ORIGINAL ARTICLE

The results of designing a new prototype device and algorithm in closed method intraperitoneal hyperthermia model in rats

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ABSTRACT

BACKGROUND: There is currently no standard medical device and method available for hyperthermic intraperitoneal therapy studies in rats. In this study, we present our designed device and algorithm that operates based on our own protocol for hyperthermic intraperitoneal treatment in rats. The aim was to demonstrate the effectiveness of the designed device, algorithm, and hyperthermia protocol by showing that the device can achieve the desired temperature inside the rat's abdomen, does not cause rat loss due to complications, operates autonomously, and provides warnings to the operator in case of emergencies.

METHODS: A closed method for intraperitoneal hyperthermia protocol was established for 6 female 8-week-old (280–310 g) albino Wistar rats. Fluid inlet and outlet tubes and a temperature probe were inserted through a 1 cm vertical incision between the xiphoid and bladder in the rat's abdomen, and the skin was sutured in a circular manner. A protocol for intraperitoneal hyperthermic treatment was established using a saline solution at a flow rate of 100 mL/min for 60 min, maintaining a temperature of 41°C±0.5 inside the rat's abdomen.

RESULTS: During the study, a temperature of 41°C±0.5 was successfully achieved in the abdomen of all rats at a flow rate of 100 mL/min±5 for 60 min. Due to three rats reaching a rectal temperature above 38.5°C during the hyperthermia protocol, external cooling was applied to the rat's tail base using ice. There were no losses until the postoperative 72nd h, and the study was successfully completed.

CONCLUSION: Our designed device and algorithm, which prioritize animal welfare, operate rapidly, safely, and with high accuracy sensitivity, have been successful in hyperthermic intraperitoneal treatment studies in rats. We believe that they can be used as a standard method and approach in hyperthermic intraperitoneal studies in rats.

Keywords: Animal welfare; device; hipec; intraperitoneal hyperthermia; rat.

INTRODUCTION

Intraperitoneal hyperthermia is a method of raising the temperature within the abdominal cavity, which includes organs such as the stomach, liver, and intestines. It is used in the treatment of specific cancer types such as ovarian and colorectal cancer, and can also be employed in experimental studies on mice to investigate the effectiveness of hyperthermia in treating cancer or other diseases. The goal of intraperitoneal hyperthermia is to selectively kill cancer cells while preserving healthy tissues.[1]

Over the past 40 years, there has been an increasing focus on intraperitoneal hyperthermia, particularly after the application of hyperthermic intraperitoneal chemotherapy

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to a 35-year-old patient with pseudomyxoma peritonei by Spratt *et al*.[1] The studies conducted by gynecologist, surgeon, and researcher Dr. Sugarbaker on peritoneal tumors, ovarian tumors, and gastrointestinal tumors have played a significant role in standardizing hyperthermic intraperitoneal chemotherapy and cytoreductive surgical procedures.[2] In addition, many researchers have contributed to investigating the efficacy of hyperthermic treatment by applying it in experimental studies on rats with various disease models.[3-6]

In humans, hyperthermic intraperitoneal treatment protocols are primarily performed using open and closed techniques, with some cases involving a combination of the two methods. The open technique, referred to as the "coliseum technique" by Sugarbaker, involves placing tubes and temperature sensors inside the abdomen without closing it after completing cytoreductive surgery and then covering it with a plastic sheet to conduct the procedure.[7] In the closed technique, tubes and temperature probes are inserted into the abdomen after the surgical procedure, and then the skin is sutured before initiating the hyperthermia process. The key difference between the closed and open methods is that the fluid delivered into the abdomen is under positive pressure in the closed technique, and the return flow is maintained under negative pressure.[8,9] However, this method is more prone to complications. For example, when fluid is delivered into the abdomen under high pressure, it can increase intra-abdominal pressure and potentially lead to sudden losses such as diaphragm elevation and cardiac arrest in the treated individual. Furthermore, due to the negative pressure used to remove the fluid from the abdomen during the procedure, there is a possibility that the intestine, mesentery, or other abdominal tissues may obstruct the tube system. In addition, various modifications of these procedures exist.[10,11]

Currently, there are numerous devices available on the market that utilizes different heating and algorithm systems for the application of hyperthermic intraperitoneal chemotherapy in humans, and new devices are being designed. Medical devices that allow the implementation of this treatment after laparoscopic surgery are particularly available today.

