

CASE REPORT**Herbal Medicines And Drug Interactions that may lead to Death**

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ABSTRACT

Panax Ginseng® (PG) is a widely used herbal medicine worldwide to stimulate immune function. We wanted to present a case with intraparenchymal bleeding due to the interaction of aspirin with PG resulting in a prolonged effect of the former drug. A 36-year-old male patient came to the emergency room with weakness in the left half of the body, which started 1 hour ago. With no prior comorbidities, it was learned that he had started aspirin and the PG extract for the last 10 days. He was drowsy with a GCS of 13/15. On the computerized tomography scan (CT) of the patient, there

was an intracerebral bleed in the right basal ganglia. The patient was admitted with neurology follow-up in the intensive care unit. The patient developed cardiac arrest on the second day of the intensive care admission and could not be recovered. Since PG can interact with aspirin pharmacokinetics, clinicians need to be aware of whether their patients are using PG in their history.

KEYWORDS

Panax Ginseng, Aspirin, Intracerebral hematoma

INTRODUCTION

Panax Ginseng® (PG) is a widely used herbal medicine worldwide. It is also used in Eastern traditional medicine and used to stimulate immune function. Ginsenoside and saponin glycoside are the main active ingredients. Its mechanism of action is not yet known. It was found that in animal experiments, it can produce cavernous relaxation by affecting NO (nitrous oxide) and could be used in the treatment of erectile dysfunction.^(1, 2) Additional uses included boosting immune function, cognitive function, physical endurance, concentration, work efficiency, and memory.⁽³⁾ It is also used for depression, chronic fatigue syndrome, diabetes mellitus, various cancers, and many other diseases.⁽⁴⁾ The main active ingredients of PG are ginsenosides.⁽³⁾ Although ginsenosides are responsible for drug interactions, it cannot be predicted whether this interaction will cause acceleration or slowdown in drug metabolism.⁽³⁾

Aspirin is a non-steroidal anti-inflammatory drug that is not only an antipyretic but also an antithrombotic and potent analgesic. Due to these effects, it is used in rheumatism, headache, and toothache.⁽⁵⁾ Similarly, aspirin is widely used in cardiovascular diseases due to its anti-thrombotic effects.⁽⁶⁾ The effect of Ginsenosides on aspirin was studied in rats and shown to affect drug metabolism.⁽⁷⁾ We

wanted to present a case with intraparenchymal bleeding due to the interaction of aspirin with PG resulting in a prolonged effect of the former drug.

CASE REPORT

A 36-year-old male patient presented to the emergency department with weakness in the left half of the body, which started 1 hour ago. The patient was drowsy and he had a GCS of 13. His pulse was 63 beats/min, oxygen saturation of 98%, and blood pressure of 200/110 mmHg. On neurological exam, light reflex and bilateral direct/indirect reflexes were normal but his pupils were anisocoric. He was able to move the limbs of the right side of the body spontaneously with a power of 5/5, while limbs of the left side were paralyzed. Lung sounds were normal with bilateral and equal air entry.

On further questioning, it was found out that he had visited his family doctor for high blood pressure and was prescribed aspirin and an antihypertensive drug, whose name was unknown. Ten days before this, the patient was already taking the PG extract. The patient had been healthy and had no comorbid conditions. The family history of the patient was questioned, and it was learned that there was no cardiac, neurologi-

cal or pulmonary disease in the family.

Electrocardiography showed normal sinus rhythm. Vascular access was obtained, and supportive treatment was started for the patient. On the computerized tomography (CT) scan of the patient, it was found that there was an acute hematoma, which appeared broadly expansive in the right basal ganglia, pressing into the right lateral ventricle and was shifting midline structures to the left (Figure.1). Despite supportive management, the patient's condition started deteriorating, he began to vomit almost immediately and was electively intubated to protect his airway. In routine laboratory examinations, his creatinine was detected as 3.09 mg/dl, BUN: 89 mg/dl. INR:1.02. All other labs were within normal limits including the blood gas. Neurology follow-up in the intensive care unit was recommended to the patient, as any neurosurgical intervention was not seen feasible by the neurosurgery department. The patient developed cardiac arrest on the second day of the intensive care hospitalization, and the patient could not be revived.

DISCUSSION

Today, PG is increasingly used due to its perceived benefit in depression, chronic fatigue syndrome, and other medical conditions. It is also believed to have antitumor, anti-fatigue, and anti-inflammatory effects. The use of aspirin is becoming more widespread especially with the increase of cardiovascular diseases. Therefore, it is important to know the interaction between these two drugs.

