Research Ideas and Outcomes 7: e71271
doi: 10.3897/rio.7.e71271

Research Idea

Sedation-Led chEmotherapy Evades Pain (S.L.E.E.P.)

Marco Cirillo ‡

‡ Heart Failure Surgery Unit Director - Cardiovascular Department - Poliambulanza Foundation Hospital, Brescia, Italy

Corresponding author: Marco Cirillo (marcocir8@gmail.com)

Reviewed v 1

Academic editor: Editorial Secretary

Received: 08 Jul 2021 | Accepted: 12 Oct 2021 | Published: 28 Oct 2021

Citation: Cirillo M (2021) Sedation-Led chEmotherapy Evades Pain (S.L.E.E.P.). Research Ideas and Outcomes 7: e71271. https://doi.org/10.3897/rio.7.e71271

Abstract

Chemotherapy and other invasive therapies are often limited by side effects, pain and negative experiences that can limit adherence to the therapy itself. Such negative components add to the patient's depressive state due to the disease. This research project proposes the use of deep sedation during chemotherapy sessions or other disabling therapies in the treatment of tumors or other severe diseases. The proposed protocol provides for an ad hoc hospitalization which could be during the night, during the day or limited to a few hours. Administration during sleep eliminates the memory and the negative impact the treatment has on the rest of the patient's daily life. This approach also agrees with the evidence of the circadian rhythm of cellular repair processes, which is greater at sunrise and sunset and linked to a good quantity and quality of sleep. In conclusion, this project aims to reduce the negative impact and increase the adherence to and efficacy of the therapy itself.

Keywords

disease, memory, cancer, chemotherapy, sedation, pain

Objective of the project

Reduce pain, side effects and memory of chemotherapy and/or particularly invasive therapies in oncological or severe pathology by deep sedation, with night/day/hourly clinic/home hospitalization (Fig. 1).

Figure 1. doi

The well-known tale of "Sleeping Beauty" is a good simile for this project. In the impossibility of canceling the death of the princess because it was determined by a higher evil will, the solution found by the godmother fairies is to make her fall asleep waiting for a solution that could come over time. Sleep protects the princess, keeps her alive and prevents her from pain. At the same time, the people who love her don't see her suffer and keep the hope that one day she can just wake up and resume her normal life without even the memory of the curse [cropped from "The sleeping beauty" by John Collier (1921), available via Wikimedia Commons, Public Domain].

Overview and background

Chemotherapy and other invasive therapies are often limited by disabling side effects, pain [Pearce et al. 2017] and the negative life experience, which can compromise the completeness of the therapy itself [Wyatt et al. 2015]. These negative effects have a great impact on the patient and add up to the state due to the disease [Breen et al. 2009, Mazzotti et al. 2012]. The curative value of therapy is sometimes questioned because of this implications. Studies have reported rates of 3%–19% for patients who partially or completely refused chemotherapy [Frenkel 2013]. It is often agreed that a different approach would be needed to address the various assessments that play a role in the refusal of treatment [Huijer and Leeuwen 2000].

Project

The project proposes the use of deep sedation during chemotherapy sessions or other disabling therapies in the treatment of tumors or other severe diseases, based on studies demonstrating a beneficial effect of moderate sedation during chemotherapy for breast cancer [Dikmen Mentes et al. 2013]. Deep sedation removes the awareness of the side effects from the patient as well as pharmacologically counteracting some of them. In fact, some agents used for deep sedation (e.g. Propofol) have a known antiemetic effect [Borgeat and Stirnemann 1998]. Moreover, it removes the lived experience and reduces the reconsolidation of emotional episodic memory [Vallejo et al. 2019]. Carrying out chemotherapy during the night would also have the advantage of maintaining the sleep-wake biorhythm, of not interfering with the patient's daily life. Several studies agree that efforts to normalize circadian sleep and activity rhythms through lifestyle intervention may be relevant to improving cancer outcomes [Innominato et al. 2014] [Jensen et al. 2014] [Wang et al. 2016] [Block et al. 2009] [Block 2018]. On the other hand, the use of procedural sedation is widespread and its modalities and side effects are known, so this state of the art could be well applied in the present project [Simmons 2005, van Haperen et al. 2019, Koers et al. 2018].

Patient management outline

The treatment scheme will be established according to the indications of the reference oncologist and to the specific agents.

Main scenario:

- the patient "goes to sleep in the hospital" in dedicated rooms and during sleep receives the chemotherapy or other indicated treatments; the sedation is stopped the next morning and the patient wakes up with the side effects controlled and reduced to a minimum and without the memory of the administered therapy; then he can live his day normally; therapy does not "break" his life but is "inserted" into it.

Alternative scenarios:

- the patient normally goes to work and at the end of the morning enters the hospital to undergo chemotherapy treatment under sedation during the period of the normal afternoon nap, then returns home as if returning from work;
- sedation-led therapy could also be performed at home, in particular cases, with a sedation assisted by healthcare personnel.

The scenarios could be adapted according to the knowledge of chronotherapy and circadian rhythms of cell regeneration, greater at sunrise and sunset [Yang et al. 2018]. Since the chemotherapy infusions last from half an hour to an hour, the next time is reserved to alter the circadian rhythm as little as possible. The sedation could be

implemented with known adjuvant sleep regulators [Innominato et al. 2016]. The use of temporary aids such as a nasogastric tube should be evaluated.

Clinical perspective

The project aims to insert chemotherapy, or other invasive therapies, into the normal life of patients by relegating it to periods of sleep, thus removing most of its negative impact and effects from consciousness. At the same time this regulates the sleep-wake cycle, often altered by the disease itself but very important for the patient's overall biological response. This advantage aims to increase adherence to therapy and therefore its effectiveness.

