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Doi Number: <http://dx.doi.org/10.38063/ejons.443>**TANI VE TEDAVİ AMAÇLI YAPILAN RADYOLOJİK İŞLEMLERİN GEBELİK ÜZERİNE ETKİLERİ**

THE EFFECTS OF RADIOLOGICAL PROCEDURES FOR DIAGNOSIS AND TREATMENT ON PREGNANCY

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457

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ÖZET

Teknolojik gelişmelerle birlikte, tıbbi uygulamalarda çok ivmeli bir şekilde iyileşmeler izlenmektedir. Sıklıkla görüntüleme yöntemlerine yenileri eklenmekte, var olanlarda da gelişmeler izlenmektedir. Gebelik esnasında tanı ve tedavi amaçlı radyolojik prosedürlerin uygulanması, günlük pratikte çok sık kullanılır hale gelmiştir. Bu yöntemleri kullanarak elde edilen veriler ciddi kazanımlar oluşturmaktadır. Ancak tüm bu radyolojik görüntüleme

yöntemlerinin, hastaya belli miktarlarda etkileri söz konusudur. Kullanılan yöntemle ilgili olarak değişik derecelerde hastaya radyasyon verilmektedir. Bu radyasyon miktarı arttıkça hastada belli sorunları da beraberinde getirmektedir. Özellikle gebelerde fetal gelişimin kompleks yapısı nedeniyle, radyasyonun fetal etkileri çok daha fazla olmaktadır. Gebelik haftası ne kadar küçükse, radyasyona bağlı fetal dokularda etkilenme riski de o kadar artmaktadır. Aynı zamanda gebelik haftası ile ilişkisi kadar, kullanılan yöntemin de hastaya verilen radyasyon miktarıyla yakın ilişkisi mevcuttur. Klinikte çok sık kullandığımız ultrasonun bile belli durumlarda gebelik üzerinde negatif etkilerinin olabileceği birkaç yayında tartışılmıştır. Radyolojik yöntemleri kullanırken, hastaya hangi dozda radyasyon verildiğinin bilinmesi ve hangi usullerle bu dozun etkisinin azaltılabileceğinin bilinmesi gereklidir. Tanı ve tedavi amaçlı olarak kullandığımız bu yöntemlerin öncelikle faydalı olması sağlanmalı, zararlarının minimize edilmesi gerekir. Bu koşulları sağlayabilmek için de kullanılacak yöntemler hakkında ayrıntılı bilgiye sahip olmak gereklidir.

Biz bu çalışmamızda, güncel veriler ışığında, günlük pratiğimizde çok sık kullandığımız radyolojik görüntüleme yöntemlerinde olası maternal/fetal riskleri inceledik. Bu yöntemleri kullanırken neler dikkat edilmesi gerektiğini araştırdık.

Anahtar Kelimeler: Radyasyon, Gebelik, Teratojenite

ABSTRACT

Technological developments provide rapid improvements in medical applications. Often, new imaging methods are added, and improvements are observed in existing ones. The application of diagnostic and therapeutic radiological procedures during pregnancy has become very common in daily practice. The data obtained using these methods constitute serious gains. However, all these radiological imaging methods have certain effects on the patient. Depending on the method used, different degrees of radiation are given to the patient. As the amount of this radiation increases, it brings certain problems in the patient. Due to the complex nature of fetal development, the fetal effects of radiation are much higher in case of pregnancy. The possibility of being affected by radiation in the early weeks of pregnancy is more than the late weeks of pregnancy. At the same time, the method used has a close relationship with the amount of radiation given to the patient as well as the pregnancy week. It has been discussed in several publications that even ultrasound, which we use frequently in the clinic, can have negative effects on pregnancy in certain situations. When using radiological methods, it is necessary to know what dose of radiation is given to the patient and to know with which methods the effect of this dose can be reduced. These methods, which we use for diagnosis and treatment, should primarily benefit, and their damages should be minimized. In order to meet these conditions, it is necessary to have detailed information about the methods to be used.

In this study, in the light of current data, we examined possible maternal / fetal risks in radiological imaging methods that we use frequently in our daily practice. We searched what should be considered when using these methods.

