Examination of Hematological Parameters after Carbon Filtered Hemoperfusion in Patients with Mushroom Poisoning

Mantar Zehirlenmesi olan Hastalarda Karbon Filtreli Hemoperfüzyon Sonrası Hematolojik Parametrelerin İncelenmesi

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Abstract

Objective: It is known that hemoperfusion with carbon filter has important benefits in the treatment of mushroom poisoning. In this study, the changes in hematological values after hemoperfusion with carbon filter in patients with mushroom poisoning were investigated.

Method: This study was planned as a retrospective study. Fifty-one patients who were hospitalized in the internal medicine service due to mushroom poisoning and underwent hemoperfusion with carbon filter between 01.01.2015 and 31.12.2021 in our hospital were included in the study. The patients were evaluated in terms of age, gender, time to onset of complaints after mushroom ingestion, time to start of hemoperfusion after mushroom ingestion, comorbid diseases, type of mushroom eaten, complaints at the time of admission, duration of hospitalization, daily hematological and biochemical parameters before and after carbon filter hemoperfusion, the lowest platelet value of the patients after carbon filter hemoperfusion and the day on which this value was observed.

Results: The mean age of the patients included in the study was 48.29 years. It was observed that 51.0% of the patients were male and 49.0% were female. Among the comorbidity distributions of the patients, hypertension (25.5%) was found the most and chronic renal failure (2.0%) the least. Among the complaints, the most nausea (76.5%) and the least abdominal pain (25.5%) were detected. When the mushroom type was examined, it was determined that

Öz

Amaç: Mantar zehirlenmesi tedavisinde karbon filtreli hemoperfüzyon yapılmasının önemli yararları olduğu bilinmektedir. Bu çalışmada mantar zehirlenmesi olan hastalarda karbon filtreli hemoperfüzyon sonrası hematolojik değerlerinin değişimi incelenmiştir.

Yöntem: Bu çalışma retrospektif bir çalışma olarak planlanmıştır. Hastanemizde 01.01.2015-31.12.2021 tarihleri arasında mantar zehirlenmesi nedeniyle iç hastalıkları servisine yatırılan ve karbon filtreli hemoperfüzyon yapılan 51 hasta çalışmaya alınmıştır. Hastalar; yaş, cinsiyet, mantar yenmesi sonrasında şikayetlerin başlama süresi, mantar yenmesi sonrasında hemoperfüzyona başlanma süresi, komorbid hastalıklar, yenilen mantarın cinsi, başvuru sırasındaki yakınmaları, hastaların hastanede yatış süresi, karbon filtreli hemoperfüzyon öncesi ve sonrasında günlük hematolojik ve biyokimyasal parametreleri, hastaların karbon filtreli hemoperfüzyon sonrası en düşük trombosit değeri ve bu değerin görüldüğü gün açısından değerlendirildi.

Bulgular: Çalışmaya dahil edilen hastaların yaş ortalaması 48,29 yıl idi. Hastaların %51,0'ı erkek, %49,0'ı kadın olduğu görülmüştür. Hastaların komorbidite dağılımları arasında en fazla hipertansiyon (%25,5), en az kronik böbrek yetmezliği (%2,0) olarak tespit edilmiştir. Şikayetler arasında en fazla bulantı (%76,5), en az karın ağrısı (%25,5) tespit edilmiştir. Mantar türü incelendiğinde ise toplama mantar %88,2, kültür mantarı %11,8 olarak tespit edilmiştir. Karbon filtreli

Cite this article as: Durlanık MB, Tiril SM, Sivritepe R, Basat S. Examination of hematological parameters after carbon filtered hemoperfusion in patients with mushroom poisoning. Bagcilar Med Bull. [Epub Ahead of Print]

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Abstract

the foraged mushrooms was 88.2% and the cultivated mushrooms was 11.8%. When the carbon filtered hemoperfusion onset time was examined, it was found that 45.1% of the patients started early and 54.9% of the patients started later. The average hospitalization day was determined as 7.18±4.16 days. It is seen that there is a statistically significant difference between the values of 0-1 day, 0-2 days, 0-3 days, 1-2 days and 1-3 days for the thrombocyte value. The highest thrombocyte value (236 $10^3/\mu L$) was seen on day 0 (p<0.001). After the first carbon filtered hemoperfusion, the mean values of the patients with the lowest thrombocyte value were 58.51 $10^3/\mu L$, and the average of the days when this value was seen was 2.5 days.

