The Effect of Aspirin on Gallbladder Volume in Patients with Acute Cholecystitis:
"Ultrasonographic Study"

AKUT KOLESİSTİTLİ HASTALARDA ASİRİNİN SAFRA KESESİ VOLÜMÜNE ETKİSİ:
"ULTRASONOGRAFİK ÇALIŞMA"

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Summary

Prostaglandins (PGs) are important mediators in the pathogenesis of the acute cholecystitis. We, therefore, decided to study the effect of aspirin on gallbladder volume and pain-relieving capacity in patients with acute cholecystitis. Ten patients with acute cholecystitis and ten healthy subjects participated in this study. The gallbladder volumes were measured using ultrasonography. Pain relief was defined as a reduction in severity from grade 3 or 2 (severe or moderate) to 1 or 0 (mild or none). After fasting the baseline measurement was taken. The patients and volunteers received 1g aspirin with 50 ml water orally. Two hours later the gallbladder volumes were rescanned in 15 min intervals for 60 min. The baseline gallbladder volumes of the healthy subjects were 19.5±5.2 ml. The mean baseline gallbladder volume of patients with acute cholecystitis was greater than that of the control group (35.0±6.4 ml). This difference was not statistically significant. After administration of aspirin significant changes in the gallbladder volume were observed. In patients with acute cholecystitis the fasting gallbladder volumes increased by 35.2%-62.8% compared to the baseline (p<0.01-0.001) and by 132.2%-196.9% compared to the control group (p<0.01-0.001). Aspirin was significantly effective in reducing pain when compared against pretreatment in the 1st hr. The mean pain grade was 1.80±0.92 in baseline and 0.00±0.00 after treatment (p<0.007).

In conclusion, aspirin significantly increased gallbladder volume in patients with acute cholecystitis. Patients were totally free of pain after treatment with aspirin. Aspirin may prevent on the relief biliary colic due to acute cholecystitis.

Key Words: Acute cholecystitis, Gallbladder volume, Aspirin

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Prostaglandins are important mediators in the inflammatory process and are also synthesised by inflamed gallbladder, cause contraction of gallbladder muscles and can induce net fluid secretion of the gallbladder mucosa. Also the ability to change PG formation by inhibi-
tion of PG synthetase activity with aspirin and other non-steroidal anti-inflammatory agents (NSAID's) is important in the treatment of any disease with an inflammatory component. An endogenous PG biosynthesis in the gallbladder wall, induced by mechanical or chemical trauma, might explain a prolonged increase in intraluminal pressure. The severe the inflammation was, the greater were the prostanoid levels (6). Furthermore, prostaglandin E2 (PGE₂) was identified in the gallbladder contents in the cases of acute cholecystitis and in response to distention of the normal gallbladder (7). Investigators have shown that though gallbladder motility in patients with gallstones is enhanced by NSAID's it is not altered in healthy volunteers (8-11). It would be important to know if the beneficial effect of NSAIDs on gallbladder contractility is seen in the patients with acute cholecystitis also. We, therefore, decided to study the effect of aspirin on gallbladder volume and pain-relieving capacity of the patients with acute cholecystitis.

**Material and Methods**

Ten patients with acute cholecystitis and ten healthy volunteers agreed to participate in the study. The trial was performed in accordance with the Declaration of Helsinki. Ethics Committee Approval was obtained where appropriate, and witnessed. Informed consent was obtained from each patient prior to the study. The patients' average age was 52.3±4.6 range (42-62) years. The healthy volunteers' average age was 45.6±8.3 (29-61) years and was not different from the patients with acute cholecystitis. All patients had fever, leucocytosis, Murphy's sign and an oedematous gallbladder as proved by ultrasonography. Patients with gastro-duodenal ulcer disease or with severe cardiopulmonary disease were excluded from the study. All patients remained in the emergency ward for a period of 24 hrs. After physical, laboratory and ultrasonographic investigations, their pain levels were determined in order to compare initial and altered test pain. Those with moderate or severe pain (grade 2 or 3 on the rating scale) described by the treatment regimen were excluded from the study. All patients had fever, leucocytosis, Murphy's sign and an oedematous gallbladder as proved by ultrasonography. Patients with gastro-duodenal ulcer disease or with severe cardiopulmonary disease were excluded from the study. All patients remained in the emergency ward for a period of 24 hrs. After physical, laboratory and ultrasonographic investigations, their pain levels were determined in order to compare initial and altered test pain. Those with moderate or severe pain (grade 2 or 3 on the rating scale) described by the treatment regimen were excluded from the study.

**Results**

Demographic and clinical details are summarized in Table 1.

The mean baseline gallbladder volume of the control group was 19.5±5.2 ml. In the acute cholecystitis group the mean baseline gallbladder volume was higher than in the control group (35.0±6.4 ml). This difference was not statistically significant. After administration of aspirin, significant changes in gallbladder volume were observed. In patients with acute cholecystitis the fasting gallbladder volume increased by 35.2%-62.8% compared to the baseline (p<0.01-0.001). Figure 1, Table 2; pain relief defined as reduction in severity from 3 or 2 to 1 or 0. Aspirin was significantly effective in reducing pain as compared to the pre-treatment in the 1st hrs. The mean pain grade was...
THE EFFECT OF ASPIRIN ON GALLBLADDER VOLUME IN PATIENTS WITH ACUTE CHOLECYSTITIS

Sait KAPICIOĞLU et al.

