Iodine and Fertility

June 28, 2018
Kathleen Kenny, PharmD, RPh
Pharmacy Times, June 2018 Women's Health, Volume 84, Issue 6

In general, infertility is described as an inability to conceive despite having frequent, unprotected intercourse for a year or more.

In general, infertility is described as an inability to conceive despite having frequent, unprotected intercourse for a year or more. However, because fertility is inversely proportionate to age, many women over 35 are evaluated for infertility after 6 months.[1]

About 12% of women aged 15 to 44 years in the United States have difficulty getting or staying pregnant, regardless of marital status.[1]

The causes of infertility vary. They can include eating disorders, emotional stress, excessive exercise, hormonal disorders, poor nutrition causing low vitamin or mineral levels, medical conditions (eg, candida, polycystic ovarian disease, and sexually transmitted diseases), obesity, and thyroid disorders.[1]

Iodine

Although there are many nutrients and trace minerals involved in conception, iodine is among the most important. Iodine is a nonmetallic trace mineral essential to the function of the thyroid. In turn, the thyroid is responsible for manufacturing the hormones thyroxine (T_4) and triiodothyronine (T_3). These hormones are responsible for regulating various enzymes and organic processes required for life. Examples include cell division and metabolism; growth, development, and repair of the body; immune system function; mental state; ovulation; and weight management.[2]

Iodine Deficiency

Mild iodine deficiency occurs at urine iodine—creatine ratios between 50 µg/g and 99 µg/g, and moderate to severe iodine deficiency occurs below 50 µg/g.

significant decline in the prevalence of iodine deficiency disorders such as hypothyroidism.[3] New research has suggested that iodine also has an important impact on fertility.[4]

Results from a recent population-based prospective cohort study by the Eunice Kennedy Shriver National Institute of Child Health and Human Development have shown that moderate to severe iodine deficiency is associated with a decrease in fecundability, or the probability of becoming pregnant within a given period of time.[5]

The study consisted of 467 American women who were trying to become pregnant. Women with moderate to severe iodine deficiency showed a 46% decrease in the likelihood of conception compared with women with normal iodine levels.[6] Even women with a mild iodine deficiency had a more difficult time conceiving, though this difference was not statistically significant, according to investigators led by James Mills of the US National Institute of Child Health and Human Development.[6]

"The Western diet has changed in the last few decades, and the adoption of vegetarian and vegan diets [has] led to a reduction in dietary iodine consumption," said Tomer Singer, director of reproductive endocrinology and infertility care at Lenox Hill Hospital in New York, New York.[6]

Recommended Daily Allowance (RDA)

The RDA of iodine varies based on age, pregnancy status, and lactation status. For a complete table of RDAs of iodine, see **Table 1**.[7]

TABLE 1. RDAS FOR IODINE[7]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	110 µg*	110 µg*		
7-12 months	130 µg*	130 µg*		
1-3 years	90 µg	90 µg		
4-8 years	90 µg	90 µg		
9-13 years	120 µg	120 µg		
14-18 years	150 µg	150 µg	220 µg	290 µg
19+ years	150 µg	150 µg	220 µg	290 µg

RDA indicates recommended daily allowance.
*Adequate intake

Iodine-Rich Foods

Because the body cannot make its own iodine, it is imperative that enough iodine is consumed in the foods we eat. One of the best sources of iodine is seaweed. Other sources include dairy products, eggs, fruits, grains, seafood, and vegetables. The iodine content of fruits, grains, and vegetables affects the iodine content of animal products and meat based on what they are fed. For a list of iodine-containing foods and their approximate iodine content, see **Table 2**.[7]

Seaweed, whole or sheet, 1 g	16-2984	11%-1989%
Cod, baked, 3 oz	99	66%
Yogurt, plain, low fat, 1 cup	75	50%
Iodized salt, 1.5 g (about ¼ = teaspoon)	71	47%
Milk, reduced fat, 1 cup	56	37%
Fish sticks, 3 oz	54	36%
Bread, white, enriched, 2 slices	45	30%
Fruit cocktail in heavy syrup, canned, ½ cup	42	28%
Shrimp, 3 oz	35	23%
Ice cream, chocolate, ½ cup	30	20%
Macaroni, enriched, boiled, 1 cup	27	18%
Egg, 1 large	24	16%
Tuna, canned in oil, drained, 3 oz	17	11%
Corn, cream style, canned, ½ cup	14	9%
Prunes, 5 dried	13	9%
Cheese, cheddar, 1 oz	12	8%
Raisin bran cereal, 1 cup	11	7%
Lima beans, mature, boiled, ½ cup	8	5%
Apple juice, 1 cup	7	5%
Green peas, frozen, boiled, ½ cup	3	2%
Banana, 1 medium	3	2%

Daily values (DVs) were developed by the FDA to help consumers compare the nutrient contents of products within the context of a total diet. The DV for iodine is 150 µg for adults and children 4 years and older. However, the FDA does not require food labels to list iodine content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered high sources of a nutrient.

