Nat. Volatiles & Essent. Oils, 2021; 8(6): 3014-3019

NVEO
Natural Volatiles &
Essential Oils

Endocrine Side Effects Of Childhood Hodgkin's Lymphoma Treatment Apply In Health Care

Hadeel sleman Muneizel

Al-Balqa Applied University- Zarqa University college, Zarqa, Jordan

Abstract: The treatment plan is composed of radiation therapy for stage II to IV disease and different types of chemotherapy according to the disease stage Hodgkin lymphoma (HL) is a curable cancer with an excellent prognosis; 90% long-term only eight eligible articles were identified and retrieved for full-text reading. Few articles addressed the endocrine side effects for HL treatment combined with other types of cancer; the articles were included in the review only if the data were presented according to the specific cancer type rather than total results. In this case, the number of HL patients was reported in addition to results for the HL in specific.

Keyword:treatment plan,health care,Endocrine Side Effects, Childhood Hodgkin, Lymphoma Treatment

1. Introduction

Hodgkin lymphoma (HL) is a curable cancer withan excellent prognosis; 90% long-term survival rate (Mauz-Körholz et al., 2015).The treatment plan is composed of radiation therapy for stage II to IV disease and different types of chemotherapy according to the disease stage (Macdonald, 2010). Of course, the treatment is not without side effects; several reports addressed the long-term effects on adult survivals of childhood HL (Mauz-Körholz et al., 2015; Mostoufi-Moab et al., 2016; Patterson et al., 2012; Shimazaki et al., 2020). The effects on endocrine function have gained special attention from researchers as they may affect the patients' quality of life and performance. According to Mostoufi-Moab et al. (2016), HL patients have the highest frequency of endocrine side effects (60.1%) than other cancer patients. This review aimed to identify endocrine side effects among patients who were treated for HL during childhood.

2. Methodology

Search to identify possible studies that investigated endocrine side effects among patients treated for HL during childhood was conducted using Scholar Google and two databases (Pubmed and Sage). The search identified a similar review conducted in 2012 (van Dorp et al., 2012); therefore, we set the search for publication date as 2012-2021. Inclusion criteria included: a research study that investigated endocrine side effects of HL treatment; the patients were treated during childhood, the publication was written in English and published from 2012-2021. The search terms were: childhood Hodgkin lymphoma, childhood cancer, endocrine complications, endocrine effects, and treatment side effects.

3. Results

The narrow search period limited the results; only eighteligible articles were identified and retrieved for full-text reading. Few articles addressed the endocrine side effects for HL treatment combined with other types of cancer; the articles were included in the review only if the data were presented according to the specific cancer type rather than total results. In this case, the number of HL patients was reported in addition to results for the HL in specific. A summary of the retrieved studies' characteristics is provided in Table (1).

Table 1. Review Studies Characteristics

Study	Design	N	Ageat diagnosis (years)	Follow-up (years)	Treatment	Outcome Variables
(Çağlar et al., 2014) Turkey	Cohort study	N=120 HL: n= 43 (36%)	8.5 (5-12)	8	Group 1: CT only, n=2 Group 2: combination therapy of CT with RT, n=41	Thyroid function
(Fernandez-Pineda et al., 2018) USA	Cohort study	N=127	16 (4-22)	10	CT RT	Ovarian function
(Inskip et al., 2019) USA and Canada	Cohort study	N=12,183 HL: n=1,580 (13%)	8 (0-20)	20	RT	Thyroid function
(Keegan et al., 2018) USA	Cross-sectional	N=5,085 HL: n= not specified	Not specified	10	CT RT	Endocribne function
(Patterson et al., 2012) USA	cross-sectional	N= 519 HL: n=33 (6.4%)	5.3 (1.3-9.3)	7.2	CT RT	Endocrine function

(Servitzoglou et al., 2015) France		N=171 HL: n=50 (29.2%)	10.8 (2–17)	9.3	CT RT	Testicular function
(Swerdlow et al., 2014) England	Cohort study	N= 2127 HL: n= 558 (26.2%)	Not specified	12.2	CT RT	Ovarian function
(van Dorp et al., 2013) Netherlands	cross-sectional	N= 201 HL: n= 24 (11.9%)	6.0 (0.0–17.5)	15.7	CT RT	Testicular function

CT: chemotherapy, **HL**: Hodgkin lymphoma, **RT**: radiotherapy,

Generally, the retrieved studies examined several side effects of HL treatment. According to Patterson et al. (2012), the hazard ratio for developing endocrine side effects of treatment among HL survivorswas 1.52 (95% CI 0.62–3.76). These endocrine side effects include gonadal dysfunction (36.4%), weight problems (21.2%), thyroid dysfunction (18.2%), and bone minerals problem (6.1%).

