


## CLINICAL ARTICLE

# A Randomized Study on the Prophylactic Use of Acetaminophen to Prevent Fever after the Removal of Drainage Tubes for Lumbar Surgery

Kaifeng Ye, PhD<sup>1,2,3</sup>, Yan Li, PhD<sup>1,2,3</sup>, Yong Xing, PhD<sup>1,2,3</sup>, Kaixi Liu, PhD<sup>4</sup>, Fang Zhou, PhD<sup>1,2,3</sup>, Yun Tian, PhD<sup>1,2,3</sup> , Yanping Zhang, BS<sup>1,2,3</sup>

<sup>1</sup>Department of Orthopedics and <sup>4</sup>Anesthesiology Department, Peking University Third Hospital, <sup>2</sup>Engineering Research Center of Bone and Joint Precision Medicine, Ministry of Education, Peking University Third Hospital and <sup>3</sup>Beijing Key Laboratory of Spinal Disease Research, Peking University Third Hospital, Beijing, China

**Background:** Many inpatients encounter a fever in the first 24 h after drainage removal. It is costly to exclude the possibility of deep infection and cultures usually fail to identify the etiology. We hypothesize that the fever is caused by a normal inflammatory response and tested whether the prophylactic use of acetaminophen could reduce the fever rate.

**Methods:** This was a prospectively randomized clinical trial performed from July 2019 to January 2020. A total of 183 consecutive patients undergoing lumbar spine surgery were prospectively randomized into two groups. Ninety-one patients were randomized into the study group; they received oral acetaminophen before removal of the drainage tubes and a second dose at 8 p.m. on the same day. The remaining 92 patients were placed in the control group, and they were given routine treatment without acetaminophen. The two groups were compared for differences in age, sex, height, weight, BMI, surgical segments, surgical time, blood loss, blood transfusion, ASA score, duration of drainage, total volume of the drainage, variation of WBC and CRP, hospital stay after the removal of the drainage tube and the rate of fever. Student's *t*-test and the Mann-Whitney *U* test were used to analyze the continuous data, while the chi-square test was used for the analysis of the ranked data.

**Results:** Regarding the comparisons of basic information, there were no significant differences between the two groups for age, height, weight, BMI, surgical segments, surgical time, blood loss, blood transfusion, total drainage volume, duration of drainage, hospital stay, WBC, and CRP variation or the duration of hospital stay after removal of the drainage tube (all  $p > 0.05$ ). However, the fever rate was significantly different ( $p = 0.006$ ), and the fever rate of the study group (14/91, 15.38%) was significantly lower than that of the control group (30/92, 32.61%). In the study group, there were no complications related to the use of acetaminophen during the hospital stay or during the outpatient follow-up period.

**Conclusion:** Fever after removal of tube drainage is caused by a normal inflammatory response, and a small dose of acetaminophen could significantly reduce the possibility of fever.

**Key words:** Acetaminophen; Fever; Inflammatory response; Lumbar drainage; Prostaglandin

## Background

Degenerative lumbar diseases are becoming increasingly common in the aging population, and the number of patients requiring surgery continues to increase.<sup>1</sup> Drainage tubes are widely used at the conclusion of spine surgery to

prevent hematoma formation, compression of the cauda equina nerves, severe neurological dysfunction, and fever.<sup>2-4</sup> However, in our clinical work, many inpatients encountered a fever in the first 24 h after the drainage tube was removed, approximately 40%.

**Address for correspondence** Yun Tian and Yanping Zhang, Department of Orthopedics, Peking University Third Hospital, Beijing, China. Email: [tiany@bjmu.edu.cn](mailto:tiany@bjmu.edu.cn); [13501301199@139.com](mailto:13501301199@139.com)

Kaifeng Ye and Yan Li contributed equally to this article.  
Received 4 August 2022; accepted 18 October 2022

When these fevers appeared, we performed many laboratory tests to exclude the possibility of deep infection but failed to confirm the etiology of the fever in most cases.<sup>5,6</sup> The rate of surgical site infection has been reported to range from 0.7% to 12%,<sup>7-9</sup> and the rate in our hospital was approximately 0.1%. If an infection occurred, it would be difficult for a patient to recover. Fortunately, almost all of the patients' temperatures gradually became normal after observation or antipyretic treatments before discharge. Similar to the reports of many previous studies, the evaluation of these fevers was costly and time-consuming, and they made the patients uncomfortable and could increase their medical expenditures, prolong their hospital stay and waste healthcare resources.<sup>3,4,10-14</sup>