Conclusion: When hematological parameters were examined after hemoperfusion with carbon filter in patients with mushroom poisoning, thrombocyte value decreased in all patients and increased to normal values within days without causing complications.

Keywords: Carbon filtered hemoperfusion, mushroom poisoning, thrombocytopenia

Öz

hemoperfüzyon başlama zamanı incelendiğinde %45,1 hastada erken, %54,9 hastada daha geç başlandığı tespit edilmiştir. Yatış gün ortalaması 7,18±4 gün olarak tespit edilmiştir. Trombosit değeri için 0-1 gün, 0-2 gün, 0-3 gün, 1-2 gün, 1-3 gün değerleri arasında istatistiksel olarak anlamlı fark olduğu görülmektedir. En yüksek trombosit değeri (236 $10^3/\mu L$) 0. gün görülmüştür (p<0,001). Hastaların ilk karbon filtreli hemoperfüzyon sonrası en düşük trombosit değerinin görüldüğü değerlerin ortalaması 58,51 $10^3/\mu L$ ve bu değerin görüldüğü günlerin ortalaması 2,5 gün olarak tespit edilmiştir.

Sonuç: Mantar zehirlenmesi olan hastalarda karbon filtreli hemoperfüzyon sonrası hematolojik parametreler incelendiğinde hastaların tümünde trombosit değerinde düşüş gözlenmiştir ve komplikasyona neden olmadan günler içerisinde normal değerlere yükselmiştir.

Anahtar kelimeler: Karbon filtreli hemoperfüzyon, mantar zehirlenmesi, trombositopeni

Introduction

The disease caused by some poisonous compounds contained in capped mushrooms is called mushroom poisoning. There are approximately 5.000 species of mushrooms in nature, and approximately 100 of them contain toxins (1). As a result of ingestion of wild mushroom species, the clinical picture of the patient varies from gastrointestinal system complaints to severe cytotoxic conditions that can result in multiorgan failure and death (2).

The most lethal mushroom poisoning occurs with Amanita (Amanita phalloides, Amanita verna, Amanita ocreata) and Galerina species, which contain cyclopeptides. Amanita phalloides is responsible for 50% of all mushroom poisonings, and all Amanita species are responsible for 95% of total mortality (3).

According to recent epidemiological studies, mushroom poisoning accounts for approximately 3-5% of all acute poisoning cases in Turkey, with the majority caused by foraged wild mushrooms. The incidence shows seasonal variability, with peaks in spring and autumn, especially in rural and forested regions where uncontrolled mushroom consumption is prevalent (4,5).

Hemoperfusion is the direct passage of blood through various adsorbents such as charcoal or resin and is used to remove toxic compounds from the circulatory system. Hemoperfusion has been used experimentally or therapeutically over the past several years to treat uremia, poisoning and drug intoxication, liver failure, and to increase the clearance of a variety of other noxious substances (6,7).

Carbon-filtered hemoperfusion is increasingly considered as an effective extracorporeal detoxification method due to its ability to adsorb protein-bound and lipid-soluble toxins such as amatoxins. Its rapid toxin clearance profile offers a clinical advantage over conventional dialysis methods in cases of mushroom poisoning with delayed symptom onset (8).

This study aimed to retrospectively investigate the changes in hematological parameters of patients who were hospitalized in the Department of Internal Medicine, University of Health Sciences Turkey, Ümraniye Training and Research Hospital due to mushroom poisoning and underwent carbon filter hemoperfusion between 2015 and 2021.