Keywords: Radiation, Pregnancy, Teratogenicity

1. INTRODUCTION

Choosing the most appropriate imaging method in pregnant women is a common clinical question that is faced every day. In general, the indications for imaging are similar to those in non-pregnant. However, it is reasonable to evaluate the effects of the method to be applied in pregnancy on the fetal tissue and to give as little radiation dose as possible (as low as reasonably achievable-ALARA). It is important to keep the amount of fetal radiation to a minimum, but it should not be out of the question of not doing the necessary procedures because of fear of the situations that fetal exposure may cause. If the radiation dose given in the method used in radiological examinations is known, the risks that may occur are evaluated in terms of profit and loss and the necessary imaging method can be applied. In most cases, the perception of fetal risk is higher than the actual risk.

The anatomical position of vital organs is also important in terms of radiation. It is important to know the exact anatomical locations of the uterus and other genital related structures. Since the uterus is in the pelvis until about the 12th week, the radiation given to the distant areas of the pelvis is less likely to pass to the fetal tissues. In addition, as the uterus is located closer to the anterior pelvis in the early weeks of pregnancy, it is possible that the radiation given from the posterior will have less effect than the one given from the front.

Besides all other factors, the most important component of the amount of radiation is the type of examination performed. In certain imaging methods, serious radiation transmission may occur even when working away from the pelvis. Of course, the opposite of this situation may be the case depending on the method used.

In this study, we searched the the possible effects of imaging methods used medically for diagnosis and treatment on pregnancy. In the light of current data, we examined the relationship between radiation - fetal/maternal complications.

459

2. RESULTS AND DISCUSSION

2.1. Units of Radiation Dose

In order to make predictions in evaluating the effects of radiation, it is necessary to have basic knowledge about radiation first. The amount of energy obtained from ionizing radiation accumulated in any tissue is called "absorbed radiation dose" or "rad". 1 rad dose absorbed means that 1 gram of material absorbs 100 erg energy by exposure to radiation. Gray (Gy) is the radiation absorption dose used in international (SI) units (Kruskal, 2021).

$$1 \text{ rad} = 0.01 \text{ gray (Gy)}$$

Equivalent dose reflects the biological effect of radiation exposure on human tissue. The unit used to measure the equivalent dose is rem (roentgen-equivalent man). Sievert (Sv) is the equivalent dose to radiation used in international (SI) units. Depending on the type of radiation (beta, gamma, alpha or neutron) the dose absorbed may be the same or lower than the equivalent dose.

$$1 \text{ rem} = 0.01 \text{ sievert (Sv)}$$

Some organs are more sensitive to radiation than others, and this difference is reflected in the effective dose. The effective dose is calculated by multiplying an organ equivalent dose by the tissue weight factor for that organ. The unit that measures the equivalent dose for a tissue is also rem or sievert. Information on radiation doses is shown in table 1 (El-Sayed, 2017).

measure	Definition	Legacy unit	SI unit
Exposure	Number of ions produced by X-ray or gamma radiation per kilogram of air	Roentgen (R)	2.58×10^{-4} C/kg
Dose	Amount of energy deposited per kilogram of tissue	Rad (rad)	Gray (Gy) 1000 mGy=1 Gy 1 Gy = 100 rad
Relative effective dose	Amount of energy deposited per kilogram of tissue normalized for biological effectiveness	Roentgen equivalent man (rem)	Sievert (Sv) 1000 mSv = 1 Sv 1 Sv = 100 rem

Table 1: Measures of radiation doses

In the United States, a person is exposed to a radiation dose equivalent to an average full body exposure of 3.1 mSv (310 mrem) each year from natural sources (USNR Commission, 2017). The United States Nuclear Regulatory Commission recommends that the radiation exposure of pregnant women (ie, work-related exposure) does not exceed 5 mSv (500 mrem) to the fetus during the entire pregnancy.