To address this challenging issue, we carried out a thorough literature review. To the best of our knowledge, no previous research has focused on fever after the removal of drainage tubes. However, we found that many studies paid attention to early postoperative fever and suggested that the main reason for postoperative fever was the inflammatory response due to tissue trauma during surgery.<sup>4,10,11,15</sup> Inflammation is a normal physiological reaction during the process of healing, and the extent of tissue trauma correlates with the possibility of fever.<sup>10</sup> Many previous studies have further proven that the main inflammatory responses are due to pyrogenic cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interferon-gamma. These mediators act directly on the preoptic area of the hypothalamus and cause a release of prostaglandins, which could raise the thermoregulatory "set point" for the body temperature and cause fever.<sup>4,11,16,17</sup> Both animal and human experiments have suggested that pretreatment with a cytokine antagonist could lower the concentration of pyrogenic cytokines and reduce the possibility of fever.<sup>16,18</sup>

Furthermore, a previous investigation indicated that the presence of hematoma appeared to be a relatively common cause of fever.<sup>19</sup> In addition, many studies have discovered a high concentration of IL-6 in the drained fluid after surgery.<sup>16,20,21</sup> Therefore, we infer that once the drainage tube is removed from lumbar patients after surgery, the pyrogenic cytokines cannot flow outside of the surgical area and then accumulate gradually. A small hematoma forms, and the cytokines can ooze into the circulatory system to cause a fever. If we use acetaminophen to counteract the effects of prostaglandins in advance and then block the production of prostaglandins, perhaps we can lower the possibility of fever when the drainage tube is removed.

The aims of this prospective, randomized study were (1) to determine the efficacy of the prophylactic use of acetaminophen before lumbar drainage tube removal to prevent fever and (2) to identify whether fever was associated with age and sex. We hypothesized that the preventive use of acetaminophen could reduce the possibility of fever after the removal of drainage tubes from surgical lumbar disease patients.

## Patients and Methods

### Study Design and Patients

We performed a single-blinded randomized controlled trial (NCT04042948) in the Department of Orthopaedics at our

hospital from July 2019 to January 2020, and the first registration day was August 2, 2019. Approval was obtained from the Ethics Committee of our hospital, and the approval number was LM2019142.

Patients who underwent lumbar operations in our hospital were recruited. We calculated the sample size with a 5% significance level and 80% power, and 78 patients per group were necessary. We finally decided to recruit 95 patients in each group to allow for dropouts. The patients were randomly divided into two groups using a computer-generated random number list: the study group and the control group. The patients in the study group received an acetaminophen pill (Tylenol, 650 mg) before the removal of the lumbar drainage tube, and another pill was administered at 8 p.m. on the same day, while the patients in the control group did not receive acetaminophen. In this study, we required the time of drainage tube removal to be from 8 a.m. to 10 a.m. in the morning to ensure that the first dose of acetaminophen was taken in the morning.

The inclusion criteria were as follows: (1) adult patients conscious enough to provide informed consent; (2) a clear diagnosis of degenerative lumbar spinal disease; (3) one to two surgical segments; (4) indwelling drainage tube after the operation; and (5) normal hepatic and renal function. The exclusion criteria were as follows: (1) age <18 years; (2) more than two surgical segments; (3) abnormal hepatic and renal function; and (4) a history of stomach disease.

### Protocol

All of the included patients signed the conformed consent form on the day before the surgery, and the first group of researchers checked the computer-generated random number list, divided the patients into their corresponding groups and informed the second and third groups of researchers. The second and third groups were blinded to the patients' allocation before receiving information from the first group. The first group was blinded to all of the clinical information about the patients postoperatively.

All operations were performed under general anesthesia by senior spine surgeons and fluoroscopy control on a radiolucent operation table. The extent of the surgery depended on the severity of the disease, and all of the patients had a closed wound drain placed below the deep fascia over the exposed dura before wound closure. No complications occurred during the operations.

All patients received routine treatment and care before the drainage tubes were removed. Our nurses recorded the patients' temperatures four times a day and the volume of the drainage collections once a day. All of the data were uploaded to the medical system. When the recorded drainage volume over 24 h was below 50 ml,<sup>22</sup> the attending physician decided to remove the drainage tube. All patients underwent laboratory tests for the concentrations of white blood cells (WBCs) and C-reactive protein (CRP) the day after drainage tube removal. For the study group, the extra intervention was a pill of acetaminophen taken before the removal of the drainage tube and another pill taken orally at 8 p.m.

