CHAPTER XVI

THE PROTOCOL OF HYPERTONIC SODIUM CHLORIDE ON PREVENTION OF DELIRIUM AFTER SURGERY

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1.INTRODUCTION

Post-operative delirium (POD) is defined as an acute neuropsychiatric syndrome characterized by a temporary and reversible brain functional disorder that can be seen after surgical intervention due to physical or physiopathological reasons (*Godfrey et al*.2020). Surgical intervention is a risk factor in the development of delirium, and risk factors for delirium due to surgical intervention may vary at different stages of the surgical process. Surgical intervention is a stress-filled stimulus that elicits an inflammatory response and as such is a form of trauma. Metabolic, immunological, neuroendocrine and inflammatory changes develop in response to overcoming this trauma in a stressed organism. The release of stress hormones and cytokines, inflammatory mediators, plays a role in the formation of these changes (Girard *et al*.2012). After the surgical intervention, the systemic inflammatory process is activated, cytokine and neurotransmitter release begins. Cytokines are polypeptide hormones secreted by glialar and macrophages in the central nervous system. Generally, extracellular levels increase in stress, inflammation, tumor, trauma and infection. Cytokines initiate the activation of microglia, increasing the permeability of the blood brain barrier to neurotoxins and cognitive impairment (Belarbi *et al*. 2012).

In the literature, it is stated that anxiety, fluid electrolyte imbalances, hypoxia, infections, and the neuroendocrine and neuroinflammatory response given to the surgical treatment by the organism increase the serum levels of inflammatory cytokines and increase the levels of S-100B from specific proteins that are neurobiochemical markers. (Cerejeira *et al*.2010, Cortese & Burger 2017). Serum S-100B protein level plays an important role in determining cerebral affection and cognitive loss in delirium (Kunihara *et al.* 2006). The main cytokines released after surgery in delirium are; interleukin-1 (IL-1), tumor necrosis factor (TNF-α), IL-6 and IL-10.The first reaction is the release of IL-1 and TNF-α from activated macrophages and monocytes in damaged tissues. These factors cross the blood-brain barrier, causing cognitive impairment. The penetration of neurotoxic agents and

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inflammatory cytokines in the impaired blood-brain barrier can cause delirium (vanMunster *et al*. 2010, Cavallazzi, *et al*. 2012).

Delirium is mostly seen in surgical clinics after intensive care units in hospitalized patients (Mulkey *et al.,*2019; Ortega *et al.*2020). In the literature, it has been stated that the prevalence of delirium is 50% in elderly hospitalized patients, affecting 3-53% of patients undergoing major surgery and 83% of critical patients in intensive care unit (Cerejeira *et al*. 2010; Sanders *et al.* 2011; Cohen *et al,*2019). Although there are many factors that cause delirium, it is observed more in some patient groups. These patient groups; elderly patients are those undergoing cardiac and hip surgery (Holroyd-Leduc *et al*. 2010; Martinez *et al.* 2015). Studies show that postoperative patients have a high relationship between high CRP (C-reactive protein) and interleukin 6 (IL-6) levels and delirium in patients undergoing hip prosthesis surgery (VanMunster *et al*. 2008; Capri *et al.* 2014). VanMunster *et al*. (2008) found that IL-6 and IL-8 levels were high in patients developing delirium in their studies with patients who were operated on for hip fracture. As a result, they report that there is a relationship between IL-6 and IL-8 level and delirium pathogenesis, which may be related to IL-6 hyperactive delirium behaviors (VanMunster *et al*. 2008).

Delirium; It has negative effects on patients, patient relatives, health system in terms of emotional, functional and financial aspects. These effects are; Increases the length of hospital stay, mortality and morbidity, and increased hospital costs (Morandi *et al*. 2009; Koster *et al*. 2011; Banerjee *et al*. 2010;Grealish *et al*.2019). Cognitive and functional losses, which have long-term effects of delirium, may continue in the period after discharge, causing patients to be hospitalized again (Koster *et al*. 2011). Because of its negative effects on health, the symptoms of delirium are not yet fully recognized and because it is mixed with different cognitive disorders, it is generally not noticed by health professionals (Fong *et al*. 2009; Banerjee *et al*. 2010).