2.2. Possible Effects on the Fetus

The result of exposure to radiation in fetuses is mostly based on observations rather than scientific research. Ethical issues prohibit research on the fetus. Therefore, most of the data on the effect of radiation on the fetus come from observations of patients suffering from Japan's Hiroshima bombardment and the Chernobyl nuclear disaster (Brent, 2009). The results of radiation exposure, based on observations from victims of high levels of radiation exposure; It can be divided into four broad groups including pregnancy loss, malformation, developmental delay and carcinogenesis. Pregnancy loss usually occurs in early pregnancy (less than two weeks) when exposed to radiation (Wilson, 2010). During the period of organogenesis (2 weeks to 8 weeks) malformations and developmental delays occur in body parts and depends on the radiation dose (De Santis, 2007). Below the radiation exposure threshold level there is minimal disturbance in organogenesis. Above the threshold, the degree of malformation is related to the radiation dose. Carcinogenesis is considered a stochastic effect. In other words, cancer can develop at any level of radiation exposure. However, as the radiation dose increases, the possibility of developing cancer increases.

Fetal radiation dose below 50 mGy is considered safe and does not cause any harm (Brent, 2015). According to the Center for Disease Control (CDC), radiation dose between 50 mGy and 100 mGy is considered insufficient in terms of effect on the fetus. Doses above 100 mGy, especially doses above 150 mGy, are seen as the minimum dosage at which negative fetal consequences will occur, based on observation. Most of the diagnostic tests performed during pregnancy are below the threshold level.

Embryogenesis is a complex process and can be divided into 3 sub-sections: pre-implantation, embryo and fetal period. This process is highly sensitive to various external factors such as teratogenic drugs, alcohol, smoking, radiation, and even the lack of proper nutrition. Different results may occur to similar effects in each of the 3 periods. The effect of exposure to radiation during pregnancy depends on the gestational age of the fetus. The embryo / fetus is most sensitive to radiation during organogenesis (2 to 8 weeks of gestational age) and in the first trimester. The fetus is more resistant to radiation during the second and third trimesters.

Radiation effects fall into 2 categories: stochastic (random effects) and deterministic (non-random effects). Stochastic effects are mutagenesis and carcinogenesis resulting from any radiation dose. Deterministic effects are dose dependent and begin to appear after the threshold value of 50-150 mSv (Osei, 1999). Potential stochastic effects lead to unrepaired or improperly repaired DNA repair and can lead to conditions such as leukemia. Intrauterine exposure at a dose of approximately 1000 mSv carries a 6% risk of leukemia (Little, 2003). Clinical deterministic effects that result in cell death can be fatal (spontaneous abortion) or cause central nervous system (CNS) abnormality, cataracts, malformations (100--200 mSv), and growth-mental retardation (table 2) (El-Sayed, 2017). Doses between 0.05-0.5 Gy are generally considered safe for the fetus during the second and third trimesters, while potentially harmful during the 1st trimester fetus. Although the fetus is more resistant to radiation in the second and third trimesters, high doses of radiation (more than 0.5 Gy or 50 rad) may cause adverse effects such as miscarriage, decreased growth, decreased IQ, and severe mental retardation (Table 3). (Sternick, 2019). Therefore, clinicians and radiologists should inform pregnant women regardless of the gestational age (Fletcher, 2010).

Gestational period	Effects	Estimated treshold dose
<i>Before implantation (0-2 weeks after fertilization)</i>	Death of embryo or no consequence (all or none)	50-100 mGy
<i>Organogenesis (2-8 weeks after fertilization)</i>	Congenital anomalies (skeleton, eyes, genitals)	200 mGy
Fetal period	Effects	Estimated treshold dose
<i>8-15 weeks</i>	Severe intellectual disability (high risk)	60-310 mGy
	Intellectual deficit	25 IQ-point loss perr 1000 mGy
	Microcephaly	200 mGy
<i>16-25 weeks</i>	Severe intellectual disability (low risk)	250-280 mGy

Table 2: Effects of gestational age and radiation dose on radiation-induced teratogenesis

Menstrual or Gestational Age	Conception Age	<50 mGy (<5 rad)	50–100 mGy (5–10 rad)	>100 mGy (>10 rad)
0–2 wk (0–14 d)	Before conception	None	None	None
3rd and 4th wk (15–28 d)	1st–2nd wk (1–14 d)	None	Probably none.	Possible spontaneous abortion.

