomiting and nausea
How does it work???

1) RA I-131 is administrated orally

2) It is rapidly and completely absorbed from the stomach

3) Quickly accumulates in the overactive thyroid gland and is used in the synthesis of thyroid hormones in the place of stable dietary iodine (uptake and organification take place – RAI is trapped in the thyroid)

4) Provokes an acute inflammatory response in the thyroid gland, (Intense radiation thyroiditis) which is followed by cellular necrosis, atrophy and fibrosis with chronic inflammatory respons.)
- 5) Loss of active thyroid gland tissue and loss of capacity to synthesize and release thyroid hormones
- 6) Thyroid sized is reduced
- 7) Hyperthyroidism is cured

The extent of this reaction depends on:

a) the % of RAI activity absorbed by the overactive thyroid
b) the radio-sensitivity of the thyroid
FACTORS THAT INFLUENCE THE EFFICACY OF THE RA –131 DOSE:

• Functioning mass of the overactive thyroid → a mean thyroid size is 15-30g. It is also difficult to establish it clinically or with a Tc-99M thyroid scan.

• The presence of uniform or multi nodular thyroid tissue (cystic/solid cold nodules present on the Tc-99M thyroid scintigraphy)

• **Uptake of RA I-131 as being calculated using a tracer dose before the actual therapy.** (we use this method as our dosage determining factor!) = The absorbed dose determination method.

• {06h00 and 24h00 I-131 uptake determination is being done}
• Tempo of radio-iodine clearance from the thyroid → influenced by exogenous Iodine factors eg drugs and dietary contents

• The radio sensitivity of the thyroid gland.

• All this factors also determine the dose of RA given to the patient

• dosage determining factors:
  - thyroid uptake,
  - effective half life of the I-131,
  - thyroid volume

• Little consensus exists among centers concerning the best method of dose selection!!!

• RAI treatment could face a 34% failure rate when it was given after pre-treatment with propyl-thio-uracil ---- > a LARGER DOSE of RAI will be required in such patients.

• Iodine skin preparations and iodinated contrast medium radiological investigations, must also be avoided.
AIM OF THIS TREATMENT/END RESULTS??

1) To induce cellular hypo function of this overactive thyroid cells.
2) To reduce the hyper secretion of the thyroid hormones
3) To achieve rapid improvement of the hyperthyroidism
4) To restore the euthyroid state in a hyperthyroid patient is very difficult!!!

This euthyroid state is frequently temporary and is followed by either hypothyroidism or hyperthyroidism again.

HYPO THYROIDISM remains the most likely result OR is considered to be the desired consequence.
COMPLICATIONS:

• Radiation thyroiditis: With transient thyroidal pain/tenderness. Treat with analgesics for local discomfort.

• Sial adenitis

• Transient exacerbation of the hyperthyroiditis symptoms due to systemic release of thyroid hormones. It is self limiting but can precipitate thyroid crisis/storm in patients > 40 years or patients with symptoms of co-existing cardiac/medical illnesses/symptoms.

  \[Rx = \text{Continue with B Blocker therapy}\]
- Transient/Permanent hypothyroidism, it is difficult to predict when the thyroid insufficiency will happen. It develops progressively, and can occur 2-6 months after treatment. It is easily corrected with (Eltroxin) replacement therapy. Do regular S-TSH levels.
- Hypo-parathyroidism, especially after treatment for post-thyroidectomy recurrence
- Risk of worsening the opthalmopathy
- Risk of residual/recurrent hyperthyroidism
- Osteoporosis risk due to elevated levels of thyroid hormones and the calcitonin dysfunction after RAI treatment
RA MEASUREMENT UNITS:

1) SI units for the absorbed dose:
   Gray (Gy)  \( 1 \text{Gy} = 100 \text{ rads} \)

2) SI unit which accounts for the biological consequences of radiation of different tissues:
   Sievert (Sv)  \( 1 \text{Sv} = 100 \text{ rem} \)

3) Amount of radio-activity: Is expressed in
   mega bequerals (MBq) OR milicurie (mCi)
   \( 1 \text{ mCi} = 37 \text{ MBq} \)
   (A 5 mCi dose = 185 MBq I-131 gives a radiation dose of the same order of magnitude as some common radiological procedures eg IVP/BA enema)