Materials and Methods

In this study, 51 patients who were hospitalized in the Department of Internal Medicine, University of Health Sciences Turkey, Ümraniye Training and Research Hospital with the diagnosis of mushroom poisoning and underwent hemoperfusion with a carbon filter between 01.01.2015 and 31.12.2021 were evaluated retrospectively. The patients were evaluated in terms of age, gender, time to onset of complaints after mushroom ingestion, time to start of hemoperfusion after mushroom ingestion, comorbid diseases, type of mushroom eaten, complaints at the time of admission, duration of hospitalization, daily hematological and biochemical parameters [leukocyte,

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hemoglobin, platelet, mean platelet volume (MPV), alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, Gamma glutamyl transferase (GGT), lactate dehydrogenase, total bilirubin, international normalized ratio, sodium, potassium, blood urea nitrogen, creatinine] for three days before and after carbon filter hemoperfusion, the lowest platelet value of the patients after carbon filter hemoperfusion and the day on which this value was observed.

The patients were first divided into three groups according to their ages: 15-25, 26-65 and over 65. The time of onset of symptoms after mushroom ingestion was then divided into two groups: 0-6 hours and over 6 hours. The time of starting carbon filter hemoperfusion after mushroom ingestion was divided into two groups as 0-20 hours and over 21 hours. Comorbid diseases were evaluated as the presence or absence of hypertension, diabetes mellitus, congestive heart failure, chronic renal failure, and asthma in patients. The type of mushrooms was divided into two groups as foraged mushrooms and cultivated mushrooms. Complaints at the time of admission were evaluated as nausea, vomiting, diarrhea and abdominal pain. The length of stay of the patients was divided into three groups: 0-5, 6-10, and 10 days and above.

The patients included in the study did not have any known liver disease. Patients who were hospitalized due to mushroom poisoning and did not undergo hemoperfusion with a carbon filter were not included in the study. Exclusion criteria included known chronic liver disease, hematologic disorders, pre-existing thrombocytopenia, or any alternative diagnosis explaining the clinical presentation. All included patients had documented ingestion of wild mushrooms, symptom onset within 24 hours, and received hemoperfusion within the first 48 hours of admission. Patient information was obtained from outpatient clinic records and hospitalization files. The Declaration of Helsinki, which regulates biomedical research on humans, was followed. Additionally, Local Ethics Committee approval of University of Health Sciences Turkey, Ümraniye Training and Research Hospital (no: B.10.1.TKH.4.34.H.GP.0.01/363, date: 16.12.2021) was obtained.

Statistical Analysis

Data were analyzed using the spss 25.0 package program. The Kolmogorov-Smirnov test was used to check whether the distribution of the data was normally distributed. While evaluating the study data, descriptive statistical methods such as median, minimum, maximum and ratio values were used. Wilcoxon test was used for comparison of two dependent groups with non-parametric distribution and Friedman test was used for comparison of more than two dependent groups. Significance was evaluated at p<0.05 levels for all values.

Results

The mean age of the patients included in the study was determined as 48.29±18.05 years. The distribution of age groups was found to be 19.6% (n=10) in the 15-25 age group, 54.9% (n=28) in the 25-65 age group, and 25.5% (n=13) in the 65 and above age group. Of the patients included in the study, 51.0% were male and 49.0% were female. Among the comorbidity distributions of the patients, the highest rate was hypertension 25.5%, and the lowest rate was chronic renal failure 2.0%. Among the complaints of the patients, the most common was nausea (76.5%) and the least common was abdominal pain (25.5%). When the mushroom species were examined, it was determined that the foraged mushrooms were 88.2% and the cultivated mushrooms were 11.8%. When symptom onset times were examined, symptoms began within the first 0-6 hours in 68.6% of patients and over 6 hours in 31.4%. When the starting times of carbon filter hemoperfusion were examined, It was observed that 45.1% of the patients were dialysed within the first 0-20 hours, and 54.9% after 21 hours. While the average length of stay was determined as 7.18±4.16 days, 39.2% of the patients were hospitalized for 0-5 days, 47.1% for 6-10 days, and 13.7% for more than 11 days (Table 1).

Laboratory values of the patients were divided into 4 groups: at the time of admission, day 1, day 2 and day 3. Wilcoxon test was used for pairwise comparison between days to detect differences. In the comparison between days, it is seen that there is a statistically significant difference in alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, creatinine, hemoglobin, potassium and lactate dehydrogenase values and the highest value is day 0 for all 8 parameters (p<0.005 for all). When the parameters of the patients were compared between days, a statistically significant difference was found between the international normalized ratio, GGT, MPV, and sodium values of the patients. It was observed that the highest value for GGT value was on the 3rd day, the highest value for MPV value was on the 2nd and 3rd days, and the highest value for Na value was on the 3rd day (p<0.005 for all).