Table 1. Patient demographics and pretreatment characteristics of the acute cholecystitis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No (%):</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>10</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Mean age(years)</td>
<td>52.3±4.6</td>
</tr>
<tr>
<td>Pretreatment severity</td>
<td></td>
</tr>
<tr>
<td>No pain</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mild</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Severe</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Stone</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Non-stone</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>BMI&gt;12%</td>
<td>1 (10)</td>
</tr>
<tr>
<td>BMI&lt;12%</td>
<td>5 (90)</td>
</tr>
</tbody>
</table>

1.80 ± 0.92 in baseline and 0.00 ± 0.00 after treatment (p < 0.007) (Figure 1).

The effect of aspirin decrease in pain level, could be detected after just 1 hr. No major side effects were recorded during aspirin treatment.

Discussion

This study demonstrated that aspirin significantly increased gallbladder volume of patients with acute cholecystitis. Aspirin was effective in providing with pain-relief in the patients with acute cholecystitis (reduction from grade 3 or 2 to grade 0) for 12 hrs. They were all totally free of pain after the treatment with aspirin. Our results agreed with previous studies (14-18).

PGs have a physiological role in the maintenance of the motility of gallbladder muscle (8-11) and play a central role in the pathogenesis of both calculous and acalculous cholecystitis. Increased production of PGs by the inflamed human gallbladder has been demonstrated in vitro (7) and in vivo (6,19,20). The severe inflammation was, the greater were the prostanoid levels (6,21). Furthermore, PGE, was identified in the gallbladder contents in cases of acute cholecystitis and in response to distention of the normal gallbladder (7). Experimentally instillation into the gallbladder lumen causes changes which increase mucosal PGE, levels and induce acute cholecystitis (22) because the changes brought about cyclooxygenase inhibitor indomethacin (19).

Prostaglandins induce active fluid secretion by the gallbladder mucosa (4,23). Exogenous administration of PGE, induces a secretory response by the gallbladder, epithelium, with stimulation of mucus secretion and contraction of the gallbladder wall (4) This active secretion by the gallbladder mucosa is abolished by PG synthetase inhibitor (24). Cessation of fluid secretion by inhibition of

Table 2. Effect of aspirin on healthy subjects and in the patients with acute cholecystitis.

<table>
<thead>
<tr>
<th>Groups</th>
<th>No</th>
<th>Baseline</th>
<th>120</th>
<th>135</th>
<th>150</th>
<th>165</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asa+Cholecystitis</td>
<td>10</td>
<td>35.0±6.4</td>
<td>44.5±11.5</td>
<td>47.3±12.2</td>
<td>51.5±10.9***</td>
<td>52.8±13.0***</td>
</tr>
<tr>
<td>Asa+Healthy</td>
<td>10</td>
<td>19.5±5.2</td>
<td>19.07±12.2</td>
<td>20.3±10.7</td>
<td>20.1±11.3</td>
<td>18.9±10.1</td>
</tr>
</tbody>
</table>

*p<0.01, **p<0.02, difference from baseline
p<0.01, **p<0.01 difference from control

prostaglandin synthesis with reduction of intraluminal pressure (24) is perhaps on action of the mechanism of cyclooxygenase inhibitors (14,25) which leads to the relief of pain in patients with acute cholecystitis. Prostanoids have their effects in early stages of acute cholecystitis, because in an animal model, inhibitors of prostanoids were beneficial only when given before the inflammation became well established (26). The data suggest that the clinical effects of PG synthesis inhibitors are minimal after the inflammatory process is well established. These explanations may explain the mechanism of aspirin-induced increase of gallbladder volume and pain relief in the patients with acute cholecystitis.

The importance of fluid secretion in the development of acute cholecystitis is supported by the observations that (1) the inflamed gallbladder secretes rather than absorbs fluid (27), (2) acute inflammation is only seen in animals that secrete fluid to the gallbladder lumen (28), and (3) a correlation exists between the rate of fluid secretion and the severity of the inflammation in animals (28) and patients (29). As noted before, implantation of a gallstone or insertion of a long-term indwelling catheter or instillation of lysolecithin to the obstructed gallbladder induces continuous and active secretion of fluid into the gallbladder (30). In addition, the fluid secretion into the lumen of an inflamed or obstructed gallbladder is enhanced by feeding and reduced by fasting (31). This active secretion is abolished by PG synthetase inhibitor (19,24). Protective mechanisms may reduce net fluid secretion when the intraluminal pressure rises (28,31).

In conclusion this study demonstrated that aspirin significantly increases gallbladder volume in patients with acute cholecystitis. The patients were totally free of pain after the treatment with aspirin. These results suggest that aspirin may prevent the relief of biliary colic due to acute cholecystitis.

REFERENCES