5th–10th wk (29–70 d)	3rd–8th wk (15–56 d)	None	Potential effects are scientifically uncertain and probably too subtle to be clinically detectable.	Possible malformations increasing in likelihood as dose increases.
11th–17th wk (71–119 d)	9th–15th wk (57–105 d)	None	Potential effects are scientifically uncertain and probably too subtle to be clinically detectable	Increased risk of deficits in IQ or mental retardation that increase in frequency and severity with increasing dose.
18th–27th wk (120–189 d)	16th–25th wk (106–175 d)	None	None	IQ deficits not detectable at diagnostic doses
>27 wk (>189 d)	>25 wk (>175 d)	None	None	None applicable to diagnostic medicine

Table 3: Summary of suspected in utero induced deterministic radiation effects

2.3. Selection of Imaging Method in Pregnancy

The need for imaging during pregnancy usually depends on the following reasons: anomalies that cannot be diagnosed by ultrasound, stroke, bleeding, vascular thrombosis, eclampsia, pituitary problems and back pain. The doses taken in the procedures performed for all these reasons are given in table 4 (Rimawi, 2016).

462

Examination	Mean Dose (cGy)
<i>Fluoroscopic examinations</i>	
<i>Barium enema (upper gastrointestinal)</i>	3.9
<i>Voiding cystourethrogram</i>	4.6
<i>Cardiac catheterization</i>	0.1
<i>Conventional x-ray examinations</i>	
<i>Abdomen (KUB)</i>	0.24
<i>Chest</i>	0.001
<i>Intravenous urogram (IVP)</i>	0.73
<i>Lumbar spine</i>	0.34
<i>Thoracic spine</i>	<0.001
<i>Pelvis</i>	0.17
<i>Hip</i>	0.13
<i>Skull</i>	<0.001
<i>Dental films</i>	<0.001
<i>Computed tomography examinations</i>	
<i>Abdomen with contrast</i>	2
<i>Abdomen without contrast</i>	1
<i>Pelvis with contrast</i>	2
<i>Pelvis without contrast</i>	1
<i>Chest</i>	<0.01
<i>Head</i>	<0.01

<i>Mammography examinations</i>	
<i>Screen-film mammography</i>	0.004
<i>Digital mammography</i>	<0.004
<i>Digital breast tomosynthesis</i>	0.25
<i>Positron emission mammography</i>	0.8

Table 4: Approximate Fetal Doses From Common Diagnostic Radiographic Procedures

It is very important that patients receive appropriate counseling about the risks of exposure to radiation before the procedure. Detailed information should be given about the possible dose and risks of the fetus. It is not clear exactly which dose of radiation for diagnostic purposes is safe for the fetus. For this reason, radiography should be avoided as much as possible.

2.3.1. Ultrasound

Considering all the different imaging methods, the most reliable / inexpensive method is ultrasound. It is a reliable method for evaluating breast masses, adnexal masses and other intrabdominal structures (Vashi, 1992). It is safe to use as a guide in detecting palpable lymph nodes during biopsy in the presence of accompanying cancer. Although proven safe, several studies have shown that ultrasound can also have certain potential effects. In studies conducted in mice, when a frequency above the frequency used in humans (6.7 mHz) is used, it has been observed that there are migration disorders in fetal brain cells (Pellicer, 2006). B-mode and M-mode imaging work on acoustic output that does not produce harmful temperature spikes. However, Doppler ultrasound has this potential; Therefore, guidelines for the use of Doppler in pregnancy have been formulated to minimize exposure time and acoustic output.

2.3.2. Magnetic Resonance (MR)

Magnetic resonance imaging (MR) uses electromagnetic radio waves instead of ionizing radiation to create detailed images. At the cellular level, the possible direct biological effects of MRI occur in two ways: 1) induction of local electric fields and currents from static and time varying magnetic fields 2) radiofrequency radiation resulting in tissue heating. Other potential maternal hazards include trauma from the projection of metal objects into the magnetic field (for example, small metal fragments may be reflected into the eyes), interference with the operation of electronic devices (e.g. pacemakers), burns, heating of conductive materials in implants, and acoustic damage from high-intensity noise (Kruskal, 2021). Despite these risks, there are no adverse maternal or fetal effects reported from MRI during pregnancy (Ray, 2016). Almost all safety studies have been carried out predominantly at 1.5 Tesla magnetic field strengths or less. Higher field strengths may increase the risk of tissue heating. For example, an animal study at 3 Tesla demonstrated warming effects in amniotic fluid and fetal tissue (Cannie, 2016). The most common use of MR during pregnancy is fetal anomalies and placenta accreta. MRI may be used when there is insufficient diagnosis by ultrasound in fetal anomalies (especially central nervous system anomalies). Image quality is less affected than ultrasound in obese patients. In placental invasion disorders, the use of MRI should be kept in mind when clear information cannot be obtained on ultrasound. In some cases, MRI is the preferred diagnostic method because it avoids the ionizing radiation of computed tomography while providing better images than ultrasonography. As an example, first trimester MRI is a