Ginsenosides with PG metabolites are thought to play a role in drug interactions.⁽³⁾ Ginsenosides and glycosylated intestinal metabolites are thought to be related to drug interactions, but studies on PG, cytochrome P450, glucuronidation or drug transport proteins are inconsistent.^(3,5,7,8) Zhu et al. showed that there is no change in warfarin metabolism on concurrent PG intake.⁽⁹⁾ Yu et al. found in the rat study that T max, which is the time for the maximum efficacy of aspirin, decreases in patients receiving PG, thus the duration of drug action is prolonged. Tian et al. showed that aspirin concentration increased due to increased gastrointestinal absorption when PG and aspirin were taken together.⁽⁸⁾

Looking at these studies, it can be concluded that there is a significant possibility of a PG- aspirin interaction. In our case, the patient took aspirin as a prophylactic dose (100 mg/day) with PG intake directing us to the possibility of drug interaction resulting in intraparenchymal bleeding on the CT scan.

For this reason, these two drugs, which are increasingly used, should be used together with care. There are case reports of herbal medicines causing kidney and/or liver

failure.⁽¹⁰⁾ If our patient had no history of using aspirin, there is a possibility that only renal failure would have developed due to herbal medicine, and not the catastrophic bleed that the patient presented within our department.

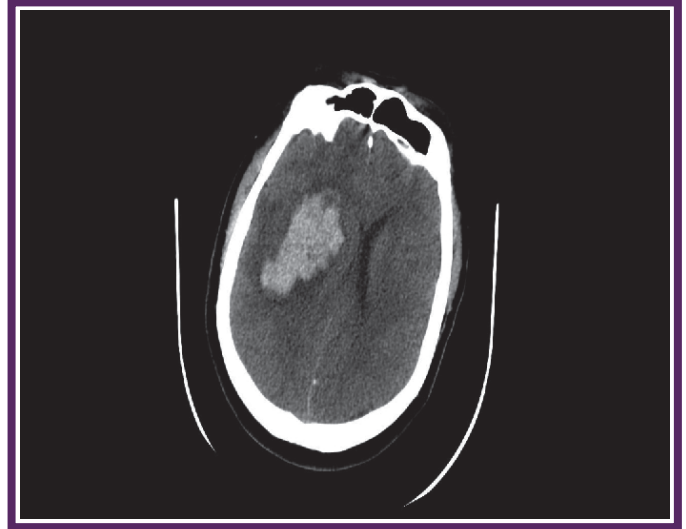


Figure 1. CT Scan showing right acute intracerebral hemorrhage in basal ganglia with midline shift

Since PG can interact with aspirin pharmacokinetics, clinicians need to be aware of whether their patients are using PG in their drug history. It is necessary to use these two drugs with caution to treat or prevent cardiovascular diseases. For the detailed interaction further case reports, clinical studies and meta-analysis are needed.

REFERENCES

1. Shamloul R. Natural Aphrodisiacs. *The Journal of Sexual Medicine*. 2010;7(1pt1):39-49.
2. Ortaç M. Erektile disfonksiyon tedavisinde fitoterapi. *Androloji Bülteni*. 2016;18(64):20-3.
3. Ramanathan MR, Penzak SR. Pharmacokinetic drug interactions with Panax ginseng. *European Journal of Drug Metabolism and Pharmacokinetics*. 2017;42(4):545-57.
4. Therapeutic Research Center. *Natural Medicines Comprehensive Database 2020*. Available from: <https://naturalmedicines.therapeuticresearch.com/-search.aspx?q=panax&go.x=0&go.y=0>. [Accessed February 02, 2020]
5. Kunutsor S, Seidu S, Khunti K. Aspirin for primary prevention of cardiovascular and all-cause mortality events in diabetes: Updated meta-analysis of random-

- ized controlled trials. *Diabetic Medicine*. 2017;34(3):316-27.
6. Kim J, Becker RC. Aspirin dosing frequency in the primary and secondary prevention of cardiovascular events. *Journal of Trombosis and Thrombolysis*. 2016;41(3):493-504.
7. Yu G, Tan L, Xue Y, Zhao M, Lu Y. The pharmacokinetics of aspirin in combination with total ginsenoside of ginseng stems and leaves in rats. *Journal of Traditional Chinese Medical Sciences*. 2017;4(4):366-71.
8. Tian Z, Pang H, Du S, Lu Y, Zhang L, Wu H, et al. Effect of Panax notoginseng saponins on the pharmacokinetics of aspirin in rats. *Journal of Chromatography B*. 2017;1040:136-43.
9. Zhu M, Chan K, Ng L, Chang Q, Chang S, Li R. Possible influences of ginseng on the pharmacokinetics and pharmacodynamics of warfarin in rats. *Journal of Pharmacy and Pharmacology*. 1999;51(2):175-80.
10. Sevinc Ok E, Tatar E, Yeniay K, Tosun A. Acute Kidney Injury Induced by Herbal Products: A Case Report. *Turkish Nephrology, Dialysis and Transplantation Journal*. 2014;23:256-8.

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