Conclusion

This new study highlights an important link between fertility and nutrition. Although this is just 1 study and further studies on larger scales are needed, the evidence suggests a causal relationship between a moderate to severe deficiency in iodine and decreased fertility. Not only is iodine very important for conception, but it is also critical during and immediately after pregnancy, as well as during lactation. The consensus is that women should take iodine and folic acid containing prenatal vitamins for 3 months before trying to conceive and continue taking them throughout lactation.

Kathleen Kenny, PharmD, RPh, earned her PharmD from the University of Colorado Health Sciences Center in Aurora. She has more than 25 years of experience as a community pharmacist and is a freelance clinical medical writer based in Colorado Springs, Colorado.

References

- Infertility FAQs. CDC website. cdc.gov/reproductivehealth/Infertility/. Updated April 18, 2018. Accessed April 29, 2018.
- Willett E. Why iodine is essential to preconception and pregnancy health. *Nat Fertil Info*. natural-fertility-info.com/iodine-preconception-and-pregnancy-health.html. Accessed April 7, 2018.
- Micronutrient facts. CDC website. cdc.gov/immpact/micronutrients/. Updated March 6, 2018. Accessed April 29, 2018.
- Mills JL, Buck Louis GM, Kannan K, et al. Delayed conception in women with low-urinary iodine concentrations: a population-based prospective cohort study [published online January 18, 2018]. *Hum Reprod*. doi: 10.1093/humrep/dex379.
- Fecundability. English Oxford Living Dictionaries website. en.oxforddictionaries.com/definition/fecundability. Accessed April 29, 2018.
- Crist C. Iodine deficiency could contribute to women's fertility problems. *Reuters* website. Published January 25, 2018. Accessed May 9, 2018.
- National Institutes of Health. Iodine. ods.od.nih.gov/factsheets/Iodine-HealthProfessional/. Updated March 2, 2018. Accessed April 29, 2018.

Related Content:
Publications | Women's Health | June 2018 Women's Health

MEK Inhibitors

May 20, 2022

Bryan Fitzgerald, PharmD, BCOP

Pharmacy Times Health Systems Edition,

Watch for alopecia, arthralgia, diarrhea, fatigue, nausea, pyrexia, rash, and vomiting, among others.

Cutaneous melanoma, a type of skin cancer arising from malignant melanocytes, is the fifth most prevalent cancer in the United States, with 99,780 new cases estimated in 2022.[1,2]

Depending on disease stage, the treatment landscape of melanoma includes immunotherapy, local therapies, surgical resection, and targeted agents. For patients with metastatic melanoma, systemic therapy with targeted agents or immunotherapy is the standard of care.[3]

Approximately half of melanoma cases possess an activating mutation in the BRAF gene, which encodes the BRAF kinase of the mitogen-activated protein kinase (MAPK) pathway.[3] Specifically, BRAF V600 mutations have been shown to respond to and benefit from targeted therapy with a BRAF inhibitor. Trial results have supported the addition of a MEK inhibitor to BRAF inhibitor therapy, leading to this combination being established as a standard-of-care option for patients with BRAF V600 mutations.[3]

The FDA has approved 3 pairs of BRAF and MEK inhibitors to treat melanoma with BRAF V600 mutations: dabrafenib and trametinib (Tafinlar, Mekinist; Novartis), encorafenib and binimetinib (Braftovi, Mektovi; Pfizer), and vemurafenib and cobimetinib (Zelboraf, Cotellic; Genentech). All 6 agents are orally administered and are available through specialty pharmacies.

BRAF and MEK inhibitors are associated with various unique toxicities that may require close monitoring and management. Common toxicities include alopecia, arthralgia, diarrhea, fatigue, nausea, pyrexia, rash, and vomiting. Rarer ones that may require nuanced monitoring plans include cardiac, dermatologic, and ocular toxicities.