When the platelet value is compared for days 0-1, days 0-2, days 0-3, days 1-2, and days 1-3, it is seen that there is a

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statistically significant difference, and the highest value is day 0 (p<0.001). The mean of the lowest platelet value after the first carbon filter hemoperfusion was 58.51 $10^3/\mu L$ and the mean of the days when this value was seen was 2.5 days. The patients' platelet values returned to normal after an average of 6.62 days, and the average platelet count on these days was found to be 198.7 $10^3/\mu L$ (Table 2).

Discussion

In this study, we aimed to observe the changes in hematological and biochemical parameters after the application of carbon filter hemoperfusion in patients hospitalized due to mushroom poisoning. In the present study, we observed a decrease in the platelet count of patients after hemoperfusion with a carbon filter. It was

Table 1. Clinical and demographic data of patients			
Age (years)	48.29±12.05		
Age group analysis	<25	25-65	65<
	10 (19.6%)	28 (54.9%)	13 (25.5%)
Sex	**Male**		**Female**
	26 (51%)		25 (49%)
Time to symptom onset	0-6 hours		6 hours <
	35 (68.6%)		16 (31.4%)
Type of mushroom	Foraged mushrooms		Cultivated mushroom
	45 (88.2%)		6 (11.8%)
Starting time for dialysis with carbon filter	0-20 hours		20 hours <
	23 (45.1%)		28 (54.9%)
Length of stay	0-5 days	6-10 days	10 days<
	20 (39.2%)	24 (47.2%)	7 (13.7%)
Comorbidity	Hypertension		Chronic renal failure
	13 (25.55)		1 (2%)
Complaints	Nausea		Abdominal pain
	39 (76.5%)		13 (25.5%)

Table 2. Comparison of laboratory values of patients by day					
	Moment of admission	**The first day**	**The second day**	**The third day**	
	Median (min-max)	**Median (min-max)**	**Median (min-max)**	**Median (min-max)**	**p-value**
Alkaline phosphatase (38-155 U/L)	67 (30-371)	60 (28-379)	55 (29-326)	53 (24-273)	**0.000***
Alanine aminotransferase (10-40 U/L)	24 (2-990)	22 (6-4000)	20 (6-3242)	22 (5-2648)	**0.011****
Aspartate aminotransferase (15-50 IU/L)	28 (11-1247)	21 (11-5516)	20 (9-2525)	22 (9-710)	**0.000***
Blood urea nitrogen (10-20 mg/dL)	32 (14-111)	29 (12-111)	26 (8-107)	23 (7.6-104)	**0.000***
Creatinine (<1 mg/dL)	0.82 (0.57-2.9)	0.74 (0.47-4.02)	0.73 (0.48-3.5)	0.72 (0.44-4.59)	**0.001****
Gamma glutamyl transferase (7-49 U/L)	26 (8-700)	23 (7-574)	24 (7-450)	30 (7-397)	**0.000***
Hemoglobin (12.4-14.8 g/L)	14.4 (9.8-17.8)	12.5 (8.9-15.9)	11.6 (8.17-14.8)	11.1 (6.5-15.4)	**0.000***
International normalized ratio	1.11 (0.89-3.95)	1.25 (0.96-5.55)	1.2 (0.99-2.95)	1.17 (0.95-3.94)	**0.000***
Potassium (3.5-5.5 mmol/L)	4.4 (3-5.8)	4.1 (3-5.2)	3.9 (2.7-5.4)	4 (3.2-5.1)	**0.000***
Lactate dehydrogenase (90-250 U/L)	322 (161-2801)	241 (134-7317)	254 (129-2118)	240 (116-1254)	**0.000***
Mean platelet volume	9.5 (6.4-13.2)	9.9 (6.67-13.,4)	10.2 (6.4-88.9)	10.2 (7.1-13.7)	**0.003****
Sodium (135-145 mEq/L)	139 (130-145)	139 (130-143)	138 (13-145)	139 (131-144)	**0.034****
Thrombocyte (150-450.000/mm³)	236 (112-422)	106 (35-284)	73 (17-135)	71 (18-181)	**0.000***
Total bilirubin (0.3-1.9 mg/dL)	0.7 (0.17-3.45)	0.97 (0.18-4.5)	0.69 (0.09-3.95)	0.61 (0.09-5)	**0.001****
Leukocyte (4.1-8.9 10³/uL)	10.11 (4.77-23.09)	10.2 (2.45-22.7)	8.45 (0.56-16.18)	7.2 (2.47-16.3)	**0.000***
Friedman test *: p<0.001, **: p<0.05, min-max: Minimum-maximum					