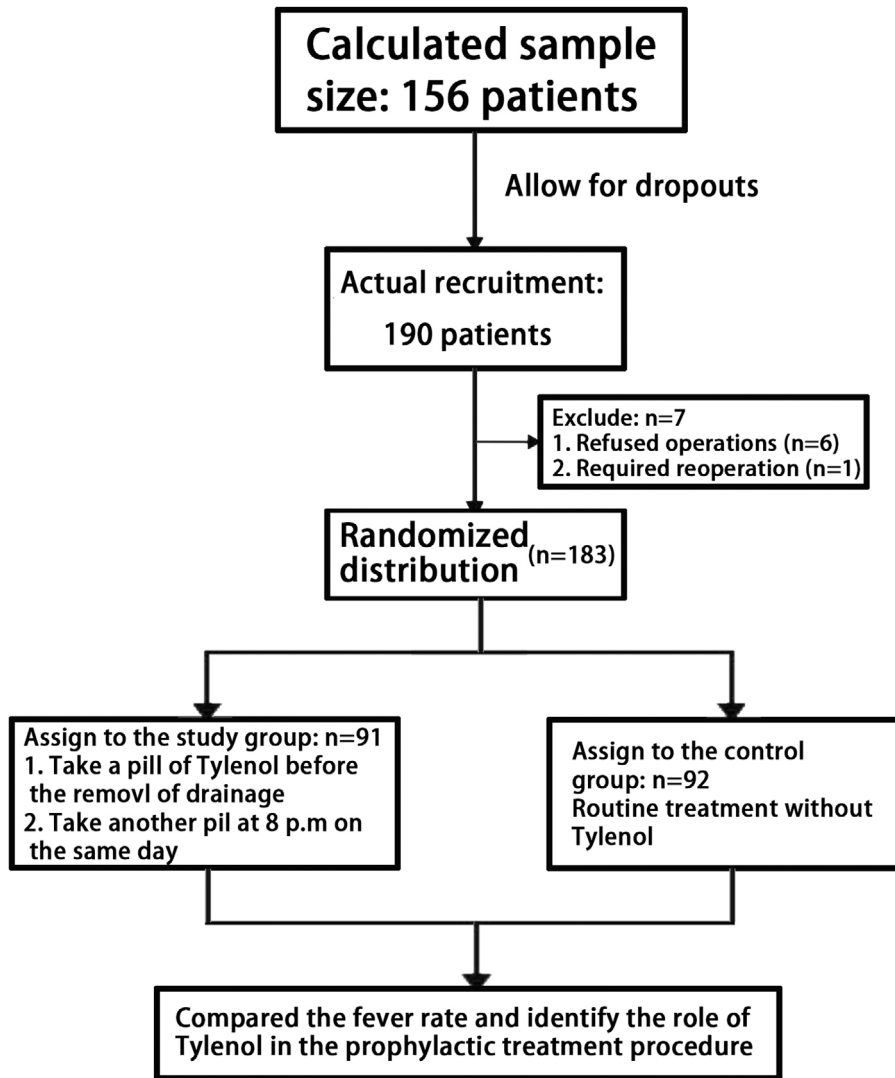


Fig. 1 The process of the study

TABLE 1 The characteristics of the two groups expressed as continuous data

Characteristic	Study group Mean (SD)	Control group Mean (SD)	Total	t/Z	p value
Age (year)	50.76 (11.70)	51.91(12.12)	51.34 (11.89)	-0.809	0.419
Height (cm)	164.79 (8.39)	166.26 (8.27)	165.53 (8.34)	-1.199	0.230
Weight (kg) <sup>#</sup>	69.34 (11.34)	70.25 (10.31)	69.80 (10.81)	0.568*	0.571
BMI (kg/m <sup>2</sup> )	25.52 (3.67)	25.39 (3.01)	25.46 (3.35)	-0.054	0.957
Surgical segments	1.29 (0.48)	1.35 (0.55)	1.32 (0.51)	-0.726	0.468
Surgical time (min)	124.44 (37.17)	121.81 (39.24)	123.19 (38.07)	-0.454	0.649
Blood loss (ml)	246.39 (143.23)	266.00 (145.62)	256.19 (144.36)	-1.023	0.307
Blood transfusion (ml)	90.83	109.24	99.46	-1.804	0.071
Total drainage volume (ml)	481.43 (302.60)	454.99 (324.47)	468.21 (313.13)	-0.837	0.402
Duration of drainage (day)	3.36 (1.01)	3.30 (0.91)	3.33 (0.96)	-0/167	0.867
Hospital stay (day)	7.68 (1.93)	8.12 (2.71)	7.91 (2.36)	-0.647	0.517
WBC ( $\times 10^9/L$ )	8.25 (2.68)	8.69 (2.78)	8.47 (2.73)	-1.165	0.244
CRP (mg/dL)	3.77 (3.61)	4.09 (3.58)	3.93 (3.58)	-0.837	0.402
Duration of hospital stay after removal of the drainage tube (day)	2.23 (1.42)	2.82 (2.61)	2.52 (2.12)	-1.438	0.151

<sup>#</sup> Student's t-test and the rest were Mann-Whitney U test.; \* The t value and the rest were Z value.