Studies have reported that cytokines, one of the inflammatory markers, can cross the blood-brain barrier after surgery and cause brain damage and delirium (Xin *et al.* 2017, Mazandarani *et al*. 2012). Therefore, it is necessary to determine the diagnostic usage possibilities of inflammatory markers and their role in delirium etiology. Thus, preventive and diagnostic evidence-based studies can be conducted to reduce cytokine release. Evidence-based studies to prevent delirium development by decreasing the level of cytokines after surgery in literature reviews are insufficient. It is stated in the literature that administration of hypertonic sodium chloride infusion to the patient before surgery can reduce cytokine

release by preventing delirium and prevent delirium (Xin *et al.* 2017; Mazandarani *et al*. 2012). Hypertonic sodium chloride has an immunomodulatory effect by blunting neutrophil activation and reducing cytokine production and preventing cytokines that are effective in the development of delirium from crossing the blood barrier system (Mazandarani *et al*. 2012).

In this article, it was aimed to give information about the intervention protocol applied in the study of the effect of hypertonic sodium chloride solution on prevention of delirium in surgical patients over 65 years of age. In order for delirium to be seen at a high rate in surgical clinics and to reduce the negativities caused by it, it is necessary to diagnose with early biological markers and screening scales and apply preventive interventions. With these preventive applications, early diagnosis will be provided for delirium, morbidity and mortality rates will be reduced, and diagnosis-treatment costs will be positively affected. In addition, this randomized controlled clinical study, which requires a multidisciplinary team approach, is an indication that nurses can take part in these studies with their educational level, knowledge, skills, clinical experience, and the roles and responsibilities they have undertaken as a member of the team in predicting and preventing delirium patients.

2. METHOD

In this article, it was aimed to explain the protocol followed as a randomized controlled clinical trial to determine the effect of hypertonic sodium chloride (NaCl) application in the prevention of delirium seen in patients over 65 years old after surgery.

2.1. Type of the Research

This research is a randomized controlled clinical study from epidemiological studies and an interventional protocol that is tracked in this clinical study with application-oriented.

2.2. Place and Date of the Research

This research was conducted in University of Health Sciences Derince Training and Research Hospital's orthopaedics and cardiovascular surgery clinics between the dates September 2018 and May 2019. Orthopaedics and cardiovascular clinics and the patients in these clinics were selected due to the reason that in literature, delirium development rate was high especially following hip fracture, hip prosthesis and cardiovascular surgery (McPherson *et al*. 2013)

The patients that are operated with orthopaedic and cardiovascular diagnosis are hospitalized generally one day before the surgery since they are prepared as elective surgery, and next day surgical intervention are

applied. All orthopaedic patients that undergo a surgery generally are not taken into intensive care unit unless it is needed, and after the operation, nurses make their admission into clinics and routine postoperative follow-ups begin. In general, the patients those come to orthopaedic clinic after surgical intervention start to oral intake with fluids after 6-8 hour, and when they tolerate the fluid, immediately normal alimentation is started. After cardiovascular intervention, most of patients are taken into intensive care unit and after extubate, they can start to oral feeding with fluids in 6-8 hour. In orthopaedic, cardiovascular and intensive care clinics' routine practice, there are post-op drug administration protocols. Patient-controlled analgesia for pain treatment is used on most of the patients undergoes cardiovascular and orthopaedic surgery. This practice is also valid for intensive care patients, and it is followed up by anaesthesiologist and nurses. Usually on the morning of the second day after the surgery, patients are mobilized by standing up with doctors and nurses. Within patient care, by taking part of in all processes during the hospitalization of hospitalized patients for the purpose of planned surgical intervention, nurses has a guiding and key role in the patient's risk assessment in terms of delirium. Patients are often discharged from hospital in the third or fourth day after surgery. In this study, patients are evaluated in terms of delirium throughout one day before surgical intervention and average three days after intervention.