Pyrexia

Pyrexia is defined as a temperature of 38.0oC or greater (≥ 100.4oF), and its incidence ranges with the 3 combinations of BRAF and MEK inhibitors.[4] The dabrafenib-trametinib combination is associated with a higher incidence (57%) than vemurafenib and cobimetinib (22%) and encorafenib and binimetinib (19%).[5-8] Pyrexia may be complicated by chills, hypotension, renal injury, or rigors. At the onset of pyrexia, holding

symptoms of pyrexia, the importance of hydration, and having a thermometer on hand to monitor temperature.

Dermatologic Toxicities

Several dermatologic toxicities are common with BRAF and MEK inhibitor therapy, including hyperkeratosis, palmar-plantar erythrodysesthesia, photosensitivity, and rash. Photosensitivity is most common with vemurafenib, with a reported incidence of up to 49%.[10] Pharmacists should advise patients to avoid intense sun exposure, use broad spectrum sunscreen with a sun protection factor of 30 or higher, and wear protective clothing when outside.

Cutaneous malignancies, including cutaneous squamous cell carcinoma (cSCC) and keratoacanthomas, have been reported with BRAF and MEK inhibitors. This risk of an additional cutaneous malignancy may be particularly alarming for patients with melanoma. The incidence of cSCC is higher with BRAF inhibitor monotherapy because of a paradoxical activation of the MAPK pathway to overcome BRAF inhibition. With the addition of a MEK inhibitor, the risk of cSCC is reduced. For example, there is an 11% incidence with vemurafenib vs 3% with vemurafenib and cobimetinib.[5] To screen for suspicious skin changes, routine dermatologic evaluation every 2 months is recommended for patients on BRAF/MEK inhibitor therapy.[9-11]

Rarely, cases of drug reaction with eosinophilia and systemic symptoms and Stevens-Johnson syndrome have been reported with BRAF and MEK inhibitors. These reactions may be life-threatening or fatal, and treatment should be discontinued if either condition occurs.[9-11] Based on the myriad potential dermatologic changes with BRAF and MEK inhibitors, pharmacists should encourage patients to self-monitor for any new skin changes or growths and to report any changes.

Cardiac Toxicities

Prolongation of the QT interval is a risk with BRAF inhibitors, particularly with vemurafenib and encorafenib, although it has rarely been reported with dabrafenib.[9-11] Baseline and routine electrocardiogram monitoring may be warranted, especially if patients are taking other QT-prolonging medications. The prescribing information for vemurafenib has explicit electrocardiogram monitoring recommendations, with QTc measurement at day 15, monthly during the first 3 months, then every 3 months thereafter.[10] Cardiomyopathy with decreased left ventricular ejection fraction is associated with the use of MEK inhibitors and when MEK inhibitors are used in combination with BRAF inhibitors. Assessment of left ventricular ejection fraction, typically with an echocardiogram, is recommended prior to starting therapy with a MEK inhibitor, 1 month after

with BRAF inhibitors, conjunctivitis, dry eye, and uveitis have been reported, whereas retinal vein occlusions and retinopathies are more frequently associated with MEK inhibitors. Uveitis from BRAF inhibitors may be managed with topical ophthalmic agents and treatment interruption.[10] Only in the prescribing information for encorafenib is routine ophthalmologic monitoring recommended at "regular intervals." However, patients may benefit from more routine monitoring. When starting these agents, patients should be monitored and counseled to report any ocular pain, photophobia, vision changes, and vision loss.

ABOUT THE AUTHOR

Bryan P. Fitzgerald, PharmD, BCOP, *is a clinical specialist in oncology at the University of Rochester Specialty Pharmacy in New York.*

REFERENCES

1. Cancer stat facts: melanoma of the skin. National Cancer Instit ute. Accessed March 14, 2022. https://seer.cancer.gov/statfacts/html/melan.html

2. Key statistics for melanoma skin cancer. American Cancer Society. Updated January 12, 2022. Accessed March 14, 2022. https://www.cancer.org/cancer/melanoma-skin-cancer/about/key-statistics.html

3. NCCN. Clinical Practice Guidelines in Oncology. Melanoma: cutaneous, version 3.2022. Accessed March 14, 2022. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf

4. Common terminology criteria for adverse events (CTCAE). National Cancer Institute. November 27, 2017. Accessed March 14, 2022. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5×11.pdf

5. Larkin J, Ascierto PA, Dréno B, et al. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. N Engl J Med. 2014;371(20):1867-1876. doi:10.1056/NEJMoa1408868