3.1 Determinants of endocrine side effects

According to Keegan et al.(2018), the risk for developing endocrine side effects differs according to sociodemographic characteristics. For instance, they found that the risk varies according to ethnicity; the hazard ratio forendocrine side effects mong Blacks was (HR=1.37, CI: 1.05–1.78) and Hispanics (HR=1.24, CI: 1.04–1.48), both higher than White patients' risk. Survivals living in a low socioeconomic status have a higher risk (HR=1.30, 95% CI: 1.10– 1.53). Further, the patients who were treated with chemotherapy alone had a higher cumulative risk for developing endocrine side effects (17.42%, 95% CI=15.65-19.27, p<.01) than those who received a combination of chemotherapy and radiotherapy (13.63%, 95% CI= 12.03-15.34, p<0.01).

4. Discussion

According to Çağlar et al.(2014), 51% of children diagnosed with HL developed primary hypothyroidism within 0.5-12.5 years of treatment (Median= 5 years). Regression analysis showed that children diagnosed with HL have a seven times higher risk of developing this disorder(95% CI 2.8-17.1, p <0.01). They also found that hypothyroidism occurred in patients who received combination therapy especially treated with RT doses of 2000-2999 cGy, while those who only received chemotherapy had zero incidences.

Further, 42% of patients with HLdeveloped thyroid nodules within nine years (1-17 years) after completing the therapy' a strong association was reported(OR=5.4, 95% CI=2.1-13.6, p <0.01). Other

thyroid disorders found among patients diagnosed with HL include parenchymal heterogeneity (n=13, 30%) and autoimmune thyroiditis (n=9, 21%).

Another study examined the incidence of hyperthyroidism among patients treated for HL. They reported the average dose to the thyroid gland among irradiated HL survivors as 36.4 Gy, which is considered one of the highest doses among cancer patients (Inskip et al., 2019). Further, the findings revealed that HL survivors had the highest risk among other cancer survivors (RR= 3.1, 95% CI: 1.6-5.9, P< 0.01).

4.1 Testicular Function

The luteinizing hormone and follicle-stimulating hormone (FSH) are central hormones for spermatogenesis with an inverse relationship. A study by Servitzoglou et al. (2015) revealed that almost 14% of HL patients had elevated luteinizing hormone levels. Further, among those with elevated luteinizing hormone, 85% had received abdominal radiotherapy (P= .03). The same study found that 95% of the patients received Procarbazine chemotherapy and that almost half of them (44%) had high serum FSH levels, which had a significant correlation with the procarbazine dose. This supports the relationship between the cumulative procarbazine dose and fertility impairment.

Another important marker is the Inhibin B level, which is associated with sperm quantity and infertility risk (van Dorp et al., 2013). It was reported that after a median follow-up time of 15.7 years, the levels are significantly low among survivors of HL (median 46 ng/L, R=10– 274). Further, after 3.3 years post the first follow-up, the levels decreased to 41 ng/L (10–269), suggesting that recovery of gonadal function among survivors of childhood HL is less likely.

5. Conclusion

Several women treated during childhood for HL reported having ovarian insufficiency; therefore, an ovarian transposition is frequently performed before radiotherapy treatment (Moawad et al., 2017). According to Fernandez-Pineda et al. (2018), exposure to alkylating agents (HR=11.2, 95% CI=3.4 to 36.8; p<0.0001) and radiotherapy doses > 1,500 cGy (HR=25.2, 95% CI=3.1 to 207.3; p=0.002) during the treatment for HL increase the risk of developing premature ovarian insufficiency during early adulthood.

Swerdlow et al.(2014) studied the incidence of premature menopause (before age 45 years) among women treated for HL. The incidence was almost 28.5% for women who started the treatment during childhood. Further, those who received the treatment during childhood (age<19 years) had a lower risk than other women who were treated during adulthood (20-35 years). Nevertheless, among patients who received a childhood treatment for HL, the future cumulative risk increases with age. For instance, at the age of 30, the risk ratio is 10.6 (95% CI= 8.2 to 13.4), which increased to 13.1 (95% CI= 10.4 to 16.2) at the age of 35 years.

Recommendations

Several clinical practice guidelines address the surveillance for late effects among childhood cancer survivors (Kremer et al., 2013). Such guidelines improve the identification of patient risk groups, specifies screening intervals and diagnostic tests, and then provide recommendations. Therefore, the

results of this review, which provide specific data about the thyroid and gonadal dysfunction, in addition to previous reviews, provide a base for developing such guidelines.

References

Çağlar, A. A., Oğuz, A., Pınarlı, F. G., Karadeniz, C., Okur, A., Bideci, A., Koçak, Ü., & Bora, H. (2014). Thyroid abnormalities in survivors of childhood cancer. JCRPE Journal of Clinical Research in Pediatric Endocrinology, 6(3), 144–151. https://doi.org/10.4274/jcrpe.1326

Fernandez-Pineda, I., Davidoff, A. M., Lu, L., Rao, B. N., Wilson, C. L., Srivastava, D. K., & Chemaitilly, W. (2018). Impact of Ovarian Transposition before Pelvic Irradiation on Ovarian Function among Long-term Survivors of Childhood Hodgkin Lymphoma: A Report from the St. Jude Lifetime Cohort Study. Pediatr Blood Cancer, 65(9), 139–148. https://doi.org/10.1002/pbc.27232.Impact