reasonable option in a pregnant patient with suspected appendicitis and whose appendicitis cannot be visualized by ultrasound examination.

Gadolinium increases the signal from tissues where blood flow is increased, especially in the case of inflammation or neoplasm. MRI is a good option to evaluate the mother's brain and spinal cord, suspected inflammatory joint disease, inflammatory bowel disease, and inflammatory and neoplastic conditions of solid organs. It may also be useful for evaluating the inflammatory and neoplastic conditions of bone, muscle, and connective tissue. Due to its magnetic properties, gadolinium, the most commonly used contrast agent for MRI, crosses the placenta and is excreted by the fetus into the amniotic fluid. It is then swallowed; so it can be reabsorbed into the fetal circulation. In light of the potentially long half-life in the fetus and the very few studies in human pregnancies, the potential profit / loss should be well calculated and its use should be avoided as much as possible (Prola, 2018).

2.3.3. Plain radiography

2.3.3.1. Nonabdominopelvic plain radiography

When viewing non-abdominopelvic areas, the patient should wear a lead apron to minimize fetal exposure from radiation emission. A quick film / screen combination or digital radiography can also be used to reduce total radiation exposure. However, diagnostic radiographs of the head, neck, chest and limbs (not including the fetus in the imaging field) produce almost no dispersion to the fetus; Therefore, any radiation received will not result in a measurable increased risk for any adverse consequences.

2.3.3.2. Abdominopelvic plain radiography

The following techniques can be used to minimize exposure to radiation in procedures where the fetus is in direct field of vision (Kruskal, 2012):

- Posterior-anterior (PA) exposure reduces the fetal radiation dose by 0.02 to 0.04 mGy (0.00002 to 0.00004 Gy, 2 to 4 mrad) compared to traditional anterior-posterior (AP) exposure because the uterus is located in the anterior pelvis.
- Shutters can be employed to collimate the radiation beam and reduce scatter.
- Avoiding magnification near the uterus and use of grids decreases the fetal dose of radiation.
- Minimize repeat examinations.

2.3.4. Fluoroscopy and Angiography

During fluoroscopic and angiographic imaging studies, changing the exposure time, the number of images obtained, the beam size, and the field of view can reduce the amount of radiation exposure.

2.3.5. Iodinated Contrast Materials

Contrast materials with iodine can be used when indicated during pregnancy. They don't appear to be teratogenic or carcinogenic. However, iodinated contrast materials cross the placenta and may have temporary depressive effects on the developing fetal thyroid gland. Although the fetal thyroid starts to retain iodine in the first trimester and produces T4 and T3 in the middle of pregnancy, no clinical sequelae have been reported from short exposures to iodinated contrast material in the second and third trimesters (Rajaram, 2012).