2.3. Population and Sample of the Research

This interventional protocol's population is composed of hospitalized patients, who accept voluntary participation and received written and oral approval, for cardiac surgery intervention to cardiovascular surgery clinic and for hip prosthesis surgery to orthopaedic clinic during the study in the institution, that research will be conduct. For the number of sample, power analysis of the study calculated in GPower 3.1. In the study of Xin *et al*. (2017) named as "Hypertonic saline for prevention of delirium in geriatric patients who underwent hip surgery", delirium prevalence difference between hypertonic saline applied group and isotonic applied group is given as 26,6%. According to results of this study, for 80% power number of samples must be at least 76, in two groups that each has 38. With considering the population representation ability of samples should be strong, in this study, number of samples was made with 100 patients, for each group has 50 patients.

In the time period that is study conduct, total 11 patient that were comply with criteria and accepted the participate the study were excluded from the study, since five of them had their operations cancelled, four of them was transferred to intensive care unit before operation due to respiratory problems and two of them is refused to undergo an operation.

Sample exclusion criteria are as follows;

i. Those who are under 65,
ii. Those who has score in Standard Mini-Mental State Examination (MMSE) less than 24,
iii. Patients with a history of delirium before the surgical intervention,
iv. Patients with neurologic and mental medical record,
v. Those who are using tranquilliser and antidepressant,
vi. Patients that are recently using glucocorticoid because of infection and chronic inflammatory
vii. Those who have anti-inflammatory drug utilization at least three days before operation, who have communication obstacle and who have addiction of alcohol or drug are excluded.

In addition, at every stage of research, termination of the research and taking related precautions in case of developing acute coronary failure, renal failure and electrolyte abnormality are taken into account.

Randomisation of the sample: Before implementation, firstly, assigning of groups that will be applied HSC and SC was realised.

Group that was applied Hypertonic Sodium Chloride (NaCl) (HSC): A group of 50 patients who receive 150 ml of 3% + 150 ml of 3% = 300 ml of 6% of hypertonic sodium chloride, which is selected randomly with MedCalc 11.5.1. Packaged software from 100 patients (150 ml of 3% hypertonic sodium chloride in mediflex bag is product of Eczacıbaşı-Baxter Hospital Products Industry and Trade Inc. and is applied intravenously).

Group that was applied Sodium Chloride NaCl (Isotonic) (SC): A group of 50 patients who receive 500 ml of 0.9% sodium chloride (isotonic) (NaCl) and which is selected randomly with MedCalc 11.5.1. Packaged software from 100 patients (500 ml of 0.9% of isotonic polypharmacy is a product of Eczacıbaşı-Baxter Hospital Products Industry and Trade Inc. and is applied intravenously).

During the research, in order to reduce affection and ethical problems, MedCalc 11.5.1 packaged software is used for the HSC and SC groups (Kanık, 2009). With this program, two different interventions from 100

patient as A (6% of hypertonic sodium chloride NaCl) and as B (0,9% of sodium chloride NaCl) was randomly assigned. Through the program that is used, between 1 and 2 random 20 number was written and when it came 1, A intervention to first patient, B intervention to second patient was applied and when it came 2, B to first patient, A to second patient was applied. By this operation, arrangements were made so that there will be two patients in each column (Table 1).

Table 1: Assigning HSC and SC Groups Randomly

Random Number	1		1		1		2		2		2		1		1		2		2	
Patient No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Assign	A	B	A	B	A	B	B	A	B	A	B	A	A	B	A	B	B	A	B	A

2.4. Data Collection Tools

In this randomize clinic study, individual Features Form, Pre- Intra- and Postoperative Risk Assessment Form, The Nursing Delirium Screening Scale (Nu-DESC) and Mini-Mental State Examination (MMSE) was used as data collection tools. Required information for pre and postoperative risk assessment forms and also laboratory findings (blood tests) of patients was obtained by doctor and nurse inspection form that taking part in patient file. Furthermore, results about pre and postoperative serum cytokines level was recorded in pre and postoperative assessment forms. During 1-10 September 2018, with 10 patients in the University of Health Sciences Derince Training and Research Hospital's orthopaedic clinic, pre-application about only using forms and comprehensibility of forms was made by researchers. Through pre-application, intelligibility of forms and expediency for the aim of the study was evaluated. In the line with the results, necessary arrangements about the forms that will be used were made.

