THE NORTHERN HOSPITAL

THYROXINE OVERDOSE

The Diagonal of May 25, 1963 (to Constantin Brancusi) 1963, Dan Flavin.

"One may not think (much) of light....but I do and it is....as plain and open and direct an Art form as you will ever find". ***Dan Flavin.***

Throughout the long history of Art, it is a recurring motif that the emergence of new Art forms is very often the result of a reaction to that which has preceded it. It was almost inevitable therefore that in 1959, at the very peak of American Abstract Expressionism, (which itself had largely succeeded Surrealism during the years of the Second World War) a new Art form would suddenly burst onto the scene. It was introduced by the "Black Paintings" of Frank Stella at an exhibition, known as "Sixteen Americans" at the Museum of Modern Art in New York City. Abstract Expressionism when it first appeared, had been disconcertingly obscure to most of the general public, but with the increasing fame of its leading protagonists, such as Jackson Pollock, Willem de Kooning, William Baziotes, Clyfford Still and Mark Rothko, if not an understanding then at least a certain familiarity had begun to be established. But then just at this point, to everyone's total confusion, a bold new statement was made…against the Abstract Expressionists! And if Abstract Expressionism had been puzzling then Minimalism took things to a whole new level again!

Minimalism's prime directive was to remove the tortured emotional subjectivism of Abstract Expressionism and replace it with cool reason and almost mathematical uncomplicated impartiality. There would be nothing at all to try to "understand" - Frank Stella himself explained simply, "what you see is what you see…." no more and no less. Every piece of Minimalist Art was to be considered without obscure agenda, without hidden emotional symbolism. Indeed the proponents often playfully admitted that they were more interested in the reactions invoked in viewers than they were in the Art object itself. Much of the Art of Minimalism took the form of three dimensional "sculptural" works rather than flat two dimension paintings. Works, though very minimal, were very, almost mathematically and geometrically, precise. This as in reaction against the uncontrolled "automatic" smattering of paint favored by the Abstract Expressionists. Minimalism also strove for something completely new, challenging even the concepts of what Art actually was, or what it could be. It sought to distance itself from traditional media, paint and stone and wood. It fascinatingly evolved in part from a number of earlier short lived Twentieth century genres. From Constructivism it evolved the idea of working with modern industrial materials, bricks, sheet metal, perspex and most innovatively of all with pure light, in the form of the haunting minimalist works of Dan Flavin. In the spirit the Dadaist "readymade" it took everyday items and turned these into Minimalist works of Art, and in the spirit of Pop Art, these everyday items could be as basic as those produced on the massive industrial scale. Even the simplest modern day industrial materials or commodities could be a work of pure Art.

Just what the viewer was meant to get out of Minimalist Art, was….well… entirely up to the viewer. There were no distractions, no unnecessary complications. Indeed unwittingly the Minimalists did take something out of their Abstract Expressionist colleagues - frequently no title, (which could influence feelings) would be given to the work, many simply being numbered by the year or by numerical order in which it was produced, although Dan Flavin did often "dedicate" his works to those he thought important to him personally. Although much derided, and mocked at the time, Minimalist Art nevertheless, had a lasting and powerful influence on subsequent late Twentieth century, and Twenty First century concepts of Art, design and architecture. It established the idea that aesthetic beauty could be seen in the pure, the simple, the uncomplicated and that this beauty could exist in its own unadorned right and for its own unadorned sake.

When we manage our patients who have taken what appears to be an alarming overdose of thyroxine, we must relax. This overdose despite what we may at first suspect does not produce significant symptoms at presentation, even with large overdoses. Thyroxine's toxic action is far more manifest in the long term chronic exposure situation. The most immediate concern will simply be the patient's psychiatric status and well being. And so we may take a most Minimalist approach - what we see is what we see - nothing more - nothing less - and that's not very much at all! Apart from a dose of oral charcoal in cooperative adults who happen to present within one hour, acute intervention is not required. TFT blood testing is not required and immediate medical admission is not required, on medical grounds, simply close outpatient follow-up with the minimum of fuss!

Untitled 1980; Donald Judd, Tate Gallery London.

Donald Judd himself did not much care for the term "minimalist"- yet much of his work was.....well...Minimalist!

THYROXINE OVERDOSE

Introduction

Overdose of **thyroxine** is rarely sufficient to produce significant symptoms of hyperthyroidism.