It should be noted that there is a possibility of harm to human health from various medical devices that come into contact with fluids to be heated, especially when they come into contact with an aluminum surface. Examples of such devices include hyperthermic intraperitoneal chemotherapy devices and fluid warmers that enable rapid blood transfusion.[12] In particular, when fluids come into contact with an aluminum heating surface, there is a possibility of aluminum mixing with the fluid, which may lead to heavy metal poisoning. Consequently, the FDA issued a statement on September 15, 2021, emphasizing the importance of this issue to healthcare providers using such devices.[13]

Unfortunately, for animal studies, which form the basis of clinical discoveries, there is a lack of widely produced hyperthermia devices. In fact, there are no standard intraperitoneal hyperthermia devices available on the market that researchers can use for animal studies.

As a result, when reviewing the literature, it can be observed that researchers have conducted hyperthermic intraperitoneal studies in rats using simple setups and basic peristaltic pumps that they have designed themselves.[3-6]

While an increase in such studies brings hope for future clinical hyperthermic research in humans, there is still no standardized device or method established for conducting intraperitoneal hyperthermia studies in rats. Although various methods have been used for heating and circulating fluid within the rat's abdomen, the adequacy of these methods and their safety remain debatable. Moreover, whether hyperthermia protocols should be performed using the open or closed technique has not been clarified.[9]

Furthermore, when examining the studies in the literature, the simplicity of the heating and fluid pumping systems used in studies involving hyperthermia in rats, as well as the lack of calibration testing, raise questions regarding whether sufficient heating or animal welfare is being ensured.

Therefore, there is a clear need for a new device, particularly for the application of hyperthermic treatment in small experimental animals such as rats and mice, whose abdominal volume ranges from 5 to 50 cc. Consequently, we would like to present our designed prototype device and intraperitoneal hyperthermia protocol for rats, demonstrating the sensitivity of our work through testing and calibration methods. Our designed device and hyperthermia protocol encompass the methodology and algorithm applied for performing closed-method intraperitoneal hyperthermia in rats.

MATERIALS AND METHODS

Ethics Committee Approval

This study was initiated with the approval of the Local Ethics Committee for Animal Experiments of Health Sciences University, Ankara, Türkiye, on May 26, 2022, with decision number etik-2022/11. All necessary measures were taken to ensure animal welfare and to avoid pain, suffering, and discomfort in the animal experiments. Surgical procedures were performed under anesthesia, and appropriate food and drink were provided before and after the procedures at the proper ambient temperature.

Design and Principles of Intraperitoneal Hyperthermic Therapy Device

In an intraperitoneal hyperthermic therapy device, the following components are required: a heating unit for heating the carrier fluid, a closed hose and pump system for circulating the fluid between the device and the rat abdomen, temperature sensors for measuring the temperature of the heated fluid, a pressure measurement system for measuring the pressure in the system, an emergency warning system for unexpected situations, and an algorithm and control unit to organize and manage the entire system (Table1), (Fig.1).

Table 1. Components of hyperthermic intraperitoneal therapy device

1. Heating unit
2. Pump system
3. Closed system disposable hose system [Figures 2-4]
4. Temperature sensors
5. Pressure sensor
6. Emergency warning system
7. Algorithm
8. Control unit

Figure 1. Intraperitoneal hyperthermic therapy device designed for rats.

Heating unit: It consists of an inner and outer part made of a heat-insulating, heat-resistant composite material, with holes allowing the passage of borosilicate glass tubes on the right and left sides and an infrared heater section.

Using a single servo motor, a specially designed peristaltic pump head, and a silicone hose of suitable thickness, it enables both the forward flow of the fluid at a flow rate of 1–3000 mL/min and the vacuuming of the fluid coming from behind.

Designed for rats, a 3 mm flat silicone drainage tube and the multipore feature at the tip of this tube aim to prevent the rat's intestines or different internal organs from getting trapped inside the tube due to negative pressure (Figures 2-4).

Figure 2. Sterilized and packaged single-use disposable rat intraperitoneal hyperthermia set.