Our nurse team kept recording the patients' temperatures four times a day and uploading the data to the medical system. The upper limit of a normal temperature was 37.7°C,<sup>15</sup> so a temperature >37.8°C at any time within the first 24 h after the removal of the drainage tube indicated that a fever had developed.

### Data and Observation

All of the patients' basic clinical information was collected, including age, sex, height, weight, body mass index (BMI), surgical segments, surgical time, blood loss, blood transfusion, American Society of Anesthesiologists (ASA) score, duration of drainage tube use, and total drainage volume.

**TABLE 2** The Shapiro–Wilk test for normality of the continuous data ( $p > 0.05$  suggests that the data were normally distributed)

Characteristic	p value	
	Study group	Control group
Age	0.001	0.004
Height	0.020	0.206
Weight	0.620	0.213
BMI	0.039	0.118
Surgical segments	0.000	0.000
Surgical time	0.006	0.000
Blood loss	0.000	0.000
Blood transfusion	0.000	0.000
Total drainage volume	0.006	0.000
Duration of drainage	0.000	0.000
Duration of hospital stay	0.000	0.000
WBC	0.000	0.000
CRP	0.000	0.000
Duration of hospital stay after removal of the drainage tube	0.000	0.000

The main observation index was temperature within the first 24 h after the drainage tube was removed. Once a fever developed, the data collection for that patient ended. The attending physicians started the diagnostic workups depending on the medical history and conducted a physical examination to identify the etiology of the fever. The possible workups included chest X-ray, urinalysis, urine culture, and blood culture. The other observation indices were the variations in WBC and CRP levels, the length of hospital stay after the removal of the drainage tube to discharge, and the whole hospital stay.

We compared the above data of the two groups to identify the efficacy of the prophylactic use of acetaminophen for preventing fever. Furthermore, we conducted subgroup analysis in the study and control groups to identify the role of age and sex in fever.

### Statistical Analysis

A descriptive analysis was performed of the main study variables. All continuous data were tested for normality with the Shapiro–Wilk test. If the data were normally distributed, Student's *t*-test was used for the analysis. The Mann–Whitney *U* test was performed for nonnormally distributed data. For ranked data, the chi-square test was used for analysis. The value of  $p < 0.05$  was considered statistically significant. All analyses were performed with SPSS Statistics (version 24.0; IBM Corp., Armonk, NY, USA).

### Results

#### Comprehensive Description

The study process is shown in Fig. 1. In total, 190 patients participated in this research, and seven patients were excluded because they refused the operation (six patients) or underwent reoperation for postoperative hematoma (one

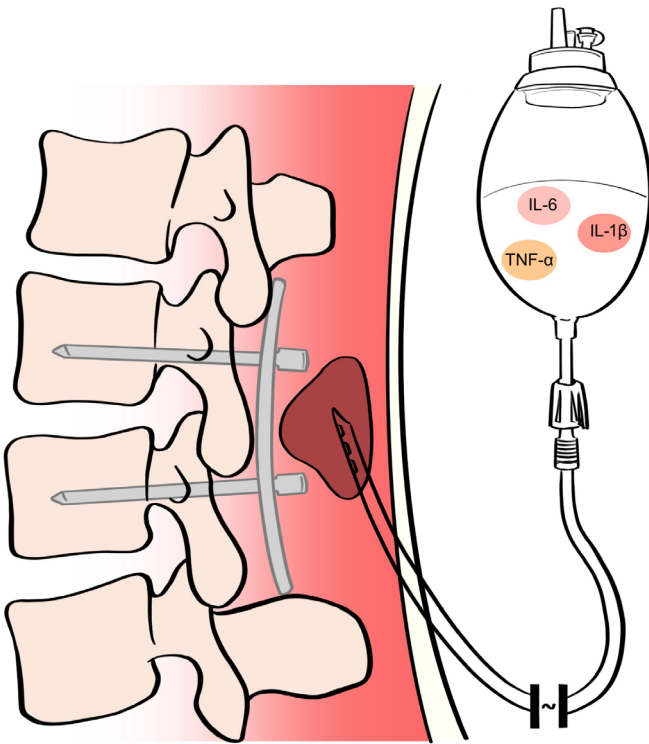
**TABLE 3** Comparisons of the ranked data

Characteristic	Study group	Control group	Total	$\chi^2$	p value
Sex (Male/Female)	39/52	41/51	80/103	0.054	0.816
ASA score (I/II)	48/43	49/43	97/86	0.005	0.945
Fever rate (Fever/Normal)	14/77	30/62	44/139	7.432	0.006

**TABLE 4** Comparison in the subgroup analysis

Groups	Subgroups	Fever	Not fever	Z/ $\chi^2$	p value
Study group	Age (year) <sup>#</sup>	50.20 (14.26)	52.74 (10.96)	-0.475 <sup>&amp;</sup>	0.635
	Sex (Male/Female) <sup>^</sup>	14/16	27/35	0.08 <sup>*</sup>	0.778
Control group	Age (year) <sup>#</sup>	53.21 (12.86)	50.31 (11.50)	-1.046 <sup>&amp;</sup>	0.296
	Sex (Male/Female) <sup>^</sup>	7/7	32/45	0.345 <sup>*</sup>	0.557

<sup>#</sup> Mann–Whitney *U* test.; <sup>&</sup> Z value.; <sup>^</sup> Chi-square test.; <sup>\*</sup>  $\chi^2$  value.