2.5. Individual Features Form

Twelve questions took part in this form, which is developed by the researcher in order to determine of patients' age, gender, marital status, educational background, medical diagnosis, comorbid chronic diseases, smoking and alcohol usage and continuous drug use status.

2.6. Pre- Intra- and Postoperative Risk Assessment Form

This form is actually three-step follow up forms that is developed by the researcher with the knowledge of literature and which consist of preoperational, intra-operational and post operational risk factors about post-op delirium (Oh *et al.*2015; Scholz *et al*. 2016; Gosselt *et al*. 2015; Raats *et al*. 2015; DeWitt, 2018). These forms are consist of the questions about presence of invasive procedure, visual and hearing impairment, risky drug usage status, presence of diseases that develops in hospitalisation time period, urinal catheter, bowel evacuation, level of mobilisation, circle of sleep, nutrition and pain status, duration of anaesthesia, duration of surgery, blood transfusion status and laboratory findings.

2.7. The Nursing Delirium Screening Scale (Nu-DESC)

This scale was used for pre and postoperative delirium screening. Gaudreau *et al.* (2005) develop this scale and it is for nurses to use. It consists of five articles that are orientation disorder, inappropriate behaviour, inappropriate communication, illusion-hallucination and psychomotor retardation. Application of it takes less than 2 minutes. Evaluation of articles is made is based on 0,1 and 2 points. In this interventional protocol, delirium screening with the scale was performed every day in 24 hour period throughout 3 days after surgery. Since delirium is usually seen second or third day after surgery (Chang et al., 2008), patients were examined in total 1200 times in the sense of delirium diagnosis three times in a day at 8 hour intervals between one day before the surgery and three days after the surgery. Presence of delirium is determined with the guidance of the DSM-IV scales as gold standard by nurses of clinics that patients stay and two-neurology specialist. It was ensured that researchers that are making the tests were blind to each other.

2.8. Mini-Mental State Examination

It is a test that used for cognitive function screening. The short test which is developed by Folstein and friends in 1975 and Turkish legitimacy and that is the most frequently used test for dementia scanning (Folstein *et al*.1975). It consists of eleven questions and it is evaluated over 30 points. Completing of the test is takes almost 10 minutes. Between twenty-nine and thirty point normal, between 18-23 points mild dementia, 17 point and

below is compatible with severe dementia. Orientation, memory, attention, calculation, recall, language, motor functions and perception, visuo-spatial abilities are tested. It's easy and quick application is the greatest advantage of it.

In this study, all patients' first assessment is made within 24 hour following their hospitalization. In the first evaluation, Standardize Mini-Mental Test was applied and patients' data were recorded. For the uneducated patients, Standardize Mini-Mental Test for uneducated (MMSE) was used. Patients who had MMSE score below 23 in first assessment were excluded from the study. If the patients who have hearing impairment were using hearing aid, it was ensured that the device was used during the application of the test.

2.9. Data Collection Method

Data was collected as randomized controlled double blind. In data collection, MedCalc 11.5.1 packaged software is used for the randomization of samples. Patients that will be performed application and be collected their data were divided into two as group that will be applied hypertonic sodium chloride (experimental) and group that will be receive sodium chloride (control). In September 2018, implementation of research was begun and in April 2019, it is finalized when it reached the planned figure. Since continuity of intervention have to be provided through 24 hour due to the feature of the studied subject, the interventions of the study was maintained with anaesthesiologists, clinic doctors and nurses. Therefore, orthopaedic, cardiovascular surgery and intensive care clinic physicians and nurses were trained. Training scheme about postoperative delirium, delirium risks, diagnosis and prevention was prepared and it was realised by ensuring that all nurses in orthopaedics and cardiovascular surgery clinics participated into them. Research was performed as double blind. Hypertonic sodium chloride (HSC) and sodium chloride (SC) group patients' files were also used on the purpose of follow-ups from their admission in the hospital till their discharge.