It must be said that given that the majority of side effects occur beyond the time of drug administration and given the presence of highly active drugs for the prevention and treatment of nausea and vomiting, this project could be applied to a limited and selected series of patients, as regards the control of the side effects themselves. Ideal candidates would be those with severe anticipatory vomiting, agitation, young people etc.

But in this pilot series the usefulness of this approach could also be tested with regard to the inclusion of drug treatment in the patient's normal life.

The impact of "going for chemo", dealing with other patients who are in different stages of the disease, "consciously" experiencing the administration of the drug that comes down from the drip, remaining "thinking" during therapy, etc. it is certainly very hard; it would be different to "go to sleep in hospital" and receive therapy during sleep, waking up without having consciously experienced the therapeutic act.

References

- Block K (2018) The Circadian System and Cancer: It's About Time! Integrative Cancer Therapies 17 (1): 3-4. https://doi.org/10.1177/1534735418755916
- Block KI, Block PB, Reynolds Fox S (2009) Making Circadian Cancer Therapy Practical. Integrative Cancer Therapies. December 2009: 371-386. https://doi.org/10.1177/1534735409352028
- Borgeat A, Stirnemann HR (1998) Antiemetische Wirkung von Propofol (antiemetic effect of propofol. Anesthetist 47 (11): 918-924. https://doi.org/10.1007/s001010050643
- Breen SJ, Baravelli CM, Schofield PE, Jefford M, Yates PM, Aranda SK (2009) Is symptom burden a predictor of anxiety and depression in patients with cancer about to commence chemotherapy? Medical Journal of Australia 190 https://doi.org/10.5694/j.1326-5377.2009.tb02480.x
- Dikmen Mentes S, Unsal D, Baran O, Argun G, Ertunc FN (2013) Effect of Sedation with Midazolam or Propofol on Patient's Comfort During Cancer Chemotherapy Infusion: A Prospective, Randomized, Double-Blind Study in Breast Cancer Patients. Journal of Chemotherapy 17 (3): 327-333. https://doi.org/10.1179/joc.2005.17.3.327
- Frenkel M (2013) Refusing treatment. Oncologist 18 (5): 634-636. [In English]. https://doi.org/10.1634/theoncologist.2012-0436

- Huijer M, Leeuwen E (2000) Personal values and cancer treatment refusal. Journal of Medical Ethics 26: 358-362. https://doi.org/10.1136/jme.26.5.358
- Innominato PF, Roche VP, Palesh OG, Ulusakarya A, Spiegel D, Lvi FA (2014) The circadian timing system in clinical oncology. Ann Med 46 (4): 191-207. https://doi.org/10.3109/07853890.2014.916990
- Innominato PF, Lim AS, Palesh O, Clemons M, Trudeau M, Eisen A, Wang C, Kiss A, Pritchard KI, Bjarnason GA (2016) The effect of melatonin on sleep and quality of life in patients with advanced breast cancer. Support Care Cancer 24 (3): 1097-1105. https://doi.org/10.1007/s00520-015-2883-6
- Jensen LD, Gyllenhaal C, Block K (2014) Circadian angiogenesis. Biomol Concepts 5 (3): 245-256. https://doi.org/10.1515/bmc-2014-0009
- Koers L, Eberl S, Cappon A, Bouwman A, Schlack W, Hermanides J, Preckel B (2018) Safety of moderate-to-deep sedation performed by sedation practitioners. European Journal of Anaesthesiology 35 (9): 659-666. https://doi.org/10.1097/eja.0000000000000835
- Mazzotti E, Antonini Cappellini GC, Buconovo S, Morese R, Scoppola A, Sebastiani C, Marchetti P (2012) Treatment-related side effects and quality of life in cancer patients. Supportive Care in Cancer 20 (10): 2553-2557. https://doi.org/10.1007/s00520-011-1354-y
- Pearce A, Haas M, Viney R, et al. (2017) Incidence and severity of self-reported chemotherapy side effects in routine care: A prospective cohort study. PLOS One 12 (10). https://doi.org/10.1371/journal.pone.0184360
- Simmons D (2005) Sedation and Patient Safety. Critical Care Nursing Clinics of North America 17 (3): 279-285. https://doi.org/10.1016/j.ccell.2005.04.009
- Vallejo AG, Kroes MC, Rey E, Acedo MV, Moratti S, Fernandez G, Strange BA (2019) Propofol-induced deep sedation reduces the reconsolidation of episodic emotional memory in humans. Science Advances 5 (3): eaav3801. https://doi.org/10.1126/sciadv.aav3801
- van Haperen M, Preckel B, Eberl S (2019) Indications, contraindications, and safety aspects of procedural sedation. Current Opinion in Anaesthesiology 32 (6): 769-775. https://doi.org/10.1097/aco.0000000000000777
- Wang Q, Ao Y, Yang K, Tang H, Chen D (2016) Circadian clock gene Per2 plays an important role in cell proliferation, apoptosis and cell cycle progression in human oral squamous cell carcinoma. Oncol Rep 35 (6): 3387-3394. https://doi.org/10.3892/or.2016.4724
- Wyatt G, Sikorskii A, Tesnjak I, Victorson D, Srkalovic G (2015) Chemotherapy interruptions in relation to symptom severity in advanced breast cancer. Supportive Care in Cancer 23 (11): 3183-3191. https://doi.org/10.1007/s00520-015-2698-5
- Yang Y, Adebali O, Wu G, Selby CP, Chiou Y, Rashid N, Hu J, Hogenesch JB, Aziz Sancar A (2018) Cisplatin-DNA adduct repair of transcribed genes is controlled by two circadian programs in mouse tissues. Proceedings of the National Academy of Sciences 115 (21): E4777-E4785. https://doi.org/10.1073/pnas.1804493115