**Fig. 2** The role of drainage tubes in preventing fever after lumbar surgery

patient). Finally, the study comprised 183 patients; 91 patients were in the study group, and the rest were in the control group. For the main diagnosis of these patients, there

were 129 with lumbar spinal stenosis, 35 with lumbar spondylolisthesis, and 19 with lumbar disc herniations.

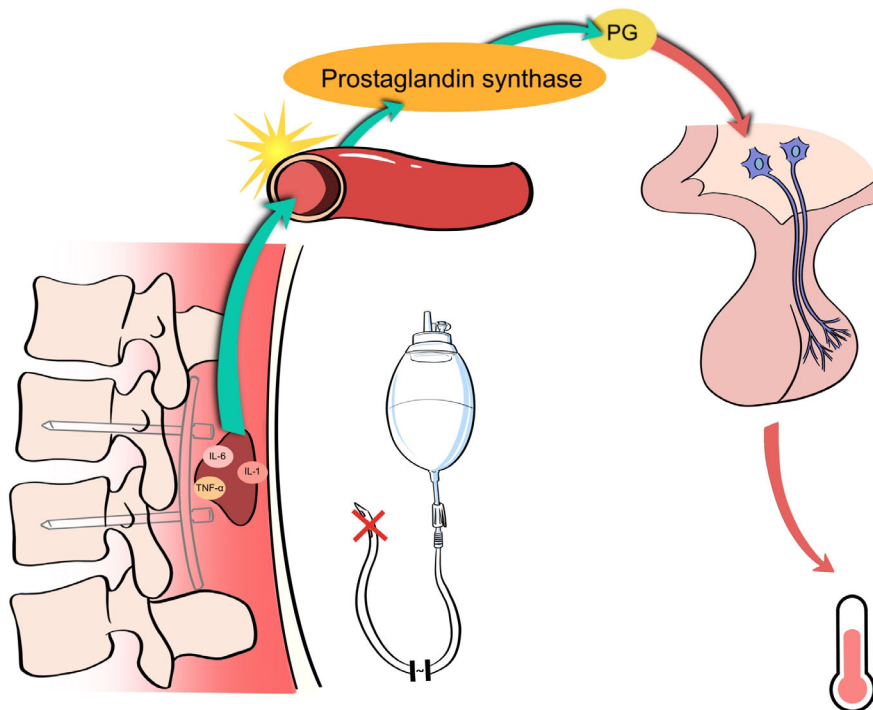
There were 80 male and 103 female patients, and the average age was 51.34 years. The average weight was 69.80 kg, and the average height was 165.53 cm, equivalent to an average BMI of 25.46 kg/m<sup>2</sup>. The basic characteristics of the patients are listed in Table 1.