Initial resuscitation or other measures are **not** usually required, as onset of symptoms, when they occur, is **delayed.**

When symptoms do occur they are:

- Mild
- **Delayed in onset (usually > 24 hours following ingestion).**
- May last up to 2 weeks.

Patients can usually be successfully managed as an outpatient and management in the ED will be more concerned with the patient's psychiatric well being.

Preparations

Thyroxine as:

Tablets:

- 50 microgram
- 75 microgram
- 100 microgram
- 200 microgram

Toxicology

- The onset of hormonal effect is delayed with maximal effects not seen for 1-3 weeks.
- Thyroxine (T4) is converted to triiodothyronine (T3) in the liver and kidney.
- T3 binds to intra-nuclear sites and influences multiple metabolic processes.

Pharmacokinetics

Absorption:

- Maximal absorption is at 2 hours post ingestion.
- Oral bioavailability is high at 80%.

Distribution:

- Thyroxine is extensively distributed and is highly protein bound.

Metabolism and elimination:

- The elimination half-life is 6-7 days following therapeutic dosing, but is only 3 days following overdose. [1]
- Although thyroxine is rapidly absorbed, it requires peripheral conversion into its more active form (T3 or tri-iodothyronine) and **so its clinical effects are delayed** (and require changes in gene expression).

Risk Assessment

- **Symptoms are not expected to occur unless > 10 mg of thyroid hormone has been ingested.**
- The majority of patients with acute thyroxine overdose remain asymptomatic or experience only mild to moderate symptoms of hyperthyroidism **2-7 days later.**
- If hyperthyroidism symptoms do appear, then the **elderly** and those with **cardiovascular co-morbidities** will be at the greatest risk.
- **Severe toxicity is more likely to occur following chronic abuse of thyroid hormones**.
- In children. ingestion of up to **5 mg** is associated with minimal symptoms only.

Clinical Features

The majority of patients will remain asymptomatic following acute ingestion.

Where symptoms do develop they are not usually seen until **> 24 hours** following ingestion

A "thyrotoxic storm" is never an *early* feature of acute thyroxine ingestion, even if the dose taken is large.

Once symptoms develop they may then last more than one week.

Symptoms seen will be predominantly those of adrenergic stimulation:

1. CVS:

- Tachycardia.
- Hypertension.
- Sweating.

2. Neurological:
   - Agitation
   - Headache.
   - Tremor
3. GIT upset.

Chronic ingestion

Chronic ingestion of thyroxine causes more severe illness, particularly in those with pre-existing cardiovascular disease.

Symptoms will be predominantly related to the cardiovascular system.

Investigations

Thyroid function tests will usually show marked elevation of thyroxine after overdose; however this does not correlate well with clinical symptoms. Thus they do not assist in management and so are not generally indicated.

ECG should be done for any palpitations that are experienced or for possible coingestion of other cardiotoxic agents.

As for any overdose consider the possibility of coingestion, **(blood alcohol, serum paracetamol level**).

Management

1. Initial resuscitation or other measures are not usually required.
2. Charcoal:
   - This should be given to **cooperative** patients who have taken **> 10 mg** of thyroxine and who have presented within **one hour** of ingestion.

     Oral activated charcoal is not indicated in *children* following *unintentional* ingestion.

3. If the patient is otherwise well and stable from a psychiatric viewpoint, admission to hospital will not be necessary.

4. **Patients should be instructed to look out for symptoms at 2-7 days and report to hospital should these occur.**

5. Propranolol

   - Will rapidly control any symptoms.
   - For adults give **10 - 40 mg orally** every **6 hours**. [1]
   - Treatment is usually for a period of **1 week.**
   - Thyroxine may be restarted *after a week*, if indicated.

6. Calcium channel blockers

   - These can be used when beta blockers are **contra-indicated.**
   - Give diltiazem **60 - 180 mg orally** every **8 hours.**

Disposition

Adult patients with *acute* overdose rarely require immediate management and disposition will be dictated by the immediate medical and psychiatric condition.

Medically and psychologically *appropriate* patients may be treated as outpatients.

Symptoms should be explained and the patient is asked to return for review over the next few days if these symptoms develop.

If symptoms develop supportive therapy with beta blockers is commenced and these will usually be required for around one week.

Thyroxine may be restarted a week after this, if the patient was taking this therapeutically.

If symptoms are moderate to severe patients should be admitted to a HDU setting.

References

1. Thyroxine overdose in L Murray et al. Toxicology Handbook 3rd ed 2015.

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