2.10. Implementation

It was ensured that preoperative intervention assessment and blood samples were taken before passing the application of hypertonic sodium chloride.

Preoperative Assessment and Collecting Blood Samples: On the behalf of delirium, risk assessment, one day before the surgery, Delirium

Screening Scale (Nu-DESC), Preoperative Delirium Risk Factors Assessment Form and for cognitive function evaluation Mini-Mental State Examination (MMSE) was applied to both groups and recorded. In preoperational period, patients who had score in screening scale over 2 and MMSE point between 23-17 and below 17 were excluded from study.

For both hypertonic sodium chloride and sodium chloride groups, venous blood sample was taken into sterile EDTA tubes before surgery and it was centrifuged at 4°C by separating the plasma in the laboratory (30 minutes at 3000 rpm) in order to determine blood level of systemic cytokine cells that are produced by macrophages and provide peripheral inflammatory activation that caused the formation of delirium. Plasma was divided into polypropylene tubes and kept in a freezer on -80°C until number of samples is completed and analysed. Centrifuging of venous blood samples and placing them into freezer was made by clinic nurses when the researcher was absent.

Prophylactic HSC and SC Application: On behalf of the application of prophylactic HSC and SC, it was ensured to order it into the files of patients who were divided into two as experiment (hypertonic sodium chloride) and control (sodium chloride) by randomized controlled. Registering the solutions into patients' file was made by researcher and anaesthesiologist who carry on the study as second consultant. In addition to routine treatment protocol, with supervision of anaesthesiologist in their clinic and researcher, 500 ml of 0,9% sodium chloride solution was applied on right upper arm intravenously to patients who were in sodium chloride group, an hour before anaesthesia in the way that it will be completed in 60 minute time period (Mazandaraniet *et al*. 2012). In the same way, 150 ml of 3% + 150 ml of 3% = 300 ml of 6% of hypertonic sodium chloride was applied on right upper arm intravenously to patients who were in hypertonic sodium chloride group, an hour before anaesthesia in the way that it will be completed in 60 minute time period in addition to routine treatment protocol (Mazandaraniet *et al*. 2012). Before this application, patients were informed about the process and their written and oral consent was received. During all these processes, patients were observed by nurses and doctors. In the case of acute heart failure, renal failure and electrolyte abnormality on patients in both groups during the realization of the stages, the treatment was ended and related precautions were taken.

Intraoperative Assessment: Hypertonic sodium chloride and sodium chloride applied patients were transferred to operating room for surgical intervention. Patients in both groups were monitored during the surgical

intervention and same anaesthetic applications were to all patients. In terms of delirium risk factors, patients were followed up during the surgical operation and findings were recorded with "Intraoperative Delirium Risk Assessment Form". In order to prevent delirium development due to blood pressure, pulse, oxygen saturation, electrocardiogram and deep sedation, bispectrality index and end-tidal CO^2 were monitored in both groups to ensure sedation control.

Postoperative Assessment and Taking Blood Samples: It is ensured that patients in both groups were transferred to their clinics and patients who need intensive care were transferred to intensive care units, and their treatments were made in accordance with the hospital routine protocol. Almost all patients who undergo cardiovascular surgery were taken into intensive care units. On the first day after surgery at 6 am, 5 ml venous blood samples were taken into sterile EDTA test tubes and it was centrifuged at 4°C by separating the plasma in the laboratory (30 minutes at 3000 rpm). Plasma was divided into polypropylene tubes and kept in a freezer on -80°C until number of samples is completed and analysed.

In order to determine postoperative delirium, between 1-3 days after surgery delirium screening was made with The Nursing Delirium Screening Scale three times a day between 08-16, 16-24 and 24-08 hours. Moreover, delirium risk was evaluated with "Postoperative Delirium Risk Assessment Form". For the diagnosis of delirium according the symptoms that were arisen on these time intervals, consultation of neurologist was requested and registered. For those patients who were diagnosed delirium, clinic doctors and nurses informed in order to begin required interventions.