4) 5-15 mCi Delivers 4000 – 20,000 rads to the thyroid
RA I-131 THERAPY DOSAGE:

• A 50 – 100 Gy dose to the thyroid can cure the over activity of a Grave’s gland (50 – 100Gy = 5,000 – 10,000 rads)

• The Usual sufficient intra-thyroid absorbed dose of 150Gy is efficient for the Hyperthyroidism of Grave’s (± 10mCi)
• There can be persistent or recurrent hyperthyroidism present after this treatment: 60Gy = 46%
• 150Gy = 14%
• This recurrence rate can cause problems in patients with heart disease, it is then necessary

• **to use an ABLATIVE regime OF 300Gy.** (±20mCi)

• ( according to Goolden and Davey → 300-400 Gy is the minimum radiation dose for complete ablation of normal thyroid tissue)
• This therapy is not to establish an euthyroid state, but to control hyperthyroidism rapidly, by inducing hypothyroidism deliberately with lifelong hormone substitution, and no second RAI dose necessary.

• This ablative regime’s incidence of hypothyroidism is:
  86% after 3/12
  93% after 18/12
• This ablative treatment should be used restrictively.
**HOW THIS CAN BE USED TO CALCULATE THE DOSE:**

<table>
<thead>
<tr>
<th>5mCi</th>
<th>10mCi</th>
<th>12mCi</th>
<th>15 mCi</th>
<th>20mCi</th>
<th>30mCi</th>
</tr>
</thead>
<tbody>
<tr>
<td>4000rads</td>
<td>8000 rads</td>
<td>9600 rads</td>
<td>12,000 rads</td>
<td>20,000 rads</td>
<td>24,000 rads</td>
</tr>
<tr>
<td>40Gy</td>
<td>80Gy</td>
<td>96 Gy</td>
<td>120Gy</td>
<td>150Gy</td>
<td>240Gy</td>
</tr>
</tbody>
</table>

**This means:**
If the 24h00 I-131 uptake is 100%, and the patient is treated with 10mCi RAI, the thyroid will get ±80Gy/8000rads of radiation.
We were afraid to give to high dosages and the final scheme looks like this:

<table>
<thead>
<tr>
<th>24h00 I-131 Uptake %</th>
<th>Total mCi dose given</th>
<th>mCi took up by thyroid</th>
<th>Gy</th>
<th>rads</th>
<th>Recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>10</td>
<td>10</td>
<td>150</td>
<td>15,000</td>
<td>14%</td>
</tr>
<tr>
<td>90</td>
<td>10</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>80</strong></td>
<td><strong>10</strong></td>
<td><strong>8</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>12</td>
<td>8,4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>12-15</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>15-20</td>
<td>10</td>
<td>150</td>
<td>15,000</td>
<td>14%</td>
</tr>
<tr>
<td>40</td>
<td>&gt;20</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RISKS OF RAI TREATMENT:

1) EFFECTS OF RADIATION EXPOSURE:
   -- teratogenicity
   -- genetic damage
   -- carcinogenesis
   -- cell dysfunctions
   a) whole body irradiation (GI system, bladder and gonads is the other organs most likely to be exposed to radiation)
   b) local effects on the thyroid itself (hypothyroidism)
TERATOGENICITY: Avoid this!!

- NB NB Verify that the patient is NOT PREGNANT! at the time of treatment!!!!!!
- You MUST OBTAIN A NEGATIVE PREGNANCY TEST!!
- OR
  - HISTORY OF MENSTRUATION WITHIN THE LAST 5 DAYS prior to the treatment BUT it is less accurate!
- OR
- ENSURE ADEQUATE CONTRACEPTION is being used
- AND
- BE CAREFUL IN POST MENOPAUSAL women whose last period finished more than 10 days previously.
• Radiation exposure:

• in early stages of pregnancy (before 9 weeks of pregnancy) → re-assure, fetus cannot be harmed by small amounts of exposure

• beware of large dose radiation exposure AFTER 10 WEEKS OF PREGNANCY!!! The fetus thyroid gland starts it’s iodine concentrating mechanism during this time (12 weeks) and can be damaged, causing fetal hypothyroidism, neonatal goiter and asphyxia