Inskip, P. D., Veiga, L. H. S., Brenner, A. V, Sigurdson, A. J., Ostroumova, E., Chow, E. J., Stovall, M., Smith, S. A., Leisenring, W., Robison, L. L., Armstrong, G. T., Sklar, C. A., & Lubin, J. H. (2019). Hyperthyroidism After Radiation Therapy for Childhood Cancer: A Report from the Childhood Cancer Survivor Study. International Journal of Radiation Oncology Biology Physics, 104(2), 415–424. https://doi.org/10.1016/j.ijrobp.2019.02.009

Keegan, T. H. M., Li, Q., Steele, A., Alvarez, E. M., Brunson, A., Flowers, C. R., Glaser, S. L., & Wun, T. (2018). Sociodemographic disparities in the occurrence of medical conditions among adolescent and young adult Hodgkin lymphoma survivors. Cancer Causes and Control, 29(6), 551–561. https://doi.org/10.1007/s10552-018-1025-0

Kremer, L. C., Mulder, R. L., Oeffinger, K. C., Bhatia, S., Landier, W., Levitt, G., & Hudson, M. M. (2013). A Worldwide Collaboration to Harmonize Guidelines for the Long-Term Follow-Up of Childhood and Young Adult Cancer Survivors: A Report From the International Late Effects of Childhood Cancer Guideline Harmonization Group. Pediatric Blood & Cancer, 60(4), 543-549. https://doi.org/10.1002/pbc

Macdonald, T. (2010). Pediatric cancer: A comprehensive review. Part I: Biology, epidemiology, common tumours, principles of treatment and late effects. Canadian Pharmacists Journal, 143(4), 176–183. https://doi.org/10.3821/1913-701X-143.4.176

Mauz-Körholz, C., Metzger, M. L., Kelly, K. M., Schwartz, C. L., Castellanos, M. E., Dieckmann, K., Kluge, R., & Körholz, D. (2015). Pediatric hodgkin lymphoma. Journal of Clinical Oncology, 33(27), 2975–2985. https://doi.org/10.1200/JCO.2014.59.4853

Moawad, N. S., Santamaria, E., Rhoton-Vlasak, A., & Lightsey, J. L. (2017). Laparoscopic Ovarian Transposition Before Pelvic Cancer Treatment: Ovarian Function and Fertility Preservation. Journal of Minimally Invasive Gynecology, 24(1), 28–35. https://doi.org/10.1016/j.jmig.2016.08.831

Mostoufi-Moab, S., Seidel, K., Leisenring, W. M., Armstrong, G. T., Oeffinger, K. C., Stovall, M., Meacham, L. R., Green, D. M., Weathers, R., Ginsberg, J. P., Robison, L. L., & Sklar, C. A. (2016). Endocrine abnormalities in aging survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. Journal of Clinical Oncology, 34(27), 3240–3247. https://doi.org/10.1200/JCO.2016.66.6545

Patterson, B. C., Wasilewski-Masker, K., Ryerson, A. B., Mertens, A., & Meacham, L. (2012). Endocrine health problems detected in 519 patients evaluated in a pediatric cancer survivor program. Journal

of Clinical Endocrinology and Metabolism, 97(3), 810–818. https://doi.org/10.1210/jc.2011-2104

Servitzoglou, M., De Vathaire, F., Oberlin, O., Patte, C., & Thomas-Teinturier, C. (2015). Dose-Effect Relationship of Alkylating Agents on Testicular Function in Male Survivors of Childhood Lymphoma. Pediatric Hematology and Oncology, 32(8), 613–623. https://doi.org/10.3109/08880018.2015.1085933

Shimazaki, S., Kazukawa, I., Mori, K., Kihara, M., & Minagawa, M. (2020). Factors predicting endocrine late effects in childhood cancer survivors from a Japanese hospital. Endocrine Journal, 67(2), 131–140. https://doi.org/10.1507/endocrj.EJ19-0228

Swerdlow, A. J., Cooke, R., Bates, A., Cunningham, D., Falk, S. J., Gilson, D., Hancock, B. W., Harris, S. J., Horwich, A., Hoskin, P. J., Linch, D. C., Lister, A., Lucraft, H. H., Radford, J., Stevens, A. M., Syndikus, I., & Williams, M. V. (2014). Risk of premature menopause after treatment for Hodgkin's lymphoma. Journal of the National Cancer Institute, 106(9). https://doi.org/10.1093/jnci/dju207

van Dorp, W., van Beek, R. D., Laven, J. S. E., Pieters, R., de Muinck Keizer-Schrama, S. M. P. F., & van den Heuvel-Eibrink, M. M. (2012). Long-term endocrine side effects of childhood Hodgkin's lymphoma treatment: A review. Human Reproduction Update, 18(1), 12–28. https://doi.org/10.1093/humupd/dmr038

Van Dorp, Wendy, Van Der Geest, I., Laven, J. S. E., Hop, W. C. J., Neggers, S., De Vries, A., Pieters, R., & Van Den Heuvel-Eibrink, M. (2013). Gonadal function recovery in very long-term male survivors of childhood cancer. European Journal of Cancer, 49(6), 1280–1286. https://doi.org/10.1016/j.ejca.2012.12.007