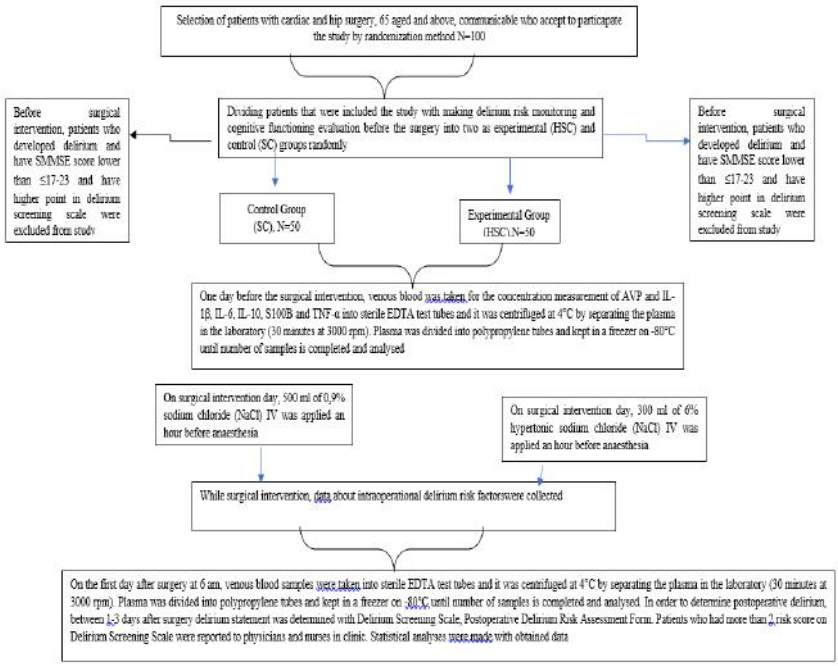
The Analysis of Blood Samples: In the blood samples of patients in both group, antidiuretic hormone level, IL-1β, IL-6, IL-10, TNF-α and S100B serum concentration measurements were made. Furthermore, in accordance with clinics' routine diagnosis and treatment protocol, apart from cytokine levels that are monitoring in blood samples taken from patients before and after surgery, other laboratory findings were taken from patients' files and recorded in delirium risk screening forms. Blood Samples of Patients: It consist of values indicating complete blood cell count, Na, K, Mg, BUN/Creatinine ratio, albumin, Hb and glucose levels. While these examinations were made in central laboratory of the hospital, measurement of cytokine levels were made in a contracted laboratory out of hospital. Financing of external laboratory tests was covered by the researcher.

Measurement Method of Patients' Blood Samples: methods of measurement were made in accordance with the suggestions of producer company. Person who conducted the tests was completely blind to information about study.

i. By using protein (Roche Elecsy 2010, Roche Diagnostics, Germany) kit, S-100B was studied in serum with immunoradiometric assay (sandwich method). S100B analyser automatically calculates based on calibration curve in every sample. Results are specified in terms of μg\L.
ii. Measurement of TNF-α with DIAsource ELISA kit, results in terms of pg/ml,
iii. IL-6 with AviBion branded kit from (Vantaa, Finland)
iv. IL-1β with Human ELISA Kit (BMS224HS Duoset, United Kingdom)
v. Level of IL-10 has been studied according to recommendations of manufacturers with commercial ELISA kits
vi. For AVP, DEH / VP / AVP ELISA kit was used.

Reference values for cytokines and for blood samples studied in the laboratory of the hospital where the research was conducted.

Figure 1. Research Flow Chart



2.11. Ethical Aspect of the Research

After acceptance of thesis topic and title by Bahçeşehir University Graduate School of Health Sciences, permission was obtained from Kocaeli University Ethical Committees of Clinical Research and from the chief physician of University of Health Sciences Derince Training and Research Hospital(Ethical approval number:KİA2018/195) . Before data collection forms were filled, patients were informed about the study and their written and oral consent were received. While studying control and experiment groups, clinic physicians and nurses were not informed about hypertonic saline application in order to prevent confusing factors. Nurses only informed about follow-ups of patient in the clinic to obtain prior information before the study.