• (Iodine deficiency at the 14 weeks pregnancy stage is the most common nutritional cause of impaired brain development)
GENETIC DAMAGE:

• The risk of genetic damage by a 3 rad exposure is estimated at 0.005%
• This risk is orders less than the spontaneous risk of such abnormalities which is about 0.8%
• If treated with I-131 for Grave’s: it is recommended that the patient DELAY ANY PREGNANCIES FOR 4-6 MONTHS
• Children treated with I-131 therapy have shown no adverse effects.
CARCINOGENESIS:

- NO evidence was found that I-131 induced leukemia or any other CA of the breast or GIT tissue
- NO links was found between RAI treatment for Grave’s and Thyroid CA --- head and neck irradiation is associated with an increased rate of thyroid ca’s)
- ( A higher rate of benign thyroid adenomas was found when RAI was given when patients were children/young adults)
CELL DYSFUNCTION:

- RAI induces cellular hypo function of the thyroid gland
- First 4-10 days post treatment: transient radiation thyroiditis may develop, with gland tenderness and exacerbation of the hyperthyroidism symptoms
- NB NB The RAI treatment only treats the hyperthyroidism in Grave’s disease = the immunological disorder persists!!!
- This increases the risk for Grave’s ophtalmopathic effects or the pre-tibial myxedema, and RAI treatment can aggravate these entities if they are already present.
- Meganism: due to the TSH receptor antibodies binding to orbital fibroblasts + local release of cytokines + progressive inflammation
- NB NB Anti thyroid drugs have an immuno-suppressive effect, and could theoretically protect against opthalmopathy(post RA treatment, wait 5 days and start with neomercazole .)
2) EFFECT OF A POTENTIAL RADIATION HAZARD CONSTITUTED BY EACH RA PATIENT AFTER RAI Rx

• This radiation hazard is to individuals who comes into contact with the RA patient – radiation sources are the patient himself (with the RA in his thyroid), as well as his secretions eg urine (and sweat and saliva in ablation dose patients)

• Patients must be advised BEFORE treatment of the following: (both verbal and written instructions must set out the limitations applicable to the treatment)

• All this limitations and restrictions is designed to reduce the dose of radiation to members of the public and their families/caretakers.

• The annual dose limit for members of the public is 5 mSv
• The total dose of radiation received by a person/individual depends on:
  --- TIME and DISTANCE spend near a RA person
  --- DOSE rates at several distances depending upon renal functions, thyroid retention of activity, patient size and the use of drugs that affects the kinetics of iodine
• RAI treatment of 800MBq (20mCi) or less can be given on an outpatient base, PROVIDED they abide by the restrictions.
• Patients receiving more than 30mCi must be hospitalized and special precautions must be taken for those involved in the administration of this dose and for the daily care of this patient!!
Restrictions:

• Avoid prolong contact with pregnant women and small children and babies, other people must be 2 meter distance away from them especially in the first 2 days after the treatment.

• Travel requirements: avoid traveling in public transport for 11-19 hours eg after 500-600 MBq(16 mCi) or public transport time with other people must not be more than 7h/day.

• Patient will need time from work to prevent contact with pregnant fellow employees and children/babies.

• Sleep apart from their partner in different beds for ±2 days.

• Hand washing and toilet flushing after frequent bladder emptying + intake of sufficient volumes of fluids during the first 2 days, to get rid of the excess RAI not trapped in the thyroid.
WHAT HAPPENS TO THE PATIENT AFTER THE RAI TREATMENT???

• 1) The effects will not be seen immediately after taking the treatment, it takes 8-12 weeks before the maximum effects can be evaluated.

• 2) If follow-up blood for S-TF is taken within the first 4 weeks post treatment, the results can be confusing, because of the radiation thyroiditis effect → the thyrotoxic state can worsen, that's why the patient must continue to use their B-Blocker therapy in this period (up to 3/12)

• 3) The best follow-up method is the S-TF, 5 weeks post treatment to detect hypothyroidism and treat it → this is being done by the referring doctors (and not at the Nuclear medicine Dept)

• 4) If the patient is still thyrotoxic 3 months post treatment, the whole procedure is started all over again, and follow-up RAI treatment can be recommended (preferable a higher dose this time in comparison to the first dose)