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observed that the thrombocytopenia returned to normal without any complications in the following days.

It is known that mushrooms are living organisms that do not carry chlorophyll, live as parasites or saprophytes, and reproduce by spores. Spores are dispersed into the environment by wind and germinate under suitable climatic conditions. That's why edible and poisonous mushrooms can grow side by side (9). Turkey is rich in mushroom flora due to its suitable ecological conditions (10). In Turkey, the habit of collecting and eating mushrooms from forests or meadows, especially in the spring months, is quite common among people with low socio-economic status. For this reason, the number of mushroom poisoning cases resulting in death is considerably high in our country. It is also known that the poisonous content of raw or cooked mushrooms does not change (10,11). In small mushrooms, symptoms appear approximately three hours after ingestion. In larger mushrooms, including Amanita phalloides, symptoms appear within 6-24 hours after ingestion. According to the onset time of symptoms, those starting up to six hours are defined as early syndromes, and those starting after six hours are defined as late syndromes. Those with late-onset symptoms are 90-95% fatal (1). In the study it was determined that approximately 48% of the mushroom species causing poisoning were Amanita phalloides and approximately 52% were non-amanita species (1). Since toxicological examination could not be performed in our hospital, in our study the diagnosis of poisoning was made based on anamnesis and clinical findings. When the mushroom species were examined in our study, we found that 88.2% of the mushrooms were foraged mushrooms and 11.8% were cultivated mushrooms. In our study, it was observed that mushrooms collected from nature and eaten caused more mushroom poisoning.

The most common symptoms in patients presenting to the emergency department due to mushroom poisoning are nausea, vomiting, abdominal pain, diarrhea, agitation, loss of consciousness and encephalopathy (12,13) In the studies 79.5% of the patients had vomiting and diarrhea, 10.3% had only vomiting, 5.1% had abdominal pain, and 5.1% had abdominal pain and vomiting at the time of admission (1,3,4). In the present study, complaints at the time of admission were nausea 76.5% (n=39), vomiting 72.5% (n=37), diarrhea 37.3% (n=19), and abdominal pain 25.5% (n=13). In our study, like other studies, we observed that patients with mushroom poisoning had more frequent complaints of nausea and vomiting.

In the study conducted by Colak et al. (14), patients were divided into two groups according to the time of onset of symptoms. In 62.1% of the patients, symptoms appeared within the first 0-5 hours, and in 37.9%, symptoms appeared within 6-24 hours. In our study, symptoms started in the first 6 hours in 68.6% of the patients and after 6 hours in 31.4%. In our study, similar to other studies, we observed that symptoms of mushroom poisoning occur more frequently within the first 6 hours.

In our study, the average hospitalization day was determined as 7.18±4.16. 39.2% of the patients were hospitalized for 0-5 days, 47.1% for 6-10 days, and 13.7% for more than 11 days. In our study, we observed that the length of hospital stays of patients hospitalized due to mushroom poisoning and who underwent hemoperfusion with a carbon filter was similar to other studies.