### Comparisons of the Study and Control Groups

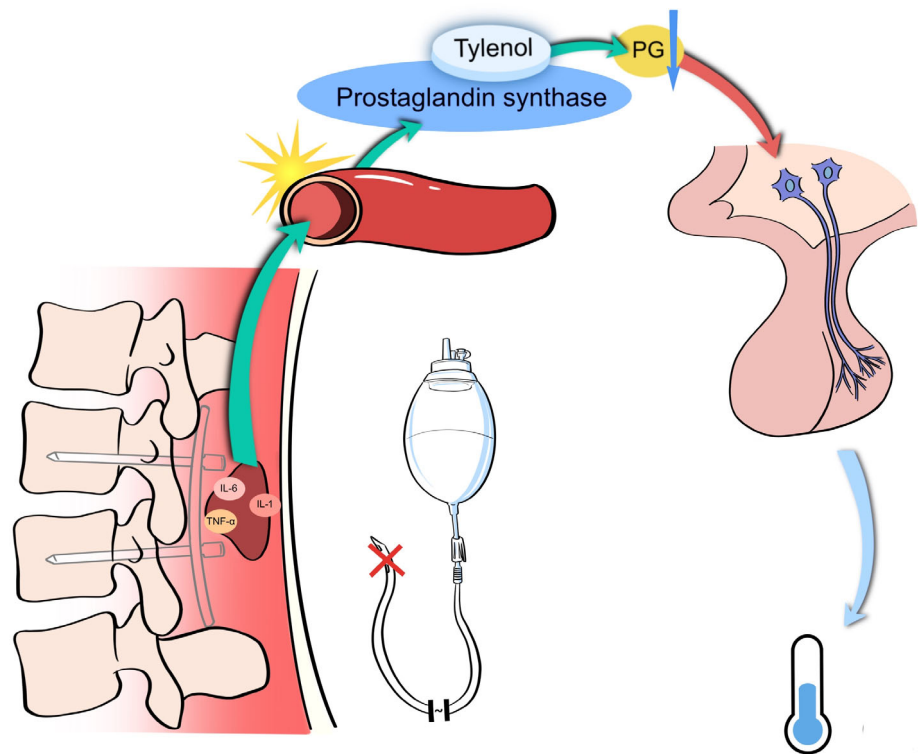
The Shapiro–Wilk (Table 2) test showed that other than weight, the remaining continuous data were nonnormally distributed ( $p < 0.05$ ), so we analyzed them with the Mann–Whitney  $U$  test, while the weight data were tested by Student's  $t$ -test. The comparison of the basic data is displayed in Tables 1 and 3. We determined that there were no differences in age, sex, height, weight, BMI, surgical segments, surgical time, blood loss, transfusion, ASA score, duration of drainage tube use, or total drainage volume between the two groups ( $p > 0.05$ ). Although the levels of WBC and CRP were lower, the length of hospital stay and the length of hospital stay after the removal of the drainage tube were shorter in the study group than in the control group, but the differences were not significant ( $p > 0.05$ ). However, the rate of fever was significantly different ( $p = 0.006$ ), and the study group (14/91, 15.38%) had a significantly lower rate of fever than the control group (30/92, 32.61%).

### Subgroup Comparisons

We divided the study group and control group into subgroups according to the condition of fever and determined



**Fig. 3** The mechanism of fever after the removal of drainage tubes for lumbar surgery (PG, prostaglandin)



**Fig. 4** The mechanism of acetaminophen in preventing fever after the removal of the drainage tube (PG, prostaglandin)

that regardless of the group, the age and sex had no significant differences between the groups, suggesting that fever was not associated with age or sex (Table 4).

### Outcomes

Among the cases of fever, there were three positive urinary cultures, one in the study group (*Escherichia coli*) and two in the control group (*Acinetobacter junii* and coagulase negative staphylococcus), which were treated by antibiotics depending on the results of the drug sensitivity test. Additionally, two patients with fever were experiencing cerebrospinal fluid leakage (discovered after the postoperative observation of fever). During follow-up in the outpatient department, no infections were discovered after discharge. In the study group, there were no complications related to the use of acetaminophen during the hospital stay or the outpatient follow-up period.

### Discussion

Similar to postoperative fever, fever after the removal of a drainage tube is always a challenge for doctors. Diagnostic workups for fever could be costly, waste time, and prolong the hospital stay of patients. Moreover, most of the evaluations fail to identify the cause of the fever. In this study, we used acetaminophen (Tylenol) as a prophylactic treatment for fever after the removal of drainage tubes for lumbar surgery, and the results showed that this approach could significantly reduce the possibility of fever.

To the best of our knowledge, our research is the first to focus on the problem of fever after the removal of a drainage tube placed during lumbar surgery. Many previous studies have focused on postoperative fever. The most consistent conclusion is that this fever is a physiological response due to the damage caused by surgical trauma, and the degree of fever is correlated with the extent of tissue trauma during surgery.<sup>4,10,15,17</sup> The inflammatory reaction stimulated by tissue trauma could trigger the release of cytokines such as IL1, IL6, and TNF- $\alpha$  in the local surgical area, and the released cytokines act as endogenous pyrogens to stimulate the preoptic area of the hypothalamus to increase prostaglandin production, raising the thermoregulatory set point for body temperature.<sup>11,17,18,23,24</sup> Based on these theories, we proposed that when the drainage tube was removed, the local inflammatory cytokines could not flow out, and then a small hematoma formed. With the increase in pressure caused by the hematoma and the increased local concentration of cytokines, the inflammatory cytokines could enter the systemic circulation and then raise the body temperature (Figs. 2 and 3). Therefore, if we use acetaminophen in advance to depress the function of prostaglandins (Fig. 4), we could lower the possibility of fever when the drainage tube is removed. The results of the study proved our hypothesis.