6. Long GV, Stroyakovskiy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. N Engl J Med. 2014;371(20):1877-1888. doi:10.1056/NEJMoa1406037

7. Robert C, Karaszewska B, Schachter J, et al. Improved overall survival in melanoma with dabrafenib and trametinib. N Engl J Med. 2015;372(1):30-39. doi:10.1056/NEJMoa1412690

8. Dummer R, Ascierto PA, Gogas HJ, et al. Encorafenib plus binimetinib

Accessed April 11, 2022.
https://www.novartis.us/sites/www.novartis.us/files/tafinlar.pdf

10. Zelboraf. Prescribing information. Genentech USA, Inc; 2016. Accessed April 11, 2022.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/202429s012lbl.pdf

11. Braftovi. Prescribing information. Array BioPharma Inc; 2018. Accessed April 11, 2022.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210496lbl.pdf

12. Mekinist. Prescribing information. Novartis Pharmaceuticals Corp; 2021. Accessed April 11, 2022.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/204114s018lbl.pdf

13. Cotellic. Prescribing information. Genentech USA, Inc; 2015. Accessed April 11, 2022.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206192s000lbl.pdf

14. Mektovi. Prescribing information. Array BioPharma Inc; 2018. Accessed April 11, 2022.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210498lbl.pdf

Download Issue: May 2022

Related Content:
Hospital | Oncology | Publications

Develop Standardized Concentrations and Overcome Barriers

IVIG Safe, Effective Treating Pregnant Patients With Severe COVID-19

Daily OTC Pearl: Uristat

Study Results Link Hormonal Changes During Menopause to Decline in Cardiovascular Health

May 20, 2022
Ashley Gallagher, Assistant Editor

But HRT is associated with positive changes to cholesterol levels, though the sample size was small, the analysis shows

leads to a decline in estrogen and an increase in follicle-stimulating hormone (FSH). The results of previous studies have shown that there is an association between menopause and heart disease, promoting levels of metabolism. However, the new study results showed a link with changes to the female sex hormones. The metabolite shifts were partially improved with hormone replacement therapy (HRT).

"Menopause is unavoidable, but it is possible that the negative metabolite shift can be diminished by eating healthily and being physically active," Eija K. Laakkonen, PhD, of the University of Jyväskylä, Finland, said in a statement. "In particular, women should pay attention to the quality of fat in their diet and getting sufficient exercise to maintain cardiorespiratory fitness. HRT is an option that women should discuss with healthcare providers at this point in their lives," Laakkonen said.

The analysis included 218 perimenopausal women who did not received HRT at baseline. Investigators obtained levels of 2 hormones, estradiol and FSH, and180 metabolites, including amino acids, lipids, and lipoproteins, via blood samples at baseline and every 3 to 6 months until early post-menopause.

The menopausal state was assessed using blood FSH levels and menstrual diaries. Early post-menopause was defined as elevated FSH levels on at least 2 consecutive occasions and no periods for more than 6 months.

A total of 35 women started HRT during the study.

"Our study investigated whether the menopausal hormonal change modulates the metabolite profile measured in blood samples taken before and after menopause. Because the menopausal transition, ie, the time with variable hormone levels and irregular menses, varies tremendously from person to person, the time points for assessment were individualized," Laakkonen said.

Investigators conducted detailed statistical analyses to determine which changes occur in metabolite levels during the menopausal transition and whether these changes related to the shift in sex hormone levels. Additionally, investigators evaluated whether the metabolite trajectory varied between HRT users and non-users.

Menopause was associated with a statistically significant change in levels of 85 metabolites. The results of the analysis showed that the menopausal hormonal shift directly explained the change in 64 of the 85 metabolites, with the effect sizes ranging from 2.1% to 11.2%, including amino acids, fatty acids, LDL cholesterol, and triglycerides.

Investigators adjusted for age at baseline, alcohol use, diet quality, duration of follow up, education level, physical activity, and smoking status. Results

sample size of women starting the therapy was small, and the study was merely observational, Laakkonen said.

Reference

Hormonal changes during menopause are directly related to decline in cardiovascular health. EurekAlert. News release. May 13, 2022. Accessed May 13, 2022. https://www.eurekalert.org/news-releases/952200

Related Content:
Women's Health | Cardiovascular Health | Retail

IVIG Safe, Effective Treating Pregnant Patients With Severe COVID-19

Daily OTC Pearl: Uristat

AHA Urges Taking Steps to Improve Access, Quality, Equity in Women's Heart Health