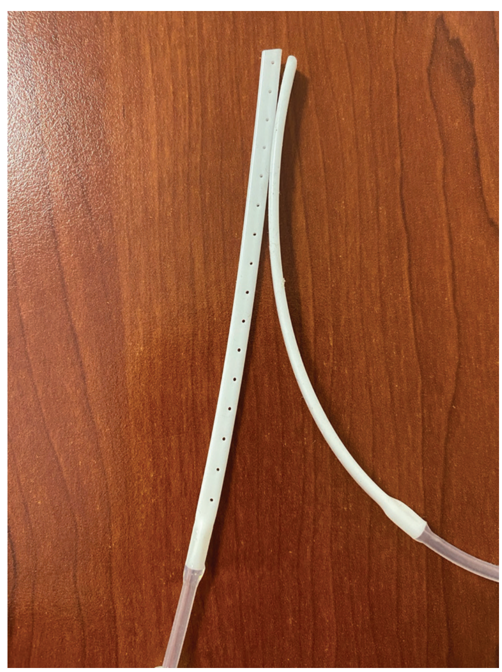

Figure 3. Ends of the hoses carrying hot water to the abdomen and providing return flow (3 mm flat silicone drain tip).

Figure 4. The disposable set specifically designed for hyperthermic intraperitoneal therapy in rats is now open.

For temperature measurement inside the rat's abdomen, measurement of the temperature of the fluid leaving the device, measurement of the temperature of the fluid returning from the rat's abdomen to the heating section of the device, measurement of the rat's rectal body core temperature, measurement of room temperature, and simultaneous temperature measurement inputs capable of performing 50 measurements per second with a temperature measurement accuracy of 0.1°C, usable for other procedures if necessary.

A pressure sensor capable of measuring the pressure by measuring the expansion of the external vessel wall simultaneously at a rate of 50 measurements per second.

According to the device's operating algorithm, if the desired temperature inside the abdomen is maintained at a temperature 0.5°C above the target for 60 s, the heating function stops and the fluid circulation continues. An audible warning is given during this process, and an alert is displayed on the control screen. When the desired temperature inside the abdomen exceeds 1°C above the target, the device stops heating and pumping the fluid. An alert is given audibly and on the control screen.

Control unit: The intraperitoneal hyperthermic therapy device can provide the desired fluid flow rate between 1 mL and 3000 mL/min. The device can apply the hyperthermic therapy protocol continuously for 12 h. It controls the heating of the fluid to be heated between 25°C and 50°C, and ensures its maintenance, adjustment, and manual interruption of the system functions in an automated manner.

Algorithm: In the intraperitoneal hyperthermic therapy device, the heating system is based on the temperature measurement by the temperature sensor that measures the temperature of the fluid exiting the heater. Accordingly, it initially operates at full power until the temperature reached inside the abdomen reaches the desired temperature. Then, when the temperature of the fluid leaving the heater reaches the target temperature inside the abdomen, it stops the heating operation. Simultaneously, it monitors both the temperature inside the abdomen and the temperature sensors after the heater. If the fluid cools down, the software provides power to the heater to heat it as required, or it shuts down the heater if the temperature rises.

Creation of Intraperitoneal Hyperthermic Treatment Protocol in Rats

A total of 6 female albino Wistar rats (8 weeks old, 280–310 g) were purchased from the Animal Research Center of Health Sciences University, Ankara, Türkiye. All rats were housed at temperatures of 20–26°C, humidity of approximately 40–70%, and a 12-h light-dark cycle, with free access to food and water.

For all surgical procedures, rats were anesthetized with intraperitoneal 3% pentobarbital sodium (Sigma-Aldrich; Merck KGaA, Darmstadt, Germany) at a dose of 35 mg/kg. In this study, an intraperitoneal hyperthermic treatment model was created by placing a temperature sensor inside the rat's abdomen, targeting a temperature of 41°C within the abdomen. A deviation of 0.5°C was considered normal. If the intra-abdominal temperature exceeded 41.5°C for 60 s, the protocol was stopped for animal welfare. In addition, if the intra-abdominal temperature exceeded 1°C above the target during hyperthermia, the protocol was intended to be stopped. A 200 mL saline solution was used as the carrier solution during the procedure.

After completing the anesthesia procedure as described above, a ventral 1 cm incision was made between the bladder and the xyphoid process. Two 3 mm silicone flat drainage tubes and one pediatric rectal temperature probe were placed inside the abdomen to facilitate the inflow and outflow of fluid. The incision site was sutured in a circular manner with 2/0 absorbable suture (GLIKOLAK, Polyglycolide Lactide, absorbable suture, BOZ Medical Equipment Company, Ankara, Türkiye), and hyperthermic treatment was applied for 60 min.