Many previous studies directly or indirectly support our proposal. The reports of Chmel *et al.*<sup>25</sup> and Gemer *et al.*<sup>26</sup> both suggested that hematoma at the wound site was the source of fever, which is in line with our thoughts. Many previous studies have noted that postoperative drainage fluid

is rich in inflammatory cytokines such as IL1, IL6, and TNF- $\alpha$ , and the levels of these cytokines are higher in fever patients.<sup>16,20,21</sup> Mark *et al.*<sup>27</sup> and Gideon *et al.*<sup>10</sup> both compared the fever rate of patients with or without drainage tubes postoperatively and declared that patients without postoperative drainage were more vulnerable to fever. More interestingly, based on Hao's<sup>22</sup> research, we found that if the drainage tube is intermittently clamped after lumbar surgery, the patient was more likely to develop a fever. All of the above conclusions could support our original idea that the removal of the drainage tube could stop the outflow of inflammatory cytokines and then cause fever.

Tylenol, a brand of acetaminophen, is a common analgesic-antipyretic medicine applied in our clinical treatment. This drug could inhibit prostaglandin synthase in the hypothalamic thermoregulation center and then reduce the production of prostaglandin. Based on what we discussed above, when the drainage tube is removed, the elevated cytokines could act on the hypothalamic thermoregulation center and cause a fever. The prophylactic acetaminophen could depress the activity of prostaglandin synthase to fight against stimulation from the cytokines and reduce the possibility of fever. The half-life of Tylenol is approximately 2 h, so the serum concentration of acetaminophen after the evening dose would be too low to have an antipyretic effect the next day. It was thus not necessary to worry if the use of acetaminophen would mask any signs of infection, and the number of infectious cases in the study group could prove this.

The concentrations of WBCs and CRP were not significantly different between groups in this study. As we observed, acetaminophen could only depress the activity of prostaglandin synthase but not suppress the inflammatory reaction caused by surgical trauma, so it was reasonable to observe this result. The length of hospital stay after drainage removal in the study group was shorter than that of the control group (2.23 days vs 2.82 days), but the difference was not significant because some patients asked to delay their discharge until the weekend or based on their personal condition. Roughly consistent with Zhu's<sup>14</sup> study, the control of fever after surgery could shorten the hospital stay.

Our study had some limitations. First, this was not a triple-blinded study. Second, due to limited funding, we did not directly test the changes in the concentrations of cytokines in response to the acetaminophen before and after the drainage tube was removed. However, we are the first to focus on fever after the removal of drainage tubes for lumbar surgery, and our research proved that prophylactic treatment with acetaminophen could significantly lower the potential for developing fever.

### Conclusion

Fever after the removal of drainage tubes is caused by a normal inflammatory response, which is not associated with age or sex. After removal of the drainage tube from surgical

lumbar patients, a small dose of acetaminophen could significantly reduce the possibility of fever. This approach could improve patient comfort, reduce the waste of medical resources, and speed up the discharge of patients. In our future research, we will try to determine the risk factors for fever after drainage tube removal and narrow the scope of patients who should receive prophylactic medicine.

### Acknowledgments

We thank Rui Wang and the other nurses for their help with this study. This manuscript has been released as a preprint at the research square (Ye *et al.*, 2021). This work was supported by the National Key R&D Program of China (2018YFE0104200).

### Conflict of Interest

There is no conflict of interest.

### Authors' Contributions

Kaifeng Ye and Yan Li collected data and wrote the article; Yong Xing was responsible for the literature review and the distribution of the patients; Kaixi Liu drew the illustrations; Fang Zhou, Yanping Zhang, and Yun Tian designed the study. All authors read and approved the final manuscript.

### Availability of Data and Materials

All data and materials used to support the findings of this study are included within the article.

### Ethics Approval and Consent to Participate

All procedures performed in this study were conducted in accordance with the ethical standards of the World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. The Ethics Committee of Peking University Third Hospital approved this study. Each author certifies that all investigations were conducted in conformity with ethical principles. All participants provided informed consent before their participation in the study.

### Consent for Publication

All authors agreed to publish "A randomized study on the prophylactic use of acetaminophen to prevent fever after the removal of drainage tubes for lumbar surgery" in *Orthopaedic Surgery*. We have received written consent from the participants to publish their clinical data (just anonymized clinical data without any identifying images or information).