2.3.6. Nuclear medicine

Nuclear medicine studies (for example, pulmonary ventilation-perfusion, thyroid, bone and kidney scans) use a radioisotope bound to a chemical. Its clinical use is less than other imaging methods. However, it should be known in detail what risks may occur in the situation that needs to be used. The effect of these substances on the fetus depends on maternal uptake and excretion, placental permeability, fetal distribution and tissue affinity, as well as the half-life, dose and type of emitted radiation. Again, as in other methods, the week of gestation in which nuclear medicine studies are performed has an importance. The risk of the procedure performed in the early weeks is higher. Substances that may be localized in specific fetal organs and tissues and therefore cause concern include iodine-131 (I131) or iodine-123 (I123) in the thyroid, iron-59 in the liver, gallium-67 in the spleen, strontium-90 and yttrium-90 in the skeleton. All of these substances may have teratogenic effects on fetal tissue in varying degrees. Fetal exposure also results from proximity to radionuclides thrown into the maternal bladder; Maternal hydration and frequent urination can reduce such exposure. After using such imaging methods, abundant hydration may be recommended for faster removal from the body. Pregnant patients may contact persons who have received radioactive materials as part of a diagnostic study; minimal residual radioactivity does not result in a measurably increased risk to the fetus. Studies have not shown a high amount of effect on people who have close contact with those exposed to such imaging methods. Radiation exposure from close contact is higher after some types of therapeutic radiation (eg, radioiodine therapy of thyroid cancer, brachytherapy implants for prostate cancer) (Cattani, 2006). Depending on the type of treatment and the dose administered, a limited contact time may be prudent.

At the 10th to 12th week of pregnancy, radioiodine isotopes are readily absorbed by the fetal thyroid. Although there are no reports of adverse fetal effects from diagnostic doses of radioactive iodine, it should not be administered to pregnant patients because induction of thyroid cancer in children is a concern (Bentur, 1994). If diagnostic screening of the thyroid is required, the preferred agent is Technetium-99m or I123 (avoid I131) (El-Sayed, 2017).

There is little information available on positron emission tomography (PET) in pregnancy. This technique involves injection of fluorodeoxyglucose F 18, a radioisotope. Animal studies have not been conducted with fluorodeoxyglucose F 18 injection. It is not known whether Ffluorodeoxyglucose F 18 injection will cause fetal harm or affect reproductive capacity when administered to a pregnant patient. The radiation dose to the uterus is 3.70 to 7.40 mGy for the usual dose range of the injected isotope. This is a low fetal dose and is not associated with adverse effects on development or growth. Due to the lack of safety data on human pregnancy, magnetic resonance imaging or computed tomography is often preferred to PET as they provide similar information, but the decision must be made on a patient-specific basis..

2.3.7. Computed tomography

The fetal radiation dose from a CT scan is affected by several variables, including the number, location, and thickness of slices. When CT imaging is performed during pregnancy, the use of a narrow collimation and wide pitch (ie, the patient moves at a faster speed in the scanner) causes the image quality to be slightly degraded, but with a large reduction in radiation exposure. Scan protocols should also be changed. As an example, if performing a CT scan with contrast, the number of acquisitions can be reduced by eliminating the precontrast series.

3. RECOMMENDATIONS

- All patients who will undergo radiological imaging during the reproductive period should be questioned in terms of possible pregnancy..
- 50 cGy (50 rad) dozdan daha fazla maruziyetler mikrosefali, mental retardasyon ve intra uterin gelişim gerliđi ile ilişkilidir. Bu dozlarda radyasyon verilmesi planlanırsa, olası kar/zarar durumu netleştirilmeli ve aileye çok ayrıntılı bir şekilde danışmanlık verilmelidir (Rimawi, 2016).
- As the gestational week progresses, the risks due to radiation exposure decrease. The most affected are between the 8th and 15th weeks.
- In pregnancies older than 15 weeks, the radiation exposure threshold dose is higher.
- The lowest possible radiation dose should be used for the diagnosis process during pregnancy (<5 rad).
- After the first 14 days, exposure to radiation above 0.5 Gy may be associated with an increased risk of congenital malformations, growth restriction and intellectual disability (Kruskal, 2021)
- Gadolinium should generally be avoided in the pregnant patient, unless its use does not significantly improve diagnostic performance and is unlikely to improve patient outcomes.
- MRI is reliable in all weeks of pregnancy and can be used in all situations that are thought to be of clinical benefit (Kruskal, 2012).

4. CONCLUSION

There are many diseases that require imaging for diagnosis and treatment during pregnancy. Although most of the diagnostic imaging poses a low risk to the mother and fetus, the risks and benefits of the imaging procedure should always be decided on a case-by-case basis. Unless necessary, it is useful to avoid imaging methods in the pregnant woman. When necessary, it should be known which method can affect how. The risks that the method to be applied may pose to the mother and fetus should be shared with the family in detail before the procedure.

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