Simultaneously during the procedure, measurements of intraperitoneal temperature using a disposable pediatric temperature probe (Metko Ltd., Ankara, Türkiye), temperature of the inflowing and outflowing fluid, rat's rectal temperature, and room temperature were taken and recorded. The ambient temperature during the procedures was measured as 23°C. Fluid circulation was maintained at a rate of 100 mL/

min inside the rat's abdomen. To stabilize the rat's body temperature, external cooling was applied to the rat's tail base using ice when the rectal temperature reached 38.5°C [Figure 8]. After the intraperitoneal hyperthermic treatment, the disposable set and saline solution used were considered medical waste and delivered to the medical waste unit. Rats were observed for 72 h after the hyperthermic treatment and then euthanized (Figures 5-8).

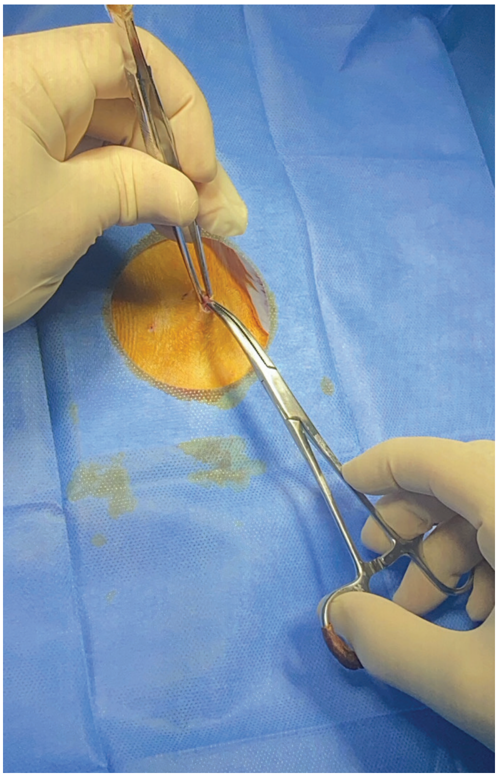

Figure 5. A 1 cm wide midline vertical incision made on the rat.

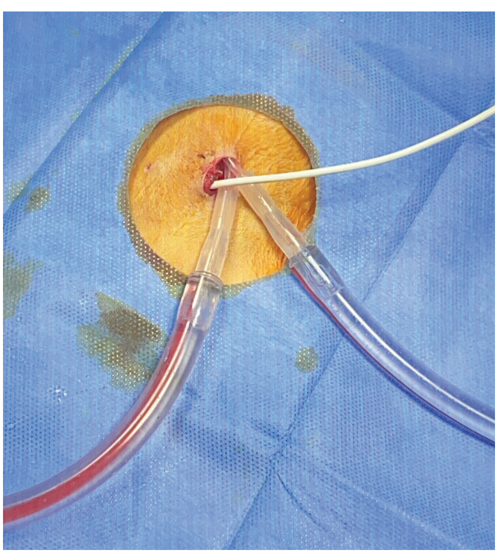

Figure 6. Placement of the tubes carrying the incoming and outgoing fluid, as well as the positioning of the temperature probe, after the incision.

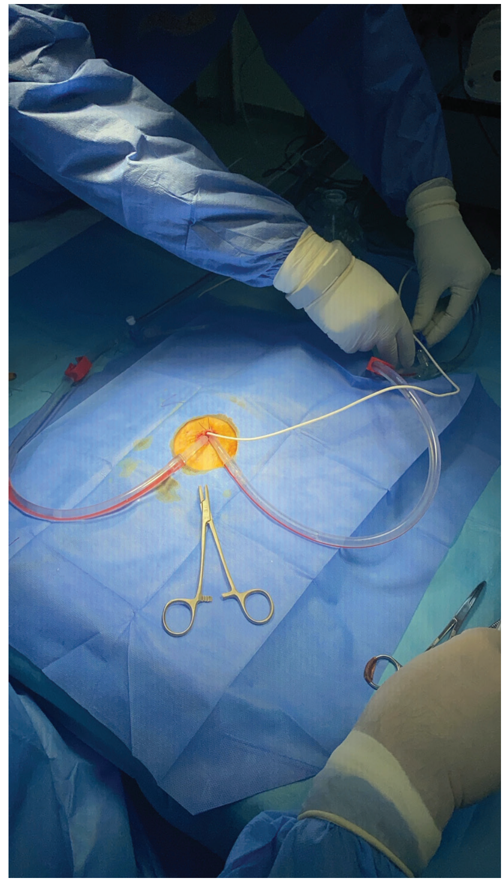

Figure 7. Placement of the tubes carrying the incoming and outgoing fluid, as well as the positioning of the temperature probe, followed by fixation with a circular suture after the incision.