### Competing Interests

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

## References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the global burden of disease study 2010. *Lancet*. 2012;380:2163–96.
2. Liu JM, Chen WZ, Fu BQ, Chen JW, Liu ZL, Huang SH. The use of closed suction drainage in lumbar spinal surgery: is it really necessary? *World Neurosurg*. 2016;90:109–15.
3. Yoo JH, Kim KT, Kim TY, Hwang JH, Chang JD. Postoperative fever after hemiarthroplasty in elderly patients over 70 years of age with displaced femoral neck fracture: necessity of routine workup? *Injury*. 2017;48:441–6.
4. Mayo BC, Haws BE, Bohl DD, Louie PK, Hijji FY, Narain AS, et al. Postoperative fever evaluation following lumbar fusion procedures. *Neurospine*. 2018;15:154–62.
5. Booth A, Ford W, Olajire-Aro T, George V, Curran T. Fever after colectomy in the enhanced recovery era: incidence and risk factors for pathologic source. *J Surg Res*. 2022;277:171–80.
6. Lee JJ, Kim JH, Jeon JH, Kim MJ, Park BG, Jung SK, et al. A retrospective controlled study of postoperative fever after posterior lumbar interbody fusion due to degenerative lumbar disease. *Medicine (Baltimore)*. 2022;101:e29231.
7. Pull ter Gunne AF, van Laarhoven CJ, Cohen DB. Incidence of surgical site infection following adult spinal deformity surgery: an analysis of patient risk. *Eur Spine J*. 2010;19:982–8.
8. Tamai K, Wang C, Heindel P, et al. Perioperative catheter use as a risk factor for surgical site infection after cervical surgery: an analysis of 39,893 patients. *Spine (Phila Pa 1976)*. 2019; 44(3) :E157–e61.
9. Gu W, Tu L, Liang Z, Wang Z, Aikenmu K, Chu G, et al. Incidence and risk factors for infection in spine surgery: a prospective multicenter study of 1764 instrumented spinal procedures. *Am J Infect Control*. 2018;46:8–13.
10. Blumstein GW, Andras LM, Seehausen DA, Harris L, Ross PA, Skaggs DL. Fever is common postoperatively following posterior spinal fusion: infection is an uncommon cause. *J Pediatr*. 2015;166:751–5.
11. Maday KR, Hurt JB, Harrelson P, Porterfield J. Evaluating postoperative fever. *Jaapa*. 2016;29:23–8.
12. Ashley B, Spiegel DA, Cahill P, Talwar D, Baldwin KD. Post-operative fever in orthopaedic surgery: how effective is the 'fever workup?'. *J Orthop Surg (Hong Kong)*. 2017;25:2309499017727953.
13. Haidar G, Singh N. Fever of unknown origin. *N Engl J Med*. 2022;386:463–77.
14. Zhu W, Huang M, Dai Y, et al. Influencing factors for delayed discharge following day surgery: a retrospective case-control study. *Int J Nurs Pract*. 2022; 28:e12951.
15. Seo J, Park JH, Song EH, Lee YS, Jung SK, Jeon SR, et al. Postoperative nonpathologic fever after spinal surgery: incidence and risk factor analysis. *World Neurosurg*. 2017;103:78–83.
16. Andres BM, Taub DD, Gurkan I, Wenz JF. Postoperative fever after total knee arthroplasty: the role of cytokines. *Clin Orthop Relat Res*. 2003;415: 221–31.
17. Narayan M, Medinilla SP. Fever in the postoperative patient. *Emerg Med Clin North Am*. 2013;31:1045–58.
18. Kahokehr A, Hill AG. Early post-operative fever. *ANZ J Surg*. 2011;81: 5–6.
19. Hausmann MJ, Kachko L, Basok A, Shnaider A, Yom-Tov G, Shefer A. Prolonged fever following kidney biopsy: a case report. *Int Urol Nephrol*. 2009;41: 423–5.
20. Handel M, Winkler J, Hornlein RF, et al. Increased interleukin-6 in collected drainage blood after total knee arthroplasty: an association with febrile reactions during retransfusion. *Acta Orthop Scand*. 2001;72:270–2.
21. Athanassious C, Samad A, Avery A, Cohen J, Chalnick D. Evaluation of fever in the immediate postoperative period in patients who underwent total joint arthroplasty. *J Arthroplasty*. 2011;26:1404–8.
22. Hao QY, Liu CY, Fu CJ, Zhang XH, Tan MS. Improved intermittent-clamped drainage in lower lumbar internal fixation: a randomized prospective study. *Chin Med J (Engl)*. 2016;129:2804–9.
23. Dionigi R, Dionigi G, Rovera F, Boni L. Postoperative fever. *Surg Infect (Larchmt)*. 2006;7(Suppl 2):S17–20.
24. Burke L. Postoperative fever: a normal inflammatory response or cause for concern. *J Am Acad Nurse Pract*. 2010;22:192–7.
25. Chmel H, Palmer JA, Eikman EA. Soft tissue hematoma as a cause of fever in the adult. *Diagn Microbiol Infect Dis*. 1988;11:215–9.
26. Gemer O, Shenhav S, Segal S, Harari D, Segal O, Zohav E. Sonographically diagnosed pelvic hematomas and postcesarean febrile morbidity. *Int J Gynaecol Obstet*. 1999;65:7–9.
27. Brown MD, Brookfield KF. A randomized study of closed wound suction drainage for extensive lumbar spine surgery. *Spine (Phila Pa 1976)*. 2004; 29(10):1066–8.