The first hemoperfusion treatment was performed in 1948 by Muirhead and Reid to remove uremic toxins from the circulation. It has been used in drug poisoning since 1951 (9). Although there has been no study since then that has revealed the real place of extracorporeal treatment in mushroom poisoning cases, the United States Association of Poison Control Centers reported that extracorporeal treatment was applied in 0.15-0.22% of all poisoning cases in their data covering the years 1985-1994 (9). Mydlík et al. (15) recommended the use of hemoperfusion filters containing Amberlite® XAD-2 within the first 24-36 hours of acute poisoning with Amanita phalloides. Monhart (16) stated that hemoperfusion reduces hepatic and renal damage, lowers the risk of mortality, and the use of Amberlite® XAD-2 instead of activated charcoal increases the chance of success in treatment. Splendiani et al. (17) applied activated charcoal hemoperfusion to one of two patients with Amanita phalloides poisoning for 3 hours every day for 5 days; to the other patient, continuous venovenous hemodialysis for 20 hours every day for 3 days, and discharged both patients on the 10th day. In our study, 45.1% of the patients started hemoperfusion with a carbon filter within the first 0-20 hours. In 54.9% of the patients, hemodialysis with a carbon filter was started after 21 hours. The mechanism by which hemoperfusion exerts its detoxifying effects includes the removal of not only amatoxins but also inflammatory mediators and hepatotoxic metabolites. Monhart (16) emphasized its potential in reducing hepatic injury when applied within the first 24 hours post-ingestion.

Hemoperfusion, which we use in the treatment of our patients, is done by passing the blood through a carbon-

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containing filter. Agents that are highly protein-bound and lipid-soluble are easier to remove from the circulation by hemoperfusion (9). The beneficial effect of hemoperfusion is not only the clearance of alpha-amanitin from plasma, but also the clearance of neurotoxic substances such as methionine, tryptophan, and phenylalanine. Hepatic encephalopathy regresses in 75% of patients with hemoperfusion (1). In the study conducted by Aji et al. (18) in our country, it was reported that thrombocytopenia did not develop in patients after hemoperfusion, but melena developed for 2-3 days. Sabeel et al. (19) reported in their study on 41 patients that the platelet count decreased by 24% after hemodialysis and hemoperfusion were combined, the lowest platelet count was 26,000 after hemodialysis and hemoperfusion were completed, and the decrease in platelets due to hemoperfusion treatment was temporary, thrombocytopenia usually resolved within 24-48 hours and was very rarely associated with bleeding. Hemoperfusion-related thrombocytopenia is generally attributed to platelet adsorption by the activated charcoal filter. This phenomenon, while transient, necessitates close monitoring, particularly in patients with baseline coagulopathy or gastrointestinal bleeding risk (18,19). In our study, it was observed that platelet values decreased after the first day after hemoperfusion with a carbon filter in patients, and the average of the values with the lowest platelet value was 58.51 $10^3/\mu L$ and the average of the days when this value was seen was 2.5 days. It was observed that the patients' platelet values returned to normal in an average of 6.62 days and the average platelet count on these days was 198.7 $10^3/\mu L$. In the present study, like other studies, we observed that platelet values decreased after hemoperfusion with a carbon filter and platelet values returned to normal within days without causing any complications.

In the study conducted by Aji et al. (18), it was reported that the highest liver enzyme levels after hemoperfusion were seen on the second and third days of treatment, followed by a gradual decrease. In our study, the highest value of all biochemical values was observed before or on the first day after hemoperfusion with a carbon filter. A decrease in values was observed within days after hemoperfusion with a carbon filter. In our study, like other studies, we observed improvement in biochemical and hematological values after the application of carbon filter hemoperfusion in patients with mushroom poisoning.

Study Limitations

The primary limitation of our study is the absence of a control group. The lack of a comparator arm restricts the ability to establish causality. However, the standard clinical practice and ethical mandates at our institution require early hemoperfusion for all patients with suspected amatoxin-related mushroom poisoning. Therefore, randomization or withholding hemoperfusion was not feasible. Future prospective studies with matched cohorts are needed to delineate its independent effect.

Conclusion

In our study, hematological and biochemical parameters were evaluated after carbon filter hemoperfusion in patients with mushroom poisoning. We found that there was a statistically significant decrease in the hematological and biochemical parameters evaluated in our study after hemoperfusion with a carbon filter. When hematological parameters were examined after hemoperfusion with a carbon filter in patients with mushroom poisoning, a decrease in platelet values was observed in all patients and increased to normal values within days without causing complications. We observed that it is beneficial to apply hemoperfusion with a carbon filter as soon as possible after the onset of symptoms in patients with mushroom poisoning.

Ethics

Footnotes

Authorship Contributions

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