Figure 8. Placement and use of ıntraperitoneal hyperthermic therapy device.

RESULTS

After the procedure, all rats were monitored in their cages for 72 h. No adverse events were encountered during the intraperitoneal hyperthermia treatment process. Furthermore, no clinical differences were observed in the rats during

Table 2. Results of intraperitoneal hyperthermic therapy in rats

Rat	Weight (gram)	Initial preparation time (minute)	Hypertermia period (minute)	Maximum rectal temperature (Celcius)	Intraperitoneal temperature (Celcius) (Min-max)	Initial heating time (second)	Maximum temperature inflow tube
No:1	280	12	60	39.3*	40.8–41.7	230	42.1
No:2	300	12	60	39*	40.6–41.7	210	42
No:3	290	10	60	37.5	40.6–41.4	200	42
No:4	310	8	60	38.2	40.7–41.7	190	42
No:5	280	7	60	38	40.3–41.6	210	42.1
No:6	290	5	60	39.2*	40.5–41.8	220	41.9

*Eksternal tail cooling procedure performed

the 72-h follow-up period after the procedures were performed. The targeted intra-abdominal temperature of 41°C was achieved between 190 and 230 s inside the abdomen, after which the hyperthermic intraperitoneal treatment process was initiated. The hyperthermic treatment process was concluded after 60 min. The temperature of the fluid entering the rat's abdomen during the procedure maximum ranged from 41.9°C to 42.1°C. In three rats, external cooling was administered by placing ice under the tail due to the rectal temperature exceeding 38.5°C during the intraperitoneal hyperthermia procedure (Table 2).

DISCUSSION

When we examine the literature, we find that there is no device available that can perform all these functions autonomously, be used in rats, and be commercially available. However, there are various hyperthermic intraperitoneal treatment devices designed specifically for use in humans, particularly for hyperthermic intraperitoneal chemotherapy, which are currently in use. Naturally, it seems technically challenging to use devices designed for approximately 70 kg humans in animals such as mice or rats weighing between 50 and 300 g. In fact, when we look at the literature, we do not come across the use of devices designed for humans in small laboratory animals such as rats or mice.

Furthermore, in hyperthermia studies conducted in rats, it is often observed that various hoses passing through heated water baths, such as a water circulation system, indirectly heat the fluid inside the hoses in an attempt to heat the liquid. Acceptably, this method, due to the heat resistance of materials such as plastic and silicone, takes time to heat the liquid and makes it difficult to achieve sufficient heating.

As an alternative, in medical hyperthermia devices used in humans, an enclosed aluminum structure is heated, and the fluid inside this container is heated accordingly and used for hyperthermia with the help of pumps. However, it is known that these types of hyperthermia devices and fluid warming devices have been withdrawn from the market and restricted in human use due to the risk of heavy metal poisoning, especially when the heated fluid comes into direct contact with the heater, such as aluminum, as stated in a bulletin issued by the FDA in 2021.[12-17]

In our designed protocol, an infrared heater is used as the heating system. Infrared heating systems inherently allow instant heating and the ability to instantly stop the generation of heat. This enables precise temperature control. The section where this infrared heater is located is covered with a heat and flame-resistant composite material. The infrared heating panel works based on the principle of heating the water as it passes through a borosilicate glass tube inside the panel. The liquid enters through one end of this borosilicate glass tube and, as it progresses under the heater with the pressure of the peristaltic pump, it exits the other end as a heated liquid. Disposable pediatric rectal temperature probes integrated into the plastic hose system through T-connectors are applied to both the inlet and outlet ends of this borosilicate glass tube. This way, our designed algorithm enables the measurement and recording of the temperature of the liquid passing through these temperature probes approximately 50 times/s, and the adjustment of the power of the heater.

In theory, our heating system can generate instant heat of approximately 200°C and heat the liquid inside the borosilicate tube very rapidly and in a controlled manner. Thanks to the algorithm and software we have developed, it can enable the circulation of liquid in body cavities at temperatures ranging from 25°C to 50°C, with a minimum flow rate of 5 mL/min and a maximum flow rate of 3000 mL/min.