3. DISCUSSION

This research was conducted to evaluate the effects of hypertonic sodium chloride on preventing develop of delirium that is seen as a very common medical complication on geriatric patient after orthopaedics and cardiovascular surgery even though it can be preventable. In line with this purpose, while searching the modulator effect of hypertonic sodium chloride on neuro-inflammatory processes that activated after surgery and its relation with delirium, we confirmed that our hypothesis which was "H_1; Application of hypertonic sodium chloride has an effect on preventing postoperative delirium.

Although type of surgical intervention is different, especially after cardiovascular and orthopaedic surgery both incidence and prevalence of delirium on geriatric patients is higher than other patient groups. Moreover, it affects elderly patients and their relatives emotionally, functionally and financially. These effects also cause prolonged hospital stay and increased hospital cost, mortality and morbidity (Banerjee *et al*. 2010). Therefore, evidence-based studies are needed to prevent the delirium.

The basic principles in health care are preventing disease, predicting medical problems and complication beforehand and taking precautions. In health care which required multi-disciplinary approach, prediction-prevent attitude is expected from healthcare professionals. Within this expectation and responsibility, knowing role and responsibilities of nurses on preventing, care and treatment of postoperative delirium is important for value-based care. These role and responsibility of nurses assist early

diagnosis of delirium and contribute to the healing process. In the sense of preventing the development of delirium, finalized pharmacological interventions are not fully available yet; however, it is priority of healthcare professionals to conduct studies that will form a basis of evidence (Champell, 2009). As a healthcare professional, nurses' involvement in evidence-based pharmacological and non-pharmacological interventions enables them to contribute the patients' healing process in value-based care and it will increase the visibility of the profession. In terms of preventing delirium, finding chance to combine critical thinking and decision-making skills with health care process by nurses will positively affect the decreasing the diagnosis-treatment costs and the rate of morbidity and mortality associated with delirium development. Through this conducted research, it is considered that awareness of duty and responsibilities of nurses is increased with giving opportunity of using critical thinking and decision-making skills effectively to nurses that play key role in clinical studies.

It is known that cytokines that is one of the indicators of inflammatory can cause brain damage and delirium after surgical intervention by passing blood-brain barrier. In the researches it states that application of hypertonic sodium chloride solution to patient before surgery reduces the cytokines release and can prevent delirium (Xin *et al*. 2017; Mazandarani *et al*. 2012). Hypertonic sodium chloride can provide a decrease in the level postoperative cytokine by modulating local and systemic inflammatory response (Kim *et al*. 2013; Zeng *et al*. 2017).

In the sense of effectiveness of this research which is conducted for evaluating the effects application of hypertonic sodium chloride after surgery on cytokines and delirium development, experimental and control groups with the same characteristics were determined by selecting randomly. To patients that were determined as experimental group 6% of hypertonic sodium chloride and to patients who were control group 0,9% of sodium chloride were applied one hour before surgical intervention. For both of groups, data about risk factors that are important on pre- intra-postoperative delirium development were recorded with data collection forms that prepared with literature review. In order to determine before and after surgery serum cytokine levels of patients that were included to study, their blood was taken and analysed. During their hospital stay, delirium risk assessment was made and patients who had more than 2 risk scores were reported to physicians and nurses in clinic to diagnosis delirium. In every stage of the research, the recorded data were analysed.

4. CONCLUSION AND SUGGESTIONS

In this study, interventional application protocol to determine the effects of hypertonic sodium chloride in preventing postoperative delirium was analysed on patients over 65 who underwent orthopaedic and cardiovascular surgery.

i. According the results with this applied protocol, POD development incidence (6,6%) on HSC group decreased significantly compared to the SC group (40%).

ii. It was out of expectation for study that from 50 patients who enrolled in the study with hypertonic sodium chloride application, POD development was seen only 3 of them. It is found that presence of the risk factors for pre-in-post delirium was higher than other patients since the average of these three people who developed delirium was 80 and above.

iii. In general it was determined that the patients who developed delirium in both groups had chronic diseases, and among these diseases there were diabetes and hypertension most, there were continuous multiple drug use, too.

iv. It was found that as a result of the application of hypertonic sodium chloride of inflammatory cytokines involved in the development of POD, development of delirium was prevented by decreasing the level of cytokines in blood of the experimental group after surgery. However, it was also found that level of cytokines was higher on control group that applied sodium chloride; therefore, incidence of delirium development was also high.

v. With hypertonic sodium chloride application, severity of delirium was also reduced beside incidence of POD, and severe delirium was never developed in the group that was applied hypertonic sodium chloride.It was determined that hypertonic sodium chloride has a modulator effect on the neuro-inflammatory processes that become active after surgery, and it prevent the delirium development.

vi. It was identified that recognition and preventing of the risk factors that effective in delirium development on pre-in-post operative periods is important to prevent and reduce of delirium that can be seen after surgery.

vii. In this national level clinical study that requires a multidisciplinary team approach, the role of the nurse in the study and the importance of the success that they contributed to the study were determined.

Based on these results;

i. Measurement of inflammatory cytokines guides preventive interventions on foreseeing, recognition and monitoring the process on delirium development. Therefore, it is suggested that measurement of serum cytokines after surgery as a supportive to delirium diagnosis tools may be beneficial at the level of protection.
ii. Conducting interdisciplinary study that includes wider patient groups and nurses by supporting application protocol of this study and getting evidence-based results are suggested.
iii. On the behalf of delirium diagnosis, it is also suggested that scales should be developed, nurses should be trained and these screening methods should be added to their daily routines.
iv. It is believed that this study guides the researchers who will use randomized controlled clinical trial from epidemiological research as a method of research. For this purpose, testing this intervention protocol on studies that will be conducted on similar or different patient groups is recommended.

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ABSTRACT

Background: The basic principle in health care; to prevent diseases, to predict medical problems and complications and to take precautions. The forecasting-prevention approach in healthcare, which requires a multidisciplinary approach, is expected from health professionals. Within the scope of this expectation and responsibility, delirium cannot be prevented and its frequency is increasing. This ongoing situation-problem "How can we prevent delirium in surgical patients?" The answer to the question was the most important factor in our search. While seeking this answer, it is important in terms of seeing the roles and responsibilities of nurses in preventing delirium and this study also confirms the concept of "key role" attributed to nursing.**Aim:** This research was performed to determine the effect of hypertonic sodium chloride (NaCl) on the prevention of delirium in surgical patients.**Material and Method:** This randomized controlled double-blind study was conducted between September 2018 and April 2019 in a training and research hospital, orthopedics and cardiovascular surgery clinics. It was determined that hypertonic sodium chloride was effective in reducing the incidence of delirium and the severity of delirium in elderly patients undergoing orthopedic and cardiovascular surgery to prevent elevation of serum plasma cytokines after surgery. All patients who were hospitalized for surgery at these dates formed the universe of the research. All patients who were hospitalized for surgery at these dates formed the universe of the study. The study group consisted of 50 patients with ≥65 years of age and 6% (NaCl) of hypertonic sodium chloride. The control group consisted of 0.9% NaCl sodium chloride (isotonic). The total of 100 patients were research sample. Delirium Screening Scale (Nu-DESC), Pre-in-Post Surgery Risk Factor Evaluation Form, Minimental Condition Assessment Test were used as data collection tools. SPPS 25.0 statistical package program was used to evaluate the data. In this article, the results of the analysis were not included because it was aimed to provide information about the protocol of the research. **Results:** It was determined that all the methods and protocols used in this study had important results in making decisions about the diagnosis, prevention and treatment of delirium.**Conclusion;** It is believed that this study will guide researchers who will use randomized controlled clinical trials from epidemiological studies as a research method. For this purpose, it is recommended to test

this intervention protocol in studies to be performed in similar or different patient groups**.**

Key Words: Delirium After Surgery, Aging, Neuroinflation, Cytokines, Hypertonic Saline: