Background: Thyroid hormones are key regulatory signaling molecules that participate in vertebrate development and homeostasis. Some anthropogenic and widely used contaminants have the potential to interfere with the endocrine function of the thyroid system. The herbicide ioxynil (IOX) and medical non-steroid estrogen diethylstilbestrol (DES) compete with thyroid hormones for transthyretin (Morgado, 2007) and cause hyperstimulation of thyroid follicular cells and down-regulation of some HPT axis genes, indicating that HPT axis homeostasis was modified in sea bream (Morgado, 2009). In zebrafish, IOX and DES altered thyroid gland development and this was associated with disruption of the function and morphology of the heart and suggested that there is an indirect endocrine disrupting action on the thyroid in teleosts (Campionho and Power, 2013). The purpose of the present study was to investigate the effect of IOX and DES on the heart, vascular system and thyroid development and the interaction between them.

Results:

1. Ventricular morphology

At 48hpf, the volume of the ventricle in IOX and DES treated zebrafish were significantly decreased.

2. Ventral aorta (VA) and thyroid follicle cell development

At 72hpf, a significant reduction in VA diameter was observed in the IOX and DES groups. The number of thyroid follicle cells and the thyroid field was significantly decreased in the IOX and DES treated zebrafish, respectively. The area of the thyroid follicle cells were significantly reduced by IOX and DES treatment.

3. Endothelial cell transcriptome of IOX and DES

3.1 Heatmap and Venn diagram of differentially expressed genes

- There were common and divergent gene expression patterns in IOX and DES treatment, which implies compound-specific toxic effects exist.
- IOX and DES affect pathways related to endothelial cell function, but compound-specific effects also exist (e.g. Vascular smooth muscle contraction)

3.2 KEGG pathway enrichment

- There were common and divergent gene expression patterns in IOX and DES treatment, which implies compound-specific toxic effects exist.
- IOX and DES affect pathways related to endothelial cell function, but compound-specific effects also exist (e.g. Vascular smooth muscle contraction)

Conclusion:

- IOX and DES directly impair vascular and heart development in zebrafish and indirectly impair thyroid gland development.
- IOX and DES have common and compound-specific effects on endothelial cells, with similar overall consequences.
- IOX and DES are thyroid disrupting compounds.

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