However, simultaneous measurement of the liquid's temperature before and after it enters the heating system does not indicate whether the desired temperature is achieved inside the rat's abdomen during intraperitoneal hyperthermia. Therefore, during intraperitoneal hyperthermia, it is necessary to place a pediatric rectal temperature probe inside the rat's abdomen. In addition, simultaneous measurement of the rat's core body temperature is required during the hyperthermia period. This is because the rat's response to intraperitoneal heating during hyperthermia will be to increase its body temperature in an attempt to combat the hyperthermia. However, due to anatomical differences and a relatively larger surface area compared to humans, rats may experience complications such as cardiac arrest during intraperitoneal hyperthermia, leading to rat mortality. Therefore, monitoring the rat's body temperature is important, and in necessary cases, cooling with ice under the rat's tail should be applied. Particularly when the body temperature of rats exceeds 38.5°C, external cooling should be applied to reduce animal welfare concerns and minimize the risk of death.[6,14]

In rat hyperthermia studies, external peristaltic pumps are commonly used as the pumping system. When an appropriate diameter hose is used in the pump head, the amount and speed of the delivered liquid can be easily controlled. However, in small animals such as rats and mice, with abdominal volumes ranging from 10 to 50 cc, pumping liquid with uncontrolled high pressure can lead to increased pressure inside the abdomen and cause cardiac arrest in rats. Therefore, it is necessary to have a pressure sensor in the hyperthermic intraperitoneal therapy device used in small animals like rats and mice, which can measure the pressure in the system and stop the heating and pumping when necessary.[6-8]

In a closed system, peristaltic pumps perform the pumping function in the forward direction and act as a vacuum for the liquid coming from behind. For this reason, using a single peristaltic pump seems sufficient. In our device, we used a pressure sensor that measures the expansion and hardening of the plastic tube externally. This way, we have designed a rat hyperthermic intraperitoneal therapy device that is both temperature-controlled and pressure-controlled.

In addition, the algorithm of the heating system is based on the desired temperature to be achieved inside the rat's abdomen and the temperature measurement of the liquid coming out of the heating unit. We used the measurement of the liquid temperature exiting the rat's abdomen to evaluate the efficiency of the system. However, our heater always operates based on controlling the temperature of the liquid exiting the heating unit. For example, when we want to apply a temperature of 41°C inside the abdomen, to prevent thermal damage to the rat, we aimed for the temperature of the heated liquid coming out to be no more than 1°C above this set temperature, and for the heating function to stop if it exceeds this limit. In case of any undesired temperature increase or hose system blockage, our algorithm automatically stops the system and provides an audible alert. According to our experience, especially the hose that allows vacuum return from inside the rat's abdomen occasionally causes blockages in the system by pulling the intestines, mesentery, or peritoneum on the abdominal sidewalls, and can even harm the rat. Therefore, we designed our hose system accordingly. Moreover, our device is designed to provide intraperitoneal hyperthermia treatment in the temperature range of 25–50°C, but it can also be used for hyperthermia studies at higher temperatures if desired.

Although rats belong to the mammalian class anatomically similar to humans, their thermoregulation mechanisms are insufficient to cope with excessive heat. Therefore, particularly in intraperitoneal hyperthermia studies, rectal temperature measurement should be performed in rats to monitor core body temperature and external cooling should be applied from underneath the tail when the temperature exceeds 38.5°C. In our study, we can say that cooling under the tail is particularly effective.[15]

When comparing the open method and closed method in intraperitoneal hyperthermia procedures, heat loss is naturally higher in the open method due to increased surface area. As a result, in the open method, higher temperature fluid needs to be introduced into the rat's abdomen. However, in our study using the closed method, we believe that delivering the fluid with a small temperature difference of maximum 1°C to achieve the desired intra-abdominal target temperature can actually protect the rat from sudden heat shocks and be safer. Particularly, this approach can help prevent thermal injuries in the rat's internal organs or intestines caused by hot fluid, especially beyond 43°C.[15]

Furthermore, while disposable sets are available for each individual in medical devices used for hyperthermic treatment in humans, unfortunately, there is currently no available device and method for rats, which poses risks to animal welfare and, especially, infections. In our hose system, we used 3 mm flat silicone drain hoses specifically designed for the inflow and outflow of the abdomen. By utilizing the multiport feature of these silicone drains, we attempted to prevent the system from being obstructed by the rat's intestines being pulled into the vacuuming hose, especially when negative pressure is applied (Medispo Medical Company).

CONCLUSION

The closed method of hyperthermic intraperitoneal chemotherapy has been successfully implemented in rats using the methodology and device we have presented. The simultaneous measurement of rectal temperature, intra-abdominal temperature, and inflow and outflow fluids is particularly important in such studies. In addition, the use of a disposable sterile tubing set for each rat helps prevent potential infection risks in rats and increases confidence in the results of the study. Furthermore, it is believed that standard equipment and standard hyperthermia methods can eliminate technical differences that determine the actual outcome of intraperitoneal hyperthermia studies in these rats and eliminate biases in the studies.

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Ethics Committee Approval: This study was approved by the Animal Experiments of Health Sciences University Local Ethics Committee (Date: 26.05.2022, Decision No: ETIK-2022/11).

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Authorship Contributions: Concept: M.U., E.N.S., B.A.G., O.A.A.; Design: M.U., E.N.S., B.A.G., O.A.A.; Supervision: M.U., E.N.S., B.A.G., O.A.A.; Resource: M.U., E.N.S., B.A.G., O.A.A.; Materials: M.U., E.N.S., B.A.G.; Data collection and/or processing: M.U., B.A.G., O.A.A.; Analysis and/or interpretation: M.U., B.A.G., O.A.A.; Literature search: M.U., E.N.S., B.A.G., O.A.A.; Writing: M.U., E.N.S., B.A.G., O.A.A.; Critical review: M.U., E.N.S., B.A.G., O.A.A.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Sıçanlarda kapalı yöntem ile intraperitoneal hipertermi modelinde yeni prototip cihaz tasarım ve algoritma çalışma sonuçları

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AMAÇ: Sıçanlarda hipertermik intraperitoneal tedavi çalışmalarında kullanılabilecek standart bir tıbbi cihaz ve yöntem bulunmamaktadır. Bu çalışmada, tasarımını ve klinik çalışmasını yaptığımız kendi algoritması ile çalışan hipetermi cihazımızı ve sıçanlarda hipertermik intraperitoneal tedavi çalışma protokolümüzü sunuyoruz. Cihazın ve algoritmasının sıçanın batını içerisinde istenilen sıcaklığı oluşturulabilmesi, cihazın yarattığı komplikasyona bağlı sıçan kaybının olmaması, cihazın otonom olarak çalışabilmesi ve acil durumlarda kendisini durdurarak operatöre uyarı vermesinin gösterilmesi ile, tasarlanan cihazın, algoritmasının ve hipertermi protokolünün etkinliğinin gösterilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: 6 adet dişi 8 haftalık (280-310 gram) albino Wistar sıçan için kapalı yöntemle intraperitoneal hipertermi protokolü oluşturuldu. Sıçan abdomeninde, ksifoid ile mesane arasında 1 cm'lik veritikal insizyondan sıvı giriş, çıkış hortumları ve ısı probu yerleştirildi ve cilt sirküler sütüre edildi. 60 dakika süre ile 100 ml/dakika akım hızında ve sıçanın batın içerisinde 41°C±0.5 sıcaklıkta sağlanacak şekilde salin solüsyonu ile intraperitoneal hipertermik tedavi protokolü oluşturuldu.

BULGULAR: Çalışma sırasında 100 ml/dakika ±5 akım hızında tüm sıçanların batını içerisinde 41°C±0.5 sıcaklık 60 dakika süre ile oluşturuldu. Hipertermi protokolü sırasında 3 sıçanın rektal ısı ölçümü 38.5°C üzerine çıktığı için sıçanlarda kuyruk altına buz uygulaması ile eksternal soğutma yapıldı. Sıçanlarda postoperatif 72. saate kadar kayıp olmadı ve çalışma başarı ile sonuçlandırıldı.

SONUÇ: Sıçanlarda intraperitoneal hipertermi tedavisi çalışmalarında hayvan refahını ön planda tutan, hızlı, güvenli ve yüksek doğruluk hassasiyetiyle çalışabilen aynı zamanda otonom olarak çalışabilen cihaz tasarımımız ve algoritmamız başarılı olmuştur. Sıçanlarda hipertermik intraperitoneal çalışmalarında standart bir yöntem ve uygulama olarak kullanılabileceğini düşünüyoruz.

Anahtar sözcükler: İntraperitoneal hipertermi; rat; cihaz; hayvan